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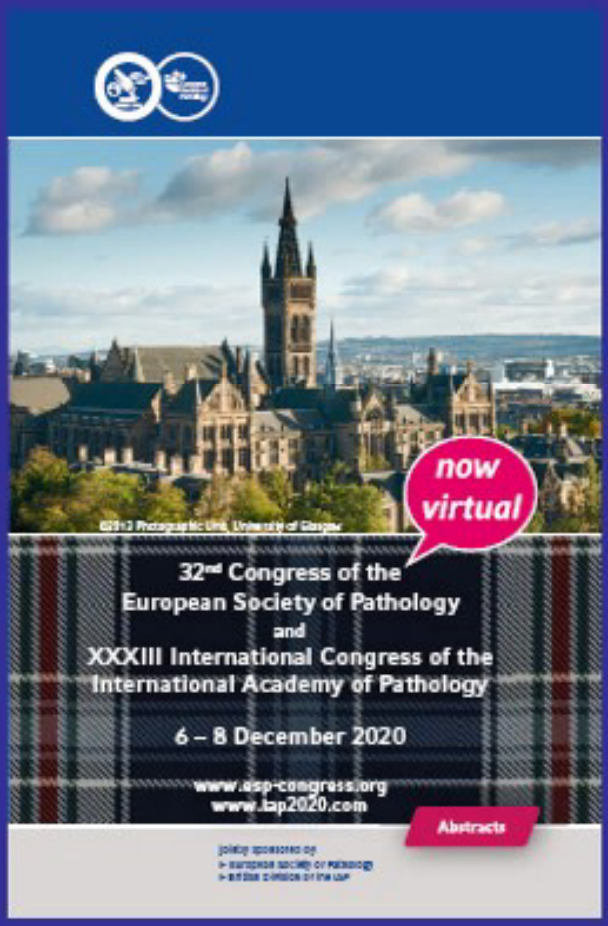

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Aims and Scope
Mission statement: To advance the scientific basis of human pathology by the publication (encouragement and dissemination) of high quality research (including molecular and translational studies) and thereby contribute to patient care.
Manuscripts of original studies reinforcing the evidence base of modern diagnostic pathology, using immunocytochemical, molecular and ultrastructural techniques, will be welcomed. In addition, papers on critical evaluation of diagnostic criteria but also broadsheets and guidelines with a solid evidence base will be considered. Consideration will also be given to reports of work in other fields relevant to the understanding of human pathology as well as manuscripts on the application of new methods and techniques in pathology. Submission of purely experimental articles is discouraged but manuscripts on experimental work applicable to diagnostic pathology are welcomed. Biomarker studies are welcomed but need to abide by strict rules (e.g. REMARK) of adequate sample size and relevant marker choice. Single marker studies on limited patient series without validated application will as a rule not be considered. Case reports will only be considered when they provide substantial new information with an impact on understanding disease or diagnostic practice.

V.i.S.d.P F. T. Bosman

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OFP-02	Joint Oral Free Paper Session: Breast Pathology / Paediatric and Perinatal Pathology
OFP-03	Oral Free Paper Session: Gynaecological Pathology
OFP-05	Oral Free Paper Session Digestive Diseases Pathology - Liver / Pancreas
OFP-06	Oral Free Paper Session: Digestive Diseases Pathology - GI
OFP-07	Joint Oral Free Paper Session: Dermatopathology / Soft Tissue & Bone Pathology
OFP-08	Joint Oral Free Paper Session: Endocrine Pathology / Head and Neck Pathology
OFP-09	Joint Oral Free Paper Session: Pulmonary Pathology / Thymic and Mediastinal Pathology
OFP-10	Joint Oral Free Paper Session: IT in Pathology / Autopsy Pathology / Pathology in Favour of Developing Countries / Cardiovascular Pathology / History of Pathology / Electron Microscopy / Other Topics
OFP-11	Joint Oral Free Paper Session: Cytopathology / Neuropathology / Ophthalmic Pathology
OFP-12	Joint Oral Free Paper Session: Molecular Pathology / Haematopathology

Oral Free Paper Sessions
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One-Day Molecular Pathology Diagnostics and Translational Research Symposium

CP-03	One-Day Computational Pathology Symposium – Selected Abstracts
MD-02	Joint Session One-Day Molecular Pathology Diagnostics and Translational Research Symposium, Molecular Pathology & Trainees: Case Presentations
MD-05	One-Day Molecular Pathology Diagnostics and Translational Research Symposium - Selected Abstracts

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Poster Sessions
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One-Day Molecular Pathology Diagnostics and Translational Research Symposium

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Abstracts

32nd Congress of the ESP and XXXIII International Congress of the IAP

Oral Free Paper Sessions

OFP-01 Joint Oral Free Paper Session: Uropathology / Nephropathology

OFP-01-001
Kidney biopsy codes for pathologists-mapping to SNOMED CT
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Background & objectives: The "Kidney Biopsy Codes (KBC)" project provides terms that allow any diagnosis and/or histomorphological pattern for a non-neoplastic kidney biopsy to be coded. We explored whether mapping to SNOMED CT is feasible, to enable aggregation and computerized exchange of data.
Methods: For KBC terms for which an unambiguous match with a pre-existing SNOMED CT concept was available, both 'parent concept' and the place in the SNOMED taxonomy were established. For remaining terms, we explored whether these could be defined by combining pre-existing (more simple) SNOMED CT concepts. This process ('post-coordination') is well supported by SNOMED CT and allows extending its content.
Results: Of glomerular terms, 88/195 (45%) could be matched to SNOMED CT. %-matching was more successful for KBC terms designating disease concepts (56%) than patterns of injury (32%). For the majority of terms that could not be mapped, we found that these could indeed be defined as a compositional expression of pre-existing SNOMED CT concepts (post-coordination). We suggested concepts that are needed for this post-coordination.
Conclusion: SNOMED CT is considered the standard for documenting, encoding and exchanging medical data in/between health information systems. This proof-of-concept shows that mapping of KBC terms to SNOMED CT is feasible, in part directly, in part through post-coordination.

OFP-01-002
Molecular analysis of renal transplant biopsies comparing the Edmonton Molecular Microscope with the NanoString Human Organ Transplant Panel
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Background & objectives: Different molecular methods like microarrays or quantitative PCRs were used by several groups on renal transplant tissues. High-resolution determination of the inflammatory infiltrate by NanoString analysis (which was developed for formalin-fixed paraffin-embedded-derived RNA) should be a sufficient approach.
Methods: We used surveillance and indication biopsies from 63 patients whose time-matched second biopsy core had been frozen and analysed by microarray in the INTERCOM/INTERCOMEX study. After re-evaluation according to recent Banff consensus, RNA isolation was performed with Maxwell FFPE kits and led to sufficient RNA yields in 53 samples which were further processed for NanoString analysis (Human Organ Transplant panel).
Results: Morphologically, of the 53 samples analysed (samples from 2011/12 and 2015), twenty-five patients showed no signs of rejection, twelve had borderline rejection, four showed cellular rejection, seven had humoral rejection, and five presented with combined rejection. Preliminary analysis of gene expression by T-distributed Stochastic Neighbour Embedding (t-SNE), Random Forest and Principal Component Analysis (PCA) showed clear differences between samples with rejection (humoral and cellular) and without rejection. Rejection samples revealed high expression of chemokine ligands compared to rejection-free tissues. Borderline rejection shared a common pattern compared to samples without rejection. First results display good correlation with the former molecular diagnosis from the INTERCOM/INTERCOMEX study.
Conclusion: Molecular approach using the NanoString platform may supplement morphological diagnosis of renal grafts especially in unclear cases and thus enhance precision diagnostics with small tissue requirement. Morphological and molecular evaluation in the same biopsy core from FFPE tissue enables direct histological-molecular correlation. Additionally, this technology also improves our understanding of pathophysiology in renal and other transplants.
Funding by: Dr. Werner Jackstädt foundation

OFP-01-003
Arteriolar C4d: a potential prognostic marker in IgA nephropathy – a retrospective study in a Portuguese tertiary centre
P. Amoroso Canão*, B. Faria, Q. Cai, C. Henriques, A.C. Matos, F. Poppelaars, M. Gaya da Costa, M. R. Daha, R. Pestana Silva, M. Pestana, M. A. Seelen
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Background & objectives: IgA Nephropathy (IgAN) is the most common glomerulonephritis worldwide. C4d has been recognized as a marker associated with significantly reduced renal survival. We aimed to study the clinical significance of arteriolar immunoexpression of C4d in a cohort of IgAN patients.
Methods: We selected all kidney biopsies with the diagnosis of IgAN, between 2001 and 2017, and reviewed their clinical features; evaluated them according to the Oxford Classification of IgAN 2016 and assessed the presence of vascular lesions. We evaluated the arteriolar and glomerular immunoexpressions of C4d and their association with the baseline and follow-up clinico-histological data thought bivariate and regression analysis.
Results: Arteriolar immunoexpression of C4d was present in 21 (17%) biopsies and associated with mean arterial pressure (MAP), chronic microangiopathy and arterial intimal fibroelastosis. After adjusting to other significant predictors, such as baseline estimated glomerular filtration rate, MAP and the presence of crescents, this immunoexpression remained significantly associated (P values <0.001) with progressive kidney disease.
Conclusion: Arteriolar immunoexpression of C4d is a potential prognostic marker in IgAN. These findings raise the possibility of including immunohistochemistry for C4d in the evaluation of IgAN biopsies.

OFP-01-004

The impact of vitamin D3 (1,25-dihydroxyvitamin D3) and its role on to the epithelial to mesenchymal transition and the development of interstitial fibrosis in renal allografts

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Background & objectives: This study aimed to understand the role and the mechanism of action of vitamin D3 (1,25-dihydroxyvitamin D3) in the development of epithelial to mesenchymal transition (EMT) and interstitial fibrosis (IF) in renal transplant (Tx) patients.
Methods: Out of 161 cases, 70 treated with vitamin D3 (Group D) and 91 cases did not receive vitamin D3 (Group A). Cytoskeletal proteins F-actin, α-SMA and paxillin expression of tubules and the tubular TGF-β, TNF-α, and E-cadherin expression evaluated. Follow-up biopsies analysed for the development of IF during 18 and 24 months after Tx.
Results: Group D patients showed higher degrees of tubular E-cadherin expression than Group A ($p<0.001$). Tubular F-actin, α-SMA, paxillin, TGF-β and TNF-α found significantly low in Group D compared to Group A ($p<0.001$). A positive correlation found between the development of IF with the tubular F-actin, α-SMA, paxillin, TNF-α and TGF-β expression ($p<0.001$). The development of IF during in follow-up biopsies found lower in Group D compared to Group A ($p<0.001$)
Conclusion: The activation of EMT and the occurrence of IF found higher in Group A cases who had cytoskeleton reorganization (increased F-actin, α-SMA, paxillin expression), and E-cadherin downregulation. E-cadherin loss during EMT suggested to promoted by high TNF-α and TGF-β expression. Contrarily, Group D patients had a lower incidence of IF. Treatment with D3 abolishes the EMT promoted by TNF-α and TGF-β. Therefore, D3 therapy is beneficial in renal transplant patients with its antifibrotic property.

OFP-01-005

Rearrangement of the endothelial cell cytoskeleton in glomerular and peritubular capillaries following antibody-mediated rejection: its significance on the development of transplant glomerulopathy and interstitial fibrosis

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Background & objectives: This study aimed to understand the rearrangement of endothelial cell cytoskeleton (EC-CSK) both in glomeruli and peritubular capillaries (PTCs) in antibody-mediated rejection (AMR) and to investigate the influence of cytoskeleton rearrangement on the development of transplant glomerulopathy and interstitial fibrosis
Methods: Total 116 allograft biopsies which diagnosed with AMR were re-evaluated and the intensity of interstitial, glomerular and PTC inflammation were graded. The endothelial cell (EC) expression of F-actin, paxillin, vinculin, HIF-1α, VEGF, and eNOS were evaluated in glomeruli and PTCs. Follow-up biopsies analysed for the development of transplant glomerulopathy (TG) and interstitial fibrosis (IF).
Results: The expression of F-actin paxillin, vinculin, HIF-1α, VEGF and eNOS in EC increased with increasing degree of C4d expression, PTC destruction, interstitial inflammation, glomerulitis and PTC-itis in glomeruli and PTCs ($p<0.001$). The risk of the development of TG, IF, proteinuria, and graft loss found higher in recipients with a high degree of F-actin, paxillin, vinculin, HIF-1α, VEGF and eNOS expression ($p<0.001$).
Conclusion: We hypothesized that PTC destruction following AMR causes chronic hypoxia that induces HIF-1α, VEGF and eNOS expression that give rise to the reorganization of EC-CSK. Upon the reorganization of EC-CSK and the increased amount of endothelial VEGF together induce the formation of gaps between adjacent ECs, which in turn initiate EC permeability and influx of leukocytes and proteinuria. As a consequence, the increasing amount of inflammatory cells induces the early development of IF, TG, and consequently the premature graft loss.

OFP-01-006

Application of artificial intelligence (AI) in assessment of renal allograft biopsies: comparison with subjective Banff criteria for graft inflammation

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Background & objectives: The Banff classification is used routinely in reporting of transplant biopsies. The variable reproducibility of Banff criteria limits its clinical value. This study evaluated the use of AI to quantify graft inflammation and correlated inflammatory cell density with Banff scores.
Methods: Digital images from 119 allograft biopsies were scored by two renal pathologists according to Banff criteria. Images were then analysed using the Visiopharm Integrator System platform. An APP was designed to quantify inflammation within normal and fibrotic cortex, and an auxiliary APP to exclude glomeruli. The model was trained through one million iterations.
Results: The inter-observer agreement for i, ti and i-IFTA scores was moderate to good (kappa-scores 0.615, 0.566, 0.552 respectively). Banff scores correlated only weakly with the density of inflammatory cells assessed using AI. i-score: only for i0 vs i3 was there a significantly different inflammatory cell density. i-IFTA and ti scores: the density was significantly greater for Banff categories 1-3 than 0, but there were no significant differences between categories 1-3.
Conclusion: he density of inflammatory cells correlates weakly with Banff scores, likely reflecting the fact that a pathologist will only recognise cortex as inflamed when there is greater than a threshold level of inflammatory cell density in a particular area. It remains to be ascertained whether inflammatory cell density assessed by AI or subjective Banff scores correlate better with clinical outcome and response to treatment.

OFP-01-007

Carcinogen-induced tumour mouse model reveals dynamic molecular changes during basal bladder cancer progression

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Background & objectives: The basal subgroup of bladder cancer is often diagnosed at the muscle-invasive stage (MIBC). Identification of molecular changes during progression from non-muscle-invasive (NMIBC) to basal MIBC is challenging.
We used the N-butyl-N-(4-hydroxybutyl)-nitrosamine (BBN) mouse model to study disease progression.
Methods: To study multiple stages of progression, 40 mice bladders were obtained at different time points following an oral BBN exposure of a maximum of 14 weeks. To characterize molecular changes occurring during progression from early stages to MIBC, we performed immunohistochemistry (IHC) - markers of basal (CK5, CK6, CK14) and luminal subtypes (FOXA1, CK20) - and RNA-seq for all stages.
Results: Morphological analysis identified a spectrum of lesions during BBN exposure: hyperplasia (n= 5), dysplasia (n=5), CIS (n=3), pTa (n=14), pT1 (n= 6), MIBC (n = 7). All tumours displayed a squamous or sarcomatoid component. IHC showed expression of basal markers

within early stages of carcinogenesis, with a decrease in FOXA1 expression during progression. Molecular classifications using RNA-seq data highlighted an early and progressive switch to the complete basal phenotype. Further analysis of RNA-seq data identified clusters of genes with expression changes during progression. Assessment of the expression dynamics of each cluster of genes provided insights into specific biological processes involved in basal bladder cancer progression and invasion.
Conclusion: We used the BBN-induced cancer mouse model to longitudinally study carcinogenesis and progression of basal bladder cancer. Our study sheds light on the underlying biology of progression from NMIBC to basal MIBC and from squamous to the aggressive sarcomatoid variant.

OFP-01-008

TERT promoter mutation analysis is a valuable diagnostic adjunct to distinguish pseudosarcomatous spindle cell proliferations from sarcomatoid urothelial carcinoma of the urinary bladder

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Background & objectives: Bladder pseudosarcomatous myofibroblastic proliferations are diagnostically challenging due to occasional ALK-negativity, frequent cytokeratin expression, worrisome histology. Sarcomatoid urothelial carcinoma (sUC) may resemble inflammatory myofibroblastic tumour (IMT). TERT promoter mutations are frequent in urothelial cancers, but pseudosarcomatous lesions have not been investigated.
Methods: We performed comparative histomorphological and immunohistochemical analysis and TERT promoter mutation testing in 17 ALK-positive and -negative spindle cell lesions and 18 sUC. Screening for genetic rearrangement and/or FISH analysis was performed by RNA sequencing in the pseudosarcomatous myofibroblastic proliferations.
Results: 9/17 sUC showed at least focal IMT-like morphology. Atypical mitoses, presence of a differentiated urothelial component and presence of heterologous elements were the most reliable morphological features of sUC, if present. ALK (D5F3), p53, p63, Ki67-index, smActin and GATA3 were differentially expressed. Pancytokeratin staining was frequent in both groups, but the staining pattern differed significantly (diffuse in 17/17 pseudosarcomatous proliferations, focal in 6/15 sUC). TERT promoter mutations were found in 17/18 sUC but in none of 17 pseudosarcomatous myofibroblastic proliferations. RNA sequencing and FISH analysis revealed genetic rearrangements in 6/7 ALK positive and 1/10 ALK negative pseudosarcomatous myofibroblastic proliferations, including a novel FN1/RET gene fusion in an ALK-negative lesion
Conclusion: TERT promoter mutations and/or ALK expression/rearrangements in spindle cell lesions of the bladder are confirmatory for sUC or IMT in the majority of cases, respectively. In equivocal cases lacking TERT and ALK alterations, clinical history, classical histomorphological and immunohistochemical features should be assessed carefully. RNA sequencing is a sensitive method for assessment of gene rearrangement, including involvement of novel genes other than ALK.

OFP-01-009

Grading of intraductal carcinoma has minor impact on grade group assignment in prostate cancer biopsy and radical prostatectomy specimens

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Background & objectives: Intraductal carcinoma (IDC) has an adverse outcome in prostate cancer patients but is not incorporated in tumour grading. Our objective was to determine the effect on global Grade group (GG) assignment in case IDC is included in grading.
Methods: A prostate cancer biopsy (n=1,031) and unrelated radical prostatectomy (n=835) cohort were reviewed for GG according to the 2014 ISUP guidelines, without IDC grade assignment. Presence and percentage of IDC were monitored. By accounting IDC as Gleason pattern 4 or 5 based on its morphology, the GG was recalculated.
Results: IDC was identified in 139/1,031 biopsies (13.5%). Assigning a Gleason pattern to IDC led to a change of GG in 17 cases (1.6%): 4/486 from GG1 to GG2, 9/375 GG2 to GG3, and 4/58 GG4 to GG5. In 213/835 (25.5%) prostatectomy specimens IDC was present. Grading of IDC based on its underlying pattern led to a GG change in 5 cases (0.6%): 1/307 from GG1 to GG2, 1/307 GG1 to GG3, 2/420 GG2 to GG3, and 1/50 GG4 to GG5.
Conclusion: We demonstrate that grading IDC led to a change in GG in <2% of prostate cancer biopsies and radical prostatectomies, indicating it has overall minimal impact on prostate cancer grade assignment.

OFP-01-010

A retrospective single-centre audit of block-taking in cystectomy specimens for malignancy

N. Herlihy*, A. Haider
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Background & objectives: There is no consensus on how many blocks should be submitted from cystectomy specimens for bladder tumours. Our department recommends ≤10 blocks. Our objective was to audit block-taking and assess how frequently the diagnosis could be reached with ≤10 blocks.
Methods: We performed a retrospective single-centre audit on cystectomy specimens for malignancy processed from January-December 2017. We performed a SNOMED search on Co-Path for all cystectomy cases for malignancy and collected data on patient demographics, presence of gross tumour, number of blocks taken from the bladder at initial cut-up and number of extra blocks (if any), and the histological diagnosis.
Results: 45 cases were suitable for inclusion. A median of 13 bladder blocks were taken per case (range, 4-28). Ten blocks or less from bladder were submitted in 10/45 cases (22.2%). More than 10 blocks were taken in a higher proportion of cases without gross tumour (16/19, 84.2%) compared to cases with gross tumour (19/26, 73.1%). Additional blocks were taken in 4/45 cases (8.8%). 2/10 specimens (20%) where less than ten blocks were taken initially required additional blocks. On review of the slides, the final histological diagnosis was achievable on the initial blocks in all four cases where additional blocks were taken. Estimated costs of oversampling for one year were £8,595.36.
Conclusion: The final histological diagnosis was achievable in all cystectomy cases for malignancy where ten blocks or less were taken from the bladder. In the majority of cases, more than ten blocks were taken, incurring significant potentially unnecessary costs. We suggest that no more than ten blocks should be taken from cystectomy specimens for malignancy, and that even fewer representative blocks can be taken if a gross lesion is identified.

OFP-01-011

Heterogeneity-analysis of molecular subtypes of muscle-invasive bladder cancer and their precursor lesions in multiregion mapped whole-organ bladders

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Background & objectives: Molecular subtypes of bladder cancer have been described which seem to have a predictive effect for chemotherapy regimens. Due to this clinical implication, the aim is to characterize in

which extent precursor lesions and tumours exhibit a heterogeneity of subtypes.
Methods: 23 positions of three whole-organ mapped specimens were histomorphologically reviewed for classifying location of normal urothelium, precursor lesions and different areas of the tumour. Immunohistochemical analysis of luminal (CK20, GATA3, FOXA1) and basal markers (CD44, CK14 and CK5/6) was carried out in selected precursor lesions and tumours to map the distribution of luminal and basal subtypes across the different positions/lesions.
Results: Out of three analysed multiregion mapped bladder tumours, one showed a heterogenous luminal and double-negative molecular subtype in multiple tumour positions as well as a mixed morphology including conventional urothelial and neuroendocrine areas. Moreover, among the second analysed bladder tumour, all tumour positions showed a high expression of basal markers whereas the included Carcinoma in situ demonstrated a luminal subtype with almost total absence of basal markers. The third analysed mapped bladder tumour demonstrated a homogenous luminal molecular subtype in all precursor and tumorous lesions.
Conclusion: This first analysis of three multiregion mapped bladder tumours shows divergent results of subtype distribution: Heterogeneity of subtypes can be observed, but other tumours and associated precursor lesions show a homogenous distribution of subtypes. To further elucidate how often subtype heterogeneity occurs in whole multiregion mapped bladder tumours, data of further bladder specimens will be presented at the meeting.

OFP-01-012
Combining hypermethylated RASSF1A detection using droplet digital PCR with miR-371a-3p testing: an improved and highly sensitive panel of liquid biopsy biomarkers for testicular germ cell tumour patients
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Background & objectives: Classical serum tumour markers used routinely in the management of testicular germ cell tumour (TGCT) patients (AFP and HCG) are elevated in only 50-60% of the cases at time of diagnosis. miR-371a-3p is the most recent promising biomarker for TGCTs, but is not sufficiently informative for detecting mature teratoma, which is therapeutically relevant. We aimed to test the feasibility to use hypermethylated RASSF1A (RASSF1AM), detected in circulating cell-free DNA, combined with miR-371a-3p, as non-invasive diagnostic markers of TGCTs.
Methods: A total of 109 patient-derived serum samples and 29 sera from healthy young-adult males were included, along with representative cell lines and tumour tissue samples. We describe a novel droplet digital PCR (ddPCR) method for quantitatively assessing RASSF1AM in liquid biopsies.
Results: Promoter methylation of RASSF1A was detected in all TGCT tissues and cell lines by EPIC array, confirmed by ddPCR. Both miR-371a-3p (sensitivity=85.7%) and RASSF1AM (sensitivity=89.8%) outperformed the combination of AFP and HCG (sensitivity=65.5%) for TGCT diagnosis. RASSF1AM detected 88% of teratomas. In this representative cohort, 14 cases were negative for miR-371a-3p, all of which were detected by RASSF1AM, resulting in a combined sensitivity of 100%.
Conclusion: Cell-free detection of RASSF1AM combined with miR-371a-3p resulted in a 100% diagnostic sensitivity for TGCT patients. These results need to be validated in patient follow-up and detection of minimal residual disease.
Funding by: FCT/MCTES, project EpiMarkGermCell (PTDC/MECONC/29043/2017). JL is recipient of a fellowship from FCT - Fundação para a Ciência e Tecnologia—(SFRH/BD/132751/2017).

OFP-01-013
Inflammation burden in benign tissue is inversely associated with significant cancer burden in the prostate: lessons from the PROMIS study
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Background & objectives: Intraprostatic inflammation enables cancer and is an attractive therapeutic target, but its burden in biopsy-naive men is poorly defined. We analysed inflammation in 158 PROMIS participants who had MRI followed by 5-mm template mapping biopsies (TPM) regardless of MRI findings.
Methods: 235 men enrolled at University College London Hospital (2012-2015) and TPM outcomes were collected for 158 (77 pilots excluded). Cancer burden was recorded in 20 Barzell zones per prostate by an experienced uropathologist (Definition 1: Gleason≥4+3 and/or maximum length ≥6mm; Definition 2: 3+4 and/or 4-5mm; insignificant: 3+3, less than 3mm). Inflammation, PIN or ASAP were noted in cancer-free Barzell zones.
Results: There was a negative association between the proportion of benign Barzell zones reported as "heavily inflamed" (out of all cancer-free zones) and TPM cancer burden (1A). The fraction of non-cancerous, inflamed Barzell zones was significantly higher in men without/insignificant cancer, compared to those with Definition 1/2 disease (1B; Kruskal-Wallis, $p<0.001$; Tukey post hoc analysis; $p<0.001$). This difference persisted when men without/insignificant cancer were compared to those with significant disease of any definition (1C). The opposite trend was true for PIN/ASAP: there was a positive association between PIN content in benign Barzell zones and cancer burden (2A), although not statistically significant (2B, 2C: Kruskal-Wallis ANOVA, $p=0.37$; Wilcoxon test, $p=0.11$).
Conclusion: Heavy inflammation affects fewer benign areas in men with significant cancer compared to those without significant tumours in their prostate. We hypothesise that such inflammatory burden differences (1) enable the progression of significant cancer in the first place (2) are a consequence of tumour-related microenvironmental changes or (3) are driven by increased inflammation in the early stages of carcinogenesis. Whether these hypotheses are true requires further investigation.
Funding by: MRC Clinical Research Training Fellowship MR/S005897/1

OFP-02 Joint Oral Free Paper Session: Breast Pathology / Paediatric and Perinatal Pathology

OFP-02-001
Congenital vascular anomaly in alveolar capillary dysplasia with misalignment of pulmonary veins
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Background & objectives: Alveolar capillary dysplasia with "misalignment of pulmonary veins" (ACDMPV) is a rare, fatal abnormal pulmonary vascular developmental disease. The pathogenic mechanisms remain largely unknown. This study aims to characterize the microvascular alterations in the lungs of ACDMPV patients.
Methods: Lung histologic structures were analysed from 16 autopsies with ACDMPV. Lung endothelial cells, smooth muscle cells, and alveolar epithelial cells were examined by immunohistochemical and

immunofluorescent stainings with antibodies recognizing different cellular markers for ACDMPV and age-matched controls. Statistical analysis was performed.
Results: The decreased capillary density or completely absence of capillary in the alveolar septa was observed while new microvascular formation with abnormal tortuosity in the thickened alveolar septa was present. Aberrant pulmonary veins were detected adjacent to small pulmonary arteries within the same bronchovascular bundle even though septal pulmonary veins were still seen in the ACDMPV lungs. Glut-1 protein, a marker for endothelial immaturity, was detected in the malpositioned and normalized pulmonary veins as well as abnormal septal neovasculature. In addition, hyperplasia of type 2 alveolar epithelial cells was observed.
Conclusion: The loss of vascular integrity and the destruction of the alveolar-capillary interface may drive abnormal growth and remodelling of the pulmonary microvasculature, which challenges the current concept of "misalignment of pulmonary veins". Future studies are needed to understand the pathogenesis.

OFP-02-002
Clinical exome sequencing for the diagnosis of foetal skeletal dysplasias
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Background & objectives: Skeletal dysplasias require genetics for definite diagnosis. Single gene sequencing (SGS), next generation sequencing (NGS) methods such as gene panel sequencing (GPS), clinical exome sequencing (CES, including all genes listed in OMIM) or whole exome sequencing are alternative approaches.
Methods: Nineteen foetuses from pregnancies interrupted because of skeletal dysplasia were genetically investigated either by SGS (eight) or NGS-based GPS (six) or CES (nine –three previously SGS and one GPS analysed-), and full autopsy including radiology.
Results: Pathogenic gene variants were found in 3/8 SGSs and in 10/12 NGS-based analysis. In six cases genetics confirmed the pathology diagnosis (thanatophoric dysplasia -twice-, spondyloepiphyseal dysplasia (SEDC), osteogenesis imperfecta (OI), and Desbuquois syndrome), that could raise to seven if two negative SGS are included. Genetics provided previously unsuspected diagnosis in eight cases: de novo achondroplasia, OI, short-rib polydactyly type 3 (SRP3), anauxetic dysplasia, and LADD, Roberts, Steel, and Schwartz-Jampel syndromes. Pathology confirmed variants of unknown significance as actual pathogenic variants in seven cases (Steel, SEDC, Schwartz-Jampel, SRP3, Roberts, OI, and Desbuquois), all among CES-analysed cases.
Conclusion: CES identifies a wide range of skeletal dysplasias and previously unreported genetic variants carrying pathogenetic significance. CES methods would likely identify variants identified in SGS whereas the contrary is unlikely. Multidisciplinary approach results in the highest diagnostic yield and precision.
Funding by: Grant from Fondo de Investigaciones Sanitarias PI17/01153, Instituto de Salud Carlos III, and Fondo Europeo de Desarrollo Regional (FEDER), Ministerio de Economia y Competitividad, Spain

OFP-02-003
CD34 immunostain increases sensitivity and/or upgrades the diagnosis of foetal vascular malperfusion in placentas from ex-utero intrapartum treatment
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Background & objectives: Previously we found an increase incidence of foetal vascular malperfusion (FVM) in placentas from EXIT (ex-utero intrapartum treatment) procedures. This retrospective analysis analyses the impact the recently introduced CD34 immunostain for the FVM diagnosis in placentas from EXIT procedures.
Methods: 105 placentas from EXIT procedures were studied. In 73 cases, the placental histological diagnosis of segmental FVM was made on H&E stained placental sections only (Group 1). In 32 cases, the CD34 component of a double E-cadherin/CD34 immunostain slides was also used to detect the segmental endothelial fragmentation (Group 2). 23 clinical and 47 independent placental phenotypes were statistically compared.
Results: The indications for EXIT procedures were: EXIT 48 to airway, 43 EXIT to ECMO and 14 EXIT to resection). Congenital diaphragmatic hernias were statistically significantly more common in Group 2 (34% vs 56%, p=0.03). There was no statistical significance between the groups in rates of segmental villous avascularity (29% vs 34%), but CD34 immunostain added and/or upgraded 12 more cases in Group 2, thus increasing the sensitivity of placental examination for FVM by 37%. There were no other statistically significantly differences in clinical and placental phenotypes, proving the otherwise comparability of the groups.
Conclusion: The use of CD34 immunostain increases the sensitivity of placental examination for FVM which thus may improve the neonatal management by revealing the increased likelihood of the potentially life-threatening neonatal complications.

OFP-02-004
A report of a very rare case of 47XYY disorder of sexual development presenting with an ambiguous genitalia and mixed gonadal dysgenesis with persistent Mullerian structures
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Background & objectives: Introduction – A report of a very rare case of 47XYY DSD presenting with an ambiguous genitalia and mixed gonadal dysgenesis with persistent Mullerian structures.
Case presentation – An 11 month old infant presented with a chief complaint of ambiguous genitalia. Physical examination of the external genitalia revealed poorly developed bifid scrotum with bilaterally non palpable testes, phallus length of 4cm with distal hypospadia and chordae. Other systemic examination was unremarkable. Hormonal analysis showed Testosterone 2.15 ng/ml and Dihydrotestestrone <6 pg/ml.cont...
Methods: cont... . Serum electrolytes were within the normal limits. Abdomino-pelvic ultrasound reported non visualized testicles. Karyotype was determined from a cheek cell with a report of 47XYY. Surgical exploration done for DSD showed Uterus with cervix, Bilateral fallopian tubes with fimbrated ends and Left side ovary like structure. No right side ovary , testicular structure or cord was seen.
Results: Histopathology showed Fallopian Tube histology and cryptorchid testis
Conclusion - 47,XYY syndrome occurs in about 1 in 1,000 newborn boys. Most males with 47,XYY syndrome have normal production of the male sex hormone testosterone and normal sexual development. Although many males with this condition are taller than average, the chromosomal change sometimes causes no unusual physical features. Mixed gonadal dysgenesis (MGD) is one of the most frequent causes of male sexual ambiguity.
Conclusion: The most common karyotype is 45,X/46,XY mosaicism
In our case the association of 47XYY DSD with ambiguous genitalia and mixed gonadal dysgenesis with persistent Mullerian structures is a rare finding, and to our knowledge, very few are reported so far

OFP-02-005

Paediatric non-Hodgkin lymphomas: a 10-year study from a terciary centre in Coimbra

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Background & objectives: Non-Hodgkin lymphoma is a common malignancy in children and adolescents in Europe. Burkitt lymphoma remains the most frequent followed by lymphoblastic lymphoma and diffuse large B-cell lymphoma. The outcome has improved, and prognosis is in general good at paediatric age.
Methods: Retrospective study of children (age<18 years old) with histopathologically diagnosis of Non-Hodgkin lymphoma from 2009 to 2019. We enrolled 43 patients in total, predominantly male (72.1%), being the youngest case with 3 years old and the oldest one with 17 years old.
Results: Diffuse large B-cell lymphoma (DLBCL) represented 25.6% of cases, Burkitt lymphoma 23.3%, lymphoblastic T-cell lymphoma 16.3%, anaplastic large cell lymphoma 16.3%, lymphoblastic B-cell lymphoma 6.9%, follicular lymphoma 4.7%, primary cutaneous anaplastic lymphoma 2.3%, plasmablastic lymphoma 2.3% and hepatoesplenic T-cell lymphoma 2.3%. Three of DLBCL were post-transplant lymphoproliferative disorders (PTLDs).
Five patients died (11.6%), two were PTLDs after cardiac transplant, one PTLD after bone marrow transplant and the others had primary cutaneous anaplastic lymphoma (death by suicide, 3 years off treatment) and hepatoesplenic T-cell lymphoma with advanced disease at the time of the diagnosis, infection and progression of the disease. B symptoms were also a factor for worse prognosis.
Conclusion: Non-Hodgkin lymphoma remains an aggressive neoplasia; however effective treatment has improved the overall survival and 5-year disease free rates. In our series, we also conclude that specific types of lymphoma have a worse outcome, as well as association with other comorbidities.

OFP-02-006

Frequency distribution of breast cancer biomarkers from a large volume laboratory – a single institution experience

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Background & objectives: Oestrogen receptor (ER), progesterone receptor (PR) and HER2 are established clinical biomarkers in breast carcinoma (BC). We evaluated trends in biomarker data (2007-2019), including newly implemented decile scoring in ER/PR, and compared internal cases (IC) and external cases (EC).
Methods: ER/PR (2011-2019) and HER2 (2007-2019) data on invasive breast carcinoma were analysed. Per ASCO/CAP guidelines, ER (clone SP1) and PR (clone 1E2) IHC were scored as <1%, 1-10%, and > 10% (or deciles of 10-100% from 2017). HER2 IHC/digital image analysis (Ventana Pathway HER2 (4B5) with Aperio software was scored 0 - 3+ ; 2+ cases were reflexed to FISH.
Results: Among 19,193 BC, (IC=6833, EC=12,360), year-to-year ER positive rates (>1%) ranged narrowly (79-81%) with PR ranging from 70-79%.By decile scoring (N=2300), ER was: score<1% (range 18-21%), score 1-10% (2.7-3.2%), score>90% (67-71%), others ≤3%. PR: score <1% (28-30%); score1-10% (7-10%); score>90% (27-31%), others ≤10%. Year-to-year HER2 IHC (total N=40,137) ranged: 0/1+ (67-80%); 2+(12-24%), and 3+(7.4-10.2%). The HER2 2+/FISH+ rate fluctuated between 13% and 28%. IC and EC results were similar.
Conclusion: Over the past decade, ER/PR IHC positive rates remained stable. The bimodal distribution of ER decile scores supports previous studies that most breast cancers are either ER negative or diffusely positive whereas PR scores vary more widely. Variations in the HER2 IHC2+ rate reflected the equivocal nature of this category, but interestingly also coincided with changes in the ASCO/CAP HER2 FISH guidelines. Frequency distributions for ER, PR and HER2 scores did not differ between internal cases and external cases.

OFP-02-007

The use of PAM50 (Prosigna®) as molecular classifier in breast cancer - the experience of 106 consecutive cases analysed at the Royal Surrey Hospital (RSH), Guildford

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Background & objectives: Hormone receptor status in breast cancer confers vital prognostic and therapeutic implications. It is currently defined using immunohistochemistry, a subjective test which may not represent true genotype. We explore discrepancies between immunohistochemical and molecular profiles using the molecular classifier Prosigna.
Methods: Since 2019 RSH has used Prosigna clinically to evaluate 106 consecutive cases of ER/PR positive, Her2 negative early breast cancer predicting risk of recurrence (ROR) and likely benefit of chemotherapy. Analysis of the Prosigna genetic signature also defines the "intrinsic" molecular subtype; luminal A, luminal B, Her2-enriched and basal-like, which we compared with immunohistochemical hormone receptor status.
Results: Of 106 cases, 101 cases had strong positive immunohistochemistry for ER (Allred score 7-8/8). PAM50 confirmed the ER positive genetic profile in all cases by categorising 66 as luminal A and 35 as luminal B. No cases were classified as Her2-enriched.
There were 5 cases with "weak" positive ER immunohistochemistry (Allred score 3-6/8). Prosigna defined these as a "basal-like" molecular profile.
Conclusion: Since eligibility for case selection was immunohistochemical ER positivity, all cases were expected to be categorised Luminal A or Luminal B as per molecular intrinsic subtype. However, Prosigna defined 5% of our cases as "basal-like". Further investigation of the "basal like" cases demonstrated that they had weak ER positivity by immunohistochemistry. This corroborates recent ASCO/CAP guidelines proposing a new reporting category "ER Low Positive" which have a gene expression profile more similar to ER-negative cancer.
Funding by: BDIAP Fellowship

OFP-02-008

Multiplex immunohistochemistry/immunofluorescence (mIHC/if) for PD-L1 testing in triple negative breast cancer: validation of a translational assay with conventional IHC

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Background & objectives: There are several immunohistochemical (IHC) assays approved as companion diagnostics to select for treatment with specific programmed death (PD)-1/PD-ligand-1 (L1) inhibitors. There is no uniformity in assessing PD-L1 across trials in triple negative breast cancer (TNBC).
Methods: Recently, we reported a comparison study (JCP 2020) demonstrating that mIHC/IF represents a promising tool in the era of cancer immunotherapy, as it can simultaneously detect and quantify PD-L1 labelling with multiple antibody clones, allowing accurate evaluation of tumour and immune cells. Hereby we conducted a validation study with bigger cohort, aiming to translate to routine diagnostic setting.
Results: Our cohort comprised of 37 TNBC cases, 20 non-small cell lung carcinomas, 9 colorectal and 29 other cancers. Three in-vitro diagnostic

PD-L1 antibody clones (22C3, SP142 and SP263) were used to perform multiplex immunohistochemistry/immunofluorescent (mIHC/IF) staining. To detect tumour, EpCAM and cytokeratin staining were applied. This was followed by digital pathological evaluation to report the combined positive score (CPS), tumour proportion score (TPS) and immune count (IC) on a single tissue section. We compared the automated scoring results to standard, manual PD-L1 scoring by pathologists using conventional IHC staining.
Conclusion: Moderate-to-strong correlations in PD-L1 positivity were found between results obtained through mIHC/IF and IHC. Individual concordance rates in the study ranged from 69-98%, with Spearman's rank correlation coefficient values up to 0.91. Further analysis within the context of therapeutic trials is required to develop PD-L1 testing as a complementary diagnostic platform in TNBC and other cancers.

OFP-02-009
Assessment of the usefulness of selected methylation features in different tissues of breast cancer patients for preoperative risk stratification
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Background & objectives: Epigenetic changes have long been believed to reflect tumour biology. We tested some of them in different tissues of breast cancer patients to analyse epigenetic background and the value of these parameters in predicting clinicopathological characteristics of tumours.
Methods: 100 Patients with breast cancer were included in the study along with age-matched controls and patients with benign breast lesions. Methylation of global DNA, repetitive elements (LINE-1 and Alu) and BRCA1 gene were studied in blood, tumour tissue and normal breast ductal epithelial cells. These parameters were analysed in comparison to clinical, histologic and phenotypic characteristics of tumours.
Results: Alu, LINE-1 and global DNA methylation showed markedly low levels in all tissues of cancer patients compared to healthy controls, with extreme hypomethylation in tumour tissue. Changes in these parameters were not always concordant. BRCA1 promoter methylation was detected exclusively in tumour tissues and in only two cases, both of which had aggressive phenotype. Methylation levels detected in blood didn't allow stratification of patients with benign and malignant breast lesions and showed rather weak relationship with clinicopathological characteristics of tumours.
Conclusion: Epigenetics signatures show distinct pattern in tumour tissue and are not homogenous in different tissues of the same patient. Given the uniform picture of DNA methylation in blood in some of investigated groups, additional data and very careful approach are required when considering using it as a diagnostic or predictive tool.
Funding: The research was supported by Shota Rustaveli National Science Foundation Of Georgia (SRNSFG) [Grant Number - PhDF2016_85].

OFP-02-010
Comparison of different pathological complete remissions in neoadjuvant breast cancer based on different assessment systems
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Background & objectives: Differences in pathological complete remission (pCR) achieved after neoadjuvant therapy (NAT) of breast cancer patients based on Miller–Payne (MP) classification, residual cancer burden (RCB), and Pinder assessment system.
Methods: 276 patients with breast cancer who underwent neoadjuvant therapy after surgical diagnosis of preoperative puncture pathology from January 2014 to January 2015 in the Fourth Hospital of Hebei Medical University were retrospectively studied. Chi-square test was used to analyse the relationship. ROC curves to analyse respective diagnostic efficacy. COX regression model was used to analyse the significance in prognostic evaluation.
Results: In this study, we found that tumour size, ER expression state, PR expression state, Ki67 index, and molecular classification of HER2 overexpression type and three negative type breast cancer were statistically significant in terms of achieving pathological complete response after neoadjuvant chemotherapy ($P<0.05$); Chi-square test showed that there was no statistically significant difference in pCR rate ($P>0.05$); ROC curve analysis shows that RCB has higher diagnostic efficiency than Pinder; COX survival analysis shows that the RCB index classification is more instructive for the prognosis of breast cancer patients after neoadjuvant treatment.
Conclusion: Evaluation of pathological response after neoadjuvant, the RCB index evaluation system has better performance than MP and Pinder evaluation system.

OFP-02-011
AI-assisted interpretation of Ki-67 standard comparison cards for different types of breast cancer
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Background & objectives: Compare the difference between the reference breast cancer standard comparison card and conventional microscope interpretation and explore the clinical applicability of breast cancer standard comparison card.
Methods: 311 breast cancer surgical resection specimens from our Hospital were selected, Ki-67 immunohistochemical staining was performed by 3 senior pathologists with conventional interpretation and comparative artificial standards. Comparison card interpretation method, by selecting two regional interpretation methods, high value-added area and average value. Intraclass correlation coefficients were used to assess reproducibility between observers.
Results: The reference standard comparison card showed excellent consistency between Ki-67 values in different types of breast cancer by selecting the average value (a high value-added area and a low value-added area, AVE) (ICC: 0.797, CI 0.753-0.834).
Conclusion: The reference standard comparison card interpretation is expected to become a common method for breast cancer Ki-67 interpretation.

OFP-02-012
ZNF703 copy number and protein expression in breast cancer
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Background & objectives: *ZNF703* is associated with proliferation and is thought to be most common in luminal breast cancer. We aimed to study *ZNF703* copy number and protein expression in breast cancer and elucidate associations with proliferation, molecular subtype and prognosis.
Methods: Using fluorescence in situ hybridization (n=702) and immunohistochemistry (IHC) (n=829), we examined *ZNF703* copy number and protein expression in primary breast cancers. We assessed associations between *ZNF703* copy number and proliferation, molecular subtype and prognosis, and between protein expression and molecular subtype. In the prognostic analyses, we estimated cumulative incidence of breast cancer death and hazard ratios.

Results: We found that 7% of primary tumours had increased copy number (mean copy number ≥6), and 76% of primary tumours were IHC positive (≥50% tumour cell nuclei positive). The highest proportion of tumours with mean copy number ≥6 was found in the Luminal A and Luminal B(HER2-) subtypes. Luminal subtypes also had the highest proportion of IHC+ cases. We found a positive association between *ZNF703* copy number increase and proliferation. Patients with *ZNF703*copy number ≥6 had poorer prognosis compared to cases without copy number increase (HR 1.6 (95% CI 1.1 -2.5)).
Conclusion: *ZNF703* copy number increase is associated with the Luminal A and Luminal B (HER2-) subtypes. Protein expression is associated with all luminal subtypes. There is an association between *ZNF703* copy number increase and proliferation, and a poorer prognosis.

OFP-02-013
The association of clinicopathological parameters and the extent of neuroendocrine differentiation with microRNA 21 and microRNA let7f expression in primary invasive breast carcinomas with neuroendocrine features
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Background & objectives: To compare primary Breast Carcinoma with Neuroendocrine Features (BCNF) cases with Invasive Ductal Carcinoma (IDC-NOS) cases without neuroendocrine differentiation matched for molecular subtype and stage as regards the clinicopathological features and the expression levels of two miRNAs.
Methods: The slides and paraffin blocks of the 29 cases with BCNF diagnosis and the 29 cases with IDC-NOS diagnosis as reported in our clinic between 2012 and 2017 were obtained from the archives and retrospectively re-evaluated. The miR-21 and miR-let7f expression levels were detected with the qRT-PCR method in paraffin blocks containing invasive tumour and normal tissue in each case.
Results: The mean age in the groups with neuroendocrine differentiation was almost 10 years higher than in the IDC-NOS group. The Ki-67 proliferation index level, nuclear grade and histological grade were higher in the group with 10% to 50% neuroendocrine differentiation than in the group with ≥ 50% neuroendocrine differentiation.
Comparison of the groups for miR-21 expression revealed that the increased expression in the IDC-NOS group was more prominent than in the other two groups with neuroendocrine differentiation. The decrease in the miR-let7f expression level in the group with 10% to 50% neuroendocrine differentiation was less than seen in the IDC-NOS group.
Conclusion: BCNF is seen at more advanced ages than IDC-NOC cases. Cases with widespread neuroendocrine differentiation within tumour tissue are associated with a lower nuclear/histological grade and Ki-67 levels. Decreased miR-let7f expression is more prominent in BCNFs while increased expression of miR-21 is more prominent in IDC-NOS cases without neuroendocrine differentiation. Our results let us to consider various treatment options (miRNA based therapy) for BCNF.

OFP-02-014
Germline mutations and pathological features of breast and female genital cancers in increased-risk patients of Asian origin
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Background & objectives: Patients of Asian ancestry comprise 10.8% of UK population in West Midlands. Breast and ovarian cancers in non-Caucasian women tend to present at earlier age with more aggressive disease. We aim to analyse patient genetics and pathologic features of those cancers.
Methods: We identified 164 increased-risk patients of Asian ancestry, out of 5618 patients genetically tested between 2006-2018 at a large reference genetics centre. All patients were screened for mutations of BRCA1/2, and a subset were also tested for (PALB2, BRIP1, RAD51D & others) as per the clinical guidelines. Histopathological and clinical data were collected and correlated with the genetic results.
Results: 51 mutations in 46 patients (median age 38) were identified of which 20/26 were BRCA1-pathogenic and 13/22 were BRCA2-VUS. Two rare pathogenic-BRCA1 variants were found repeated. BRIP1 & PALB2 mutations were pathogenic, and RAD51D was VUS. The 46 patients presented mostly by breast cancers. Breast cancers were predominantly grade3(75%), >15mm in 57.9%(11/19) and with 43% lymph node positivity and high proportion of the triple-negative phenotype (TNBC)(36.4%).
The 118/164 patients (negative for germline mutations) presented at median age of 40 years. The breast cancers were mostly grade3(52.7%), of invasive size (>15mm) in 64.6%(31/48) and node negative(55.3%;26/47). There was a higher proportion of the luminal phenotype(63.8%) and lower proportion of the TNBC(25.5%).
Conclusion: Increased-risk Asian patients presented with high grade breast cancers, at young age with larger proportions of the unfavourable triple negative molecular subtype (TNBC). Patients with pathogenic mutations had a higher proportion of TNBC. Two cases were negative for BRCA1/2 mutations but later tested positive for BRIP1 (pathogenic) and RAD51D (VUS). Extended panel testing is warranted and informs genetic counselling and optimal management in this patient group.

OFP-03 Gynaecological Pathology

OFP-03-001
Multiplexed immunohistochemistry for immune cell phaenotyping, quantification and spatial localisation in a rare tumour, clear cell ovarian cancer
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Background & objectives: Little is known about the unique immunophenotypical features of clear cell ovarian cancer (CCOC).We conducted multiplexed IF/IHC to 1) describe the tumour microenvironment (TME) of CCOC and 2) compare CCOC to high grade serous OC (HGSOC).
Methods: Tissue micro-arrays with triplicate tumour samples from 29 CCOC and 30 HGSOC were stained using multiplex IF/IHC panels including: CD3, CD4, CD8, FOXP3, Granzyme B (GrzB), CD68, CD163 and CK. IC topography was described as intraepithelial if <20uM from tumour cells (TC), or stromal (>20uM from TC). Image analysis (Visiopharm) performed to quantify IC in number/mm2 or % surface positive
Results: There were significantly fewer CD8+ IC in CCOC vs HGSOC (median 15 vs. 48 cells/mm2; p=0.01) and 34% (10/29) of CCOC were "immune-excluded" with CD8+ IC present only in the stromal compartment. However, despite lower CD8+ IC, CCOC showed significantly greater GrzB expression (marker of effector T cell cytotoxicity) (p=0.0007), and significantly reduced FOXP3+ T cells (p=0.03) resulting in favourable effector/suppressor ratio compared to HGSOC (median GrzB+/FoxP3+: 10.7 vs 0.04; P<0.0001). CCOC also showed

significantly higher levels of CD68+ macrophages (M1) (<0.0001), resulting in a significantly more favourable M1/M2 ratio than HGSOC (median CD68+/CD163+: 3.6 vs. 0.8; p=0.0001).
Conclusion: One third of CCOC are "immune excluded". However, when present, the effector to suppressor balance of both T cells (GrzB+/FoxP3+) and macrophages (CD68+/CD163+) is in favour of anti-tumour immune response.

OFP-03-002
Micropapillary variant of serous borderline tumour (MSBT) with BRAF mutations, a molecularly distinctive and less aggressive precursor of low-grade serous carcinoma (LGSC)
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Background & objectives: Despite the MSBT has been recently identified as a "synonymous" of non-invasive LGSC (niLGSC; WHO, 2014), on the base of the clinical-prognostic reports, few molecular studies are carried out on this pathological entity.
Methods: KRAS, NRAS and BRAF mutational analysis and HER2 and p53 expression were assessed on 50 LGSCs, 42 MSBTs, 50 Serous Borderline Ovarian Tumours (SBT). On these groups, we performed the Human Cancer Pathway- and miRNA- Finder PCR array (Qiagen). Altered miRNAs and pathways were confirmed by real-time PCR or immunohistochemistry. Results were correlated with the clinical and pathological features.
Results: We found a higher rate of BRAF mutation in SBT (65%) than in MSBT (30%) and LGSC (5%). Conversely, RAS mutations rate significantly increased from SBT (6%) to MSBT (25%) to LGSC (40%). We did not find HER2 and p53 alterations. MSBTs with BRAF mutations had a miRNAs and cancer pathway alterations significantly similar to those SBT cases with BRAF mutations, but different to those MSBT group with RAS mutations. Contrariwise, MSBT with RAS mutations had a miRNAs and cancer pathway alterations significantly similar to those RAS mutated LGSC cases. Finally, MSBT with RAS mutations are significantly associated to a worse PFS respect to MSBT cases with BRAF mutations (p=0.003).
Conclusion: Our data suggested the idea that MSBTs is a heterogeneous group of patients that when associated to RAS mutations represent a more aggressive malignant precursor of the LGSC. Conversely, MSBTs with BRAF mutations are molecularly and clinically more similar to SBTs.

OFP-03-004
How much tumour do we need to submit during grossing to correctly evaluate Silva pattern in endocervical adenocarcinomas?
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Background & objectives: Endocervical adenocarcinoma(EA) Silva pattern stratifies tumours based on morphology and correlates with clinical outcome. It's unknown if entire tumour submission is necessary to assign the appropriate Silva pattern. Our aim is to clarify EAs gross submission to correctly diagnose Silva pattern.
Methods: We retrospectively reviewed a cohort of 37 patients that underwent surgery and were diagnosed with HPV-related EAs at IPOP between 2005 and 2019. Macroscopic information and histological slides were re-evaluated, particularly regarding tumour size and submitted sections. Silva pattern was evaluated in each tumour section. Probability models were created using random sampling without replacement.
Results: Patients underwent hysterectomy(n=29) or conization only(n=8). Mean tumour size was 17mm (range:2,55mm). Twenty-one tumours were macroscopic. Twenty-seven tumours were totally submitted (mean size=12mm) and 10 were partially submitted(mean size=29mm). Mean tumour sections was 6 (range:1,13). Tumour's final Silva pattern included: 7 pattern-A, 7 pattern-B, 23 pattern-C. Intratumoral comparison of Silva pattern between sections showed 15 homogeneous(8-pattern C; 7-pattern A) and 22 heterogeneous tumours. Larger tumour size is associated with pattern C(p=0.006). In large tumours(~2cm) this pattern composes in median 67% of sections. Probability models showed that submission of at least half the tumour identifies the correct Silva pattern in 88% of all cases, and in 81% of heterogenous larger tumours.
Conclusion: Our findings support the current practice of partially including large tumours, since they are most frequently extensively pattern C. Total inclusion is recommend for small tumours and for larger tumours that are heterogeneous.

OFP-03-005
Integrated histopathologic and molecular classification of endometrial carcinoma: identification of prognostic subgroups
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Background & objectives: The TCGA project discovered four distinct prognostic endometrial carcinoma (EC) classes: POLE-mutant, mismatch repair deficient-MMRd, p53-mutant and no specific molecular profile-NSMP groups. Our aims were to integrate the histological and molecular classifications, and to identify markers relevant for risk stratification.
Methods: Comprehensive clinicopathologic and follow-up data including immunohistochemical (IHC) analysis and/or Next-Generation Sequencing (NGS) were analysed in a retrospective cohort of 110 ECs. IHC and/or NGS were used to assign TCGA groups and to investigate molecular alterations of multiple target genes including POLE, PTEN, ARID1A, ß-catenin, TP53, MLH1, PMS2, MSH2, MSH6 and L1CAM.
Results: TCGA class assignment of EC cohort: 8 (7.3%) POLE, 34 (30.9%) MMRd, 23 (20.9%) p53abn and 45 (40.9%) NSMP. Molecular subgroups were significantly associated with different grade, tumour-infiltrating lymphocites (TILs), mitoses, Ki-67 index, pattern of invasion, L1CAM expression. NSMP class was further subdivided based on ARID1A and on ß-catenin alterations. ARID1A loss was associated with higher grade, increase of TILs, necrosis, higher mitotic and Ki-67 index, specific patterns of invasion. Ten of 110 (9.1%) ECs recurred: 5 NSMP with ARID1A mutation, 2 MMRd, 3 p53abn. NSMP cases with ARID1A mutation showed the worst outcome with early recurrence (log-rank p<0.01).
Conclusion: An integrated EC classification may better define risk assessment, representing a step towards precision medicine. The analysis of ß-catenin and ARID1A alterations in NSMP class identified subsets of ECs statistically correlated with specific histopathological parameters and different disease recurrence.

OFP-03-006
Correlation of MMR protein deficiency with histopathologic parameters in endometrial carcinoma
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Background & objectives: The aim of the study was to analyse the correlation between DNA mismatch repair (MMR) proteins status and clinicopathological characteristics of endometrial cancers (ECs).
Methods: The relationship between clinicopathologic parameters and MMR proteins status was investigated in 198 consecutive patients who underwent surgery for ECs.
75 out of 198 (33%) cases showed immunohistochemical alteration of MMR proteins: 65=(32.8%) cases lost MLH1&PMS2, 10(5.1%)cases lost other proteins(8MSH2 & MSH6, 1MSH6, 1PMS2).On univariate

analysis, we more frequently observed high grade endometrioid carcinoma in cases with MLH1&PMS2 losses, low grade endometrioid carcinoma in cases with other losses (p=0.021).
Results: Larger tumour size and increased tumour infiltrating lymphocytes(TILs) were more frequently observed in patients with MLH1 & PMS2 losses than other losses (p=0.004, p=0.009, respectively). On multivariate binary logistic regression analysis, loss of MLH1 & PMS2 revealed statistically marginal significance for larger tumour size than MMR protein intact and other losses (odds ratio [OR]=3,052, 95% confidence interval [CI]=0.817–11.396,p=0.097,OR=0,135, 95% CI=0.014–1.263,p= 0.079, respectively).TILs was independently correlated with MMR protein loss, there was a marginal significance between infiltrative glands type myoinvasion and MMR protein loss(OR=3.104, 95% CI=1.431–6.736, p=0.011,OR=0.307, 95%CI=0.116-0.808, p=0.064, respectively).
Conclusion: The presence of infiltrative glands type myoinvasion showed predisposition to be associated with MMR protein loss. Cases with MLH1&PMS2 losses tend to be larger and higher-grade tumours than cases with MMR intact status and other losses. These results have to be proven in larger cohorts.

OFP-03-007
Correlation of PD-L1 expression with MMR protein subtype deficiency in endometrial carcinomas

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Background & objectives: Programmed death-ligand 1 (PD-L1) was studied in several cancer types, however there is stil limited data about endometrial cancer (EC). The purpose of this study was to evaluate PD-L1 expression of tumour cells(TC) and immune cells(IC) at different cut-off values.
Methods: By using immunohistochemical staining, in 176 resection specimens of EC patients, PD-L1 results were correlated with mismatch repair (MMR) protein status and several prognostic parameters including myometrial invasion patterns.
Results: On both univariate and multivariate analysis, TC and IC PD-L1 positivity with a 5% cut-off were significantly associated with MMR protein loss(univariate: p=0.015, and p=0.001; multivariate: p=0.027, CI=0.003-0.583, and p=0.002, CI=1.498-5.557 respectively). MLH1&PMS2 loss subgroup had higher rates of positivity for IC PD-L1 expression, however other MMR loss subgroup(MSH2 and/or MSH6,PMS2) tended to have higher rates of positivity for TC PD-L1 expression. MELF type myoinvasion were marginally significant for TC PD-L1 expression at 5% cut-off (univariate:p=0.089; multivariate: p=0.062, CI:0.022-10.101).
Conclusion: This study demonstrated that tumoral PD-L1 expression was more common in patients with other MMR loss subgroup, IC PD-L1 expression was more common in patients with MLH1&PMS2 loss subgroup. Also, the presence of MELF type myoinvasion showed predisposition to be associated with TC PD-L1 positivity. These results have to be proven in larger cohorts.
This research was funded by Istanbul Medeniyet University Scientific Research Project Fund.

OFP-03-008
Increased FOXJ1 protein expression is associated with improved overall survival in high-grade serous ovarian carcinoma: an ovarian tumour tissue analysis consortium study

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Background & objectives: NanoString mRNA analyses have identified FOXJ1 (ciliated cell transcription factor) and GMNN (DNA replication inhibitor) as prognostic markers in tubo-ovarian high-grade serous carcinoma (HGSC). We aimed to evaluate FOXJ1 and GMNN expression by immunohistochemistry and survival associations within ovarian carcinomas.
Methods: Ovarian Tumour Tissue Analysis Consortium tissue microarrays containing high-grade serous, low-grade serous, mucinous, endometrioid, and clear cell carcinomas were stained for FOXJ1 (N=5,544) and GMNN (N=3,787). Nuclear staining was scored in 5%-increments then categorized (FOXJ1: 0%, 5%, 10-15%, 20-45%, 50-100%; GMNN: 0%, 5%, 10-15%, 20-25%, 30%, 35-100%). The log-rank test and Cox proportional hazards regression compared expression levels and survival.
Results: FOXJ1 and GMNN expression was heterogeneous across histotypes. Increased FOXJ1 expression was associated with improved overall 5-year survival in HGSC: 47.1% in patients with high (50-100%) FOXJ1 expression versus 34.7% in those with absent FOXJ1 expression (HR= 0.78, 95%CI 0.66-0.93, p<0.0001). However, GMNN expression was not significantly associated with survival. No significant association with overall survival was observed in any other histotype, for both markers.
Conclusion: FOXJ1, but not GMNN, can be translated into an immunohistochemical biomarker to stratify prognosis in HGSC.

OFP-03-009
Technical and interpretation performance characteristics of P16 immunohistochemistry: a joint project by the British Association of Gynaecological Pathologists (BAGP) and United Kingdom External Quality Assessment Service (UKNEQAS)

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Background & objectives: Immunohistochemistry for the biomarker p16 is a surrogate for high-risk Human Papillomavirus (HPV)-mediated anogenital precancerous and malignant lesions. The accuracy of this biomarker is dependent on the technical quality of the immunostaining as well as well as correct interpretation.
Methods: BAGP members were invited to participate. Unstained sections from a tissue microarray containing 74 cores from anogenital neoplasms, non-invasive and invasive, as well as control cases, were sent to each of 40 laboratories. Participating laboratories were asked to submit details of their staining protocol as well as interpretation results electronically, the latter for each core as "Normal/reactive", "Abnormal" or "Other/Uninterpretable".
Results: Results were received from a total of 37 laboratories and 109 individuals (93 pathologists and 16 Biomedical Scientists). Two antibody clones were used; BDPharmingen: G175-405 (n=4) and Ventana CINtec: E6H4 (n=26). (No methods from 7 laboratories). IHC staining platforms from 3 suppliers were represented: Ventana Benchmark: 70%; Leica Bond: 27%; Dako autostainer: 3%.
Slides were returned by 35 laboratories enabling assessment of results of 74 cores from 102 individuals (n=7548). 30/35 laboratories (86%) showed >95% concordance with the reference result for 52 assessable cores. Excluding uninterpretable cores, there was 94% (5331/5673 core results) absolute agreement between individual and central review results.
Conclusion: This study shows excellent technical performance of p16 immunohistochemistry using different antibody clones and automated staining platforms. Interpretation accuracy for abnormal results was high overall, and discrepant results are explained largely through technical reasons.

OFP-03-010
Indicators of the intensity of intoxication of the term placenta by tobacco smoke

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Background & objectives: Intrauterine exposure to tobacco smoke can cause not just metabolic, immunological and endocrine diseases but also epigenetic changes in new-borns DNA.

Our objective was to establish an indicator of toxic changes in the form of Placental intoxication index (PII).
Methods: 290 postpartum women were divided into four groups with respect to smoking habits during pregnancy: NS, non-smokers; PS, passive smokers; AS, active smokers; APS, combined smokers. Placenta samples were analysed pathohistologically (H/E), immunohistochemically (p53, bcl-2, Hsp-70 and Metallothionein) and statistically.
PII was established for each placenta. It incorporates the sum of Placental morphologic index (PMI) and Placental immunohistochemical index (PIHI).
Results: Statistical comparison of PII for each group enabled the distinction of placentas exposed to tobacco smoke during the intrauterine period from those that were not exposed; the PII of placentas exposed to passive smoking differed statistically significantly from PII of placentas exposed to active smoking, while there was no difference between PII of placentas exposed to active smoking and combined forms of smoking.
PII in placentas exposed to tobacco smoke indicated intensity of intoxication since it showed a statistically significant correlation with the level of tobacco smoke exposure regardless of the mode of exposure.
Conclusion: PII detected intoxicated placentas that would otherwise be considered unexposed to the effect of tobacco smoke during 40 weeks of pregnancy because neonatal and macroscopic placental parameters did not indicate significant changes. Therefore, PII enables the early detection of risky new-borns who require enhanced care up to adulthood because of the harmful intrauterine effects of tobacco smoke.

OFP-03-011

Inter-observer variability in differentiated vulvar intraepithelial neoplasia

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Background & objectives: Differentiated vulvar intraepithelial neoplasia (dVIN) progresses rapidly to carcinoma but manifests a subtle histologic appearance. We assessed the variability of the diagnosis of dVIN amongst pathologists and sought to identify the most reproducible histologic features.
Methods: Two pathologists selected a set of dVIN (n=30) and no-dysplasia (n=10) slides with a range of histologic appearance and prepared a check-list of histologic features of dVIN. Nine external participants independently judged these slides as 'dVIN' or 'no-dysplasia' and noted which features they used for the diagnosis. 'Consensus diagnosis' was defined as 70% agreement. Inter-observer agreement (Fleiss' Kappa) was calculated.
Results: Consensus was reached for 23 (77%) dVIN cases and for all the no-dysplasia cases. For the diagnosis of dVIN moderate agreement (κ=0.46) was obtained; pair-wise agreement ranged from slight to substantial (mean κ=0.51; range: 0.14–0.71). Among all histologic features, moderate agreement was obtained only for parakeratosis (κ=0.51). Fair agreement was obtained for nuclear features such as atypia discernable under 100X magnification (κ=0.39), nuclear angulation (κ=0.38), abnormal chromatin (κ=0.38), and suprabasal mitoses (κ=0.32). Histologic features related to disturbed maturation and architectural changes, such as deep squamous eddies (κ=0.39), elongated/anastomosing rete-ridges (κ=0.33), altered cellular alignment (κ=0.32), cobblestone appearance (κ=0.29), and individual cell keratinization (κ=0.27), also had fair agreement.
Conclusion: Histologic diagnosis of dVIN suffers from considerable inter-observer variability. Moderate agreement was obtained only for parakeratosis, and there was only fair agreement for most histologic features. Future studies should focus on ancillary immunohistochemical and molecular biomarkers to facilitate accurate diagnosis.

OFP-05 Digestive Diseases Pathology - Liver / Pancreas

OFP-05-001

A new marker for intrahepatic cholangiocarcinoma: cystic fibrosis transmembrane conductance regulator

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Background & objectives: Biliary tract cancer are aggressive and heterogeneous neoplasms and a specific marker for the biliary epithelium is missing. We performed immunohistochemical analysis of the cystic fibrosis transmembrane conductance regulator (CFTR) in a series of 74 biliary and non biliary tumours.
Methods: We collected a cohort of 40 intrahepatic cholangiocarcinomas and 7 combined hepatocellular-cholangiocarcinomas, then compared them with 8 perihilar adenocarcinomas, 5 hepatocellular carcinomas, 1 case of biliary adenofibroma, 1 case of colorectal liver metastasis, 5 pulmonary adenocarcinomas and 7 pancreatic ductal adenocarcinomas. 3-μm-thick tissue sections were incubated with monoclonal antibody anti-CFTR (NeoBiotechnologies, mouse monoclonal antibody, CFTR/1643, diluition 1:100).
Results: Intrahepatic cholangiocarcinomas were 10 "large duct type" and 30 "small duct type". Of the "small duct type" 6 cases partially resembles biliary adenofibroma and 6 had a cholangiolocellular carcinoma component. CFTR was expressed in 67% of "small duct type", whilst never expressed in the"large duct type", nor in the perihilar adenocarcinomas (p=0.009). Moreover, CFTR was positive both in the biliary adenofibroma and cholangiocellular components of the intrahepatic cholangiocarcinomas (p=0,011) and was positive in the case of biliary adenofibroma. In the combined cancers, CFTR was expressed in 4 of 7 cases. HCCs, colorectal liver metastasis and pulmonary adenocarcinomas were negative; 1 of the 7 cases of pancreatic adenocarcinoma was positive.
Conclusion: CFTR is a reliable marker for intrahepatic biliary tumours and can be useful both in routine practice and for understanding their biology, which is fundamental to understand the results coming from genomic studies and for the personalization of therapies.

OFP-05-002

Histological and molecular profiling of intrahepatic cholangiocarcinomas in patients with a history of asbestos exposure

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Background & objectives: There are recent evidences of a role of asbestos in the cancerogenesis of intrahepatic cholangiocarcinoma (iCC). Here we present the preliminary results of a study on the histopathological features and mutational status of iCC in asbestos-exposed patients.
Methods: We retrospectively selected the iCC patients from our Institution with a proven history of asbestos exposure according to modified RENAM questionnaire. Clinical and histological features were revised. Immunohistochemistry for CK7, CK19, pCEA and CD56 was automatically performed. Next-Generation Sequencing was performed for mutational status.
Results: Until now, 19 patients were selected; 12 cases with concomitant risk factors for liver disease (alcohol, steatosis/steatohepatitis, HBV/HCV infection) and 7 cases with only asbestos exposure in anamnesis.

Six out of 7 asbestos-only exposed cases were iCC of the small-duct subtype, 1 case was an undifferentiated peripheral iCC, without a specific morphological subtype for small or large bile ducts.
Some gene mutations were more typical of multifactorial iCCs: BAP1 was mutated in 6/12 (50.0%) multifactorial cases and 1/7 (14.3%) asbestos-only cases (p=0.004, t-test); MUC genes were mutated in 6/12 (50.0%) and 1/7 (14.3%) cases respectively (p=0.004). Conversely, ATN1 was mutated in 4/12 (33.3%) and 3/7 (42.9%) cases respectively (p=0.05).
Conclusion: These preliminary results suggest an association between asbestos exposure and small-duct subtype iCC: thus, asbestos could be considered a "non-biliary" risk factor. Moreover, the different incidence of some gene mutations in presence of other risk factors suggests different carcinogenetic mechanisms.

OFP-05-003
Combined hepatocellular-cholangiocarcinoma (CHCC-CC): are the cellular components important?
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Background & objectives: Primary liver carcinomas (PLC) with unequivocal presence of both hepatocytic and cholangiocytic differentiation within the same tumour are classified as combined hepatocellular-cholangiocarcinoma (cHCC-CC). In this study the clinicopathologic characteristics and immunophenotypes of combined CC-HCC cases were analysed.
Methods: Clinicopathologic data of 19 combined CC-HCC cases were retrospectively analysed. Thirty tumour nodules from 19 cases were retrospectively reviewed for the morphological features of their hepatocytic, cholangiocytic and stromal components based primarily on routine stains.
Results: There were 12 male, 7 female patients (mean age 57, range 34-76). Tumours were, multifocal in 3 (15.79%) cases. Histopathological analyses showed presence of combinations of classical-Hepatocellular carcinoma, classical-cholangiocarcinoma (cCC) and components composed of intermediate cells, intermixed/transitional nests and immature (embryonal-like) cells. Twelve cases were classical cHCC-CC, two were combined intermediate carcinoma-CC, 3 were Intermixed/Transitional Nests combined with cCC and two had embryonal liver-like hepatocytic/cholangiocytic components. Classical HCC-CC was more multifocal (25% vs 0%), smaller (mean diameter 6,38 cm vs 8.64 cm), had more major vascular invasion, satellite nodules, intrahepatic metastases and perineural inavasion (33.33% vs. 14.48%, 16.66% vs. 0%, 33.33% vs. 0%16.66% vs. 14.28 %, respectively) than other subtypes.
Conclusion: Histopathological components of cHCC-CC may have an influence on the biological behaviour of the tumour and merits analysis in larger series

OFP-05-004
Importance of recipients' clinical profile in the allocation of liver grafts with fibrosis from dyslipidemic donors
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Background & objectives: A novel role of graft fibrosis and dyslipidemic profile in extended-criteria donors (ECD) in predicting early allograft dysfunction (EAD) was previously demonstrated.
Aim: to validate our previous results on a prospective cohort, matching graft histology to recipients' characteristics.
Methods: We prospectively enrolled all ECD whose liver grafts underwent to transplant after biopsy in 2 years.
Histological variables of the graft, donors' and recipients' clinical data, and follow-up data were recorded, including EAD (at 7 days). Multivariate and univariate analyses were applied. ROC curves were built to calculate bilirubin and creatinine cut-offs.
Results: We enrolled 103 ECD and corresponding recipients. Fourteen (13.6%) had portal fibrosis ≥2 (according to Ishak) and dyslipidemia (dyslipidemic donors with fibrosis, DDF); 42.8% DDF recipients experienced EAD versus20.9% of the other recipients (p=0.076); in particular, DDF recipients had more episode of AST raise within 7 days (p=0.048).
At multivariate ad univariate analyses, EAD correlated with pre-OLT bilirubin levels (p=0.030) in non-DDF recipients, and with pre-OLT creatinine and INR in DDF recipients (p=0.024 and p=0.016).
In particular, DDF recipients with >0.85 mg/dL pre-OLT creatinine had 71.4% EAD episodes, compared to 14.3% in DDF recipients with <0.85 mg/dL creatinine (p=0.009).
Conclusion: Our prospective cohort confirmed the importance of DDF model in predicting EAD. Moreover, the choice to transplant DDF grafts likely depends on recipients' clinical profile, in particular creatinine level, according to our model.

OFP-05-005
Histopathologic evaluation of resected colorectal cancer liver metastases
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Background & objectives: Colorectal liver metastasis (CRLM) presents histopathologic patterns with prognostic implications. The objective of this study is to evaluate the influence of pathological findings on mortality rate (MR).
Methods: Analysis of clinical and outcome data from 30 patients who underwent CRLM resection, 25 of whom were treated with chemotherapy before hepatic resection. Pathological review: resection margins; tumour regression grade (TRG); growth pattern (GP); necrosis and mucinous pattern.
Results: Thirty patients: 12 women and 18 men. Mean age: 65 years. Median survival following hepatic resection: 41 months. Resection margins: positive in nine specimens, associated with higher mortality rate (MR) (56% vs 29%). TRG: fourteen showed complete/partial response (TRG1-3) and eleven showed poor response (TRG4-5). TRG1-3 had lower MR (21%) vs TRG4-5 (54%). GP: five pushing, twelve desmoplastic, seven replacement and six mixed. Replacement GP showed higher MR (57%). Oxaliplatin-based chemotherapy was associated with desmoplastic GP (56%). Necrosis: sixteen had >10% and fourteen <10% (MR 63% vs 8%). Mucinous pattern: present in six, all four with mucinous pattern >50% died.
Conclusion: The pathological features associated with higher MR were positive resection margins, TRG4/5, replacement GP, >10% of tumour necrosis and mucinous pattern >50%. Prospective studies of patients with CRLMs are warranted to evaluate the prognostic value of histopathological features.

OFP-05-006
Role of cellular senescence in the natural history of primary sclerosing cholangitis
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Background & objectives: Cellular senescence (CS) represents an irreversible cell cycle arrest to prevent replication of injured cells, whose role in chronic liver diseases was recently suggested. We aimed to evaluate hepatic CS-marker expression in primary sclerosing cholangitis(PSC) and its correlation with clinical-pathological features.
Methods: Thirty-five PSC patients with at least one liver biopsy(LB)/explant at diagnosis and/or during follow-up were enrolled. Clinical/

laboratory data(including prognostic models) at the time of LB were collected. Endpoint was survival without liver transplantation or cirrhosis decompensation. Grading/staging according to Nakanuma were performed. Immunohistochemistry for CS-markers(p16,p21) were performed and scored based on positivity extent in native bile duct(NBD) and ductular reaction(DR).

Results: p16 and p21 expression in NBD and DR was directly correlated with hepatitis activity, cholestasis-related histological lesions, fibrosis, and disease stage ($p<0.05$ for all). By multivariate analysis, p16 expression in DR was independently associated with advanced disease stages [p=0.002,HR 13.6 (95%CI 2.6-72.6)]. p16 and p21 expression in DR was directly related to Mayo Risk Score (p=0.02 for both) and Amsterdam-Oxford Model (AOM;$p<0.001$ and p=0.007, respectively). p16 and p21 expression in NBD was directly related to AOM (p=0.03 for both). p21 expression in DR was independently associated with adverse outcome-free survival [p=0.005,HR 4.6 (95%CI 1.6-13.6)].

Conclusion: In PSC, CS marker expression in cholangiocytes is related to clinical and histological severity, disease progression and patients' prognosis, suggesting a role for CS in the natural history of the disease.

OFP-05-007

Biomarkers to predict response to immunotherapy identify pancreatic cancer patient subgroups with prolonged progression-free survival

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Background & objectives: Immunotherapy alone or in combination with chemotherapy can improve treatment response in pancreatic ductal adenocarcinoma (PDAC). Therapy success has been linked to microsatellite instability (MSI), inflamed tumour microenvironment (TME), high tumour mutational burden (TMB) and PD-L1 expression.

Methods: The study cohort comprised 115 resected PDACs, TNM stage I-III, including 25 long-term survivors (progression-free survival>60 months). TMB was assessed using the oncomine mutation load assay. PD-L1, immune cell densities and MSI-status were assessed immunohistochemically (PD-L1, MLH1, PMS2, MSH2, MSH6, CD3, CD4, CD8, FOXP3, CD68) on tissue microarrays.

Results: MSI-H was present in 2.6% of all patients and more frequent among LTSs (8%). 75% of MSI-H-cases were also TMB-H (i.e. >10), showing T-cell-inflamed TME. TMB-H was found in 15% of PDACs; 60% also expressing PD-L1. PD-L1-positivity was found in 37% (20% were also TMB-H). PD-L1-high (expression-score >4; 7%) was associated with an inflamed TME. Better overall (OS) and progression-free survival (PFS) was found for TMB-H cases (p=0.01817 and p=0.00664).

Conclusion: The morphologic/microenvironmental and clinicopathologic features of MSI-H and TMB-H patients indicate a better anti-tumour immune response. Based on concurrent biomarker expression, TMB-H patients might further profit from checkpoint inhibition, while other strategies inducing immune response might be an option for the remaining majority of patients. Combinations of biomarkers indicating potential immunotherapy response along with TMB can assist the selection of target groups as part of an individualized, precision oncology approach.

OFP-05-008

Predicting morphological classifications of pancreatic ductal adenocarcinoma (PDAC) using deep learning

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Background & objectives: We recently proposed a revised, pattern based morphological classification for PDAC, associated with transcriptional subtypes and overall survival1.We aim to assess if deep learning can automate our system to enhance reproducibility and accessibility to pathologists for patient care.

Methods: 365 H&E slides from 58 patients (range 3-11 slides/patient) with tx-naïve PDAC were digitized. Tiling was automated to generate a total of 1.6 x 105 image 524 um2 patches tiles and tumour-containing image patches extracted. Five-fold cross validation approach was used to assess the performance of our classifier in predicting the A and B morphologic subtypes of our entire cohort.

Results: Using unsupervised hierarchical clustering and dimensionality reduction, histological features, defined by 512 deep learning feature vectors (DLFV) generated by convoluted neural network (CNN) developed in our department2, were used to subgroup PDAC that mirrored our morphological subtypes. When both stromal and epithelial components were included, 68% were classified as Group A and 78% were classified as group B accurately. However, when stromal elements, to only include epithelial elements, it was able to classify 80% of Group A and 85% of Group B patients accurately, with an area under the receiver operator characteristic (ROC) curve (AUC) of 0.83.

1. N Kalimuthu S et al 2019
2. Faust et al 2019

Conclusion: We have demonstrated a proof of concept that deep learning, when applied to PDAC can objectively classify the morphological subtypes previously described on H&E slides. This could provide rapid survival data and act as a surrogate to tailor targeted therapy.

OFP-05-009

Reliability of EUS-guided fine-needle biopsy specimens to assess ATRX/DAXX and PDX1/ARX by immunohistochemistry in pancreatic neuroendocrine tumours: a proof of concept study

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Background & objectives: Somatic inactivating mutations in ATRX/DAXX genes and altered expression of transcription factors ARX and PDX1 are associated with poor outcomes in PanNETs. We sought to assess ATRX/DAXX and PDX1/ARX expression by immunohistochemistry in EUS-FNB and paired surgical specimens of PanNETs.

Methods: EUS-FNB and corresponding surgical specimens of twenty-six patients with PanNETs were retrieved at the University Hospital of Verona (2017-2018). ATRX, DAXX, ARX and PDX1 protein expression and Ki-67 proliferation index were detected by immunohistochemistry on biopsy and paired surgical specimens. Tumour grade was classified according to the WHO 2019.

Results: All EUS-FNB cases provided adequate material for immunohistochemistry examination. ATRX, DAXX, PDX1, and ARX concordance between biopsy and surgical specimens was 92% ($K = 0.705$; $p < 0.001$), 96% ($K = 0.866$; $p < 0.001$), 100% ($K = 1.000$; $p < 0.001$), and 82% ($K = 0.400$; $p = 0.050$), respectively. Likewise, tumour grade concordance was 92% ($K = 0.752$; $p < 0.001$), since 2 cases were under-staged on biopsy.

Conclusion: The assessment of ATRX/DAXX and PDX1/ARX protein expression by immunohistochemistry can be accurately performed on EUS-FNB. The concordance between EUS-FNB and surgical specimens is substantial for ATRX and tumour grade, and almost perfect for DAXX and PDX1.

OFP-05-010

Through the needle biopsy (TTNB) specimens. A new procedure in the setting of pre-operative histological diagnosis of the cystic lesions in the pancreas and retroperitoneum

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Background & objectives: Endoscopic ultrasound guided through the needle biopsy (TTNB) with microforceps procedure ecruits specimens from the cyst wall for the histological evaluation.
Hereby, we describe our experience at the University of Verona Hospital trust with TTNB of pancreatic and retroperitoneal cysts.
Methods: Electronic files were searched for TTNBs performed between January 2016 and January 2020. The clinical, serological, imaging and cyto-histological data were collected for the selected cases.
Results: 99 TTNB procedures were performed and the histological yield was 99% (98/99 cases). The histological diagnosis was performed in 83/99 (84.7%) cases. The aspecific histological characteristics of the biopsy prevented the conclusive diagnosis in 15 cases (15.3%).
In 30 cases, the patients underwent surgery and TTNB diagnosis was confirmed in 27/30 cases (90%). Grading of epithelial dysplasia between biopsy and surgical specimen was discordant in 2/30 cases (6.7%).
Conclusion: TTNB is a reliable diagnostic tool for the pre-operative diagnosis of cystic lesions in the pancreas and retroperitoneum and it allows to avoid unnecessary surgery. However, due to the histological heterogeneity of the cyst wall, pathologists must be aware that TTNB microforceps could miss epithelial dysplasia or sample non diagnostic areas, favouring misdiagnosis. A multidisciplinary approach helps reduce misdiagnosis.

OFP-06 Digestive Diseases Pathology - GI

OFP-06-001

Serrated polyposis syndrome: morphologic and molecular heterogeneity of dysplasia-carcinoma progression

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Background & objectives: Serrated polyposis syndrome (SPS) predisposes to colorectal cancer (CRC) and is characterized by multiple serrated polyps (SP) according to WHO criteria proposed in 2010 and revised in 2018. We aim to characterize the pathologic and molecular progression of SPS neoplasia.
Methods: 32 SPS patients were identified using WHO criteria in 2345 consecutive patients with at least 1 SP. Clinicopathologic assessment of advanced neoplasia (AN) in SPS patients was performed, including CRC and/or SP with dysplasia of any grade (SSPD), intestinal (I) or serrated (S) type. 10 AN were subjected to next generation sequencing (NGS) using a 50 gene hot spot panel.
Results: SPS incidence was 1.4% (18:14 female:male, mean age 67 years). 9 SPS patients had AN, including 7 CRC, 8 SSPD-I and 3 SSPD-S. BRAF V600E mutation was detected in 9 cases (5 SSPD-I, 1 SSPD-S, and 3 CRC) and KRAS Q61H in 1 CRC. Additional mutations were found in CRC cases in the following genes: p53 (2 cases), FBXW7 (2), and SMAD4, PTEN, RB1, and RET (1 each).
Conclusion: In our cohort, 13% SPS patients had AN, including CRC and SSPD. All AN had activating mutations involving the RAF-RAS - MAPK signalling pathway, with majority with BRAF mutations and one case with a KRAS mutation. Our study confirms that while BRAF V600E is a common early mutation in SPS neoplasia, analysis of CRC in SPS patients demonstrates a diverse mutational profile. Our results support the conclusion that progression of carcinogenesis in SPS involves heterogenous molecular pathways.

OFP-06-002

Computer-assisted hot-spot selection for tumour budding assessment in colorectal cancer

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Background & objectives: Tumour budding (TB) is an established prognosticator for colorectal cancer. Detection of the hot-spot to score TB is based on visual inspection, hindering reproducibility of this important factor. We present an algorithm that can potentially assist pathologists in this task.
Methods: We used a previously developed algorithm for the detection of tumour buds in pan-cytokeratin stained whole slide images, calculating the number of buds for each location using a circle with 0.785mm2 surface area. From these numbers, density heatmaps were produced. The algorithm was applied to 270 slides from Bern University hospital, in which hot-spots and tumour buds were visually identified.
Results: Heat maps were created and we located the hand-selected hotspot and noted the associated TB number. The differences and similarities between computer identified and manually selected hot-spots were visually assessed as well as via histograms. Preliminary results show that the heatmaps are helpful, as locations with the highest TB density (the top 15%) also include the hand-selected hotspots. The full results will be presented during the conference.
Conclusion: The presented algorithm can assist the pathologist in selecting the hot-spot with the highest tumour bud count with more ease at low magnification and can help to reduce the high inter-observer variability among pathologists in scoring tumour budding.
This project has received funding from the Dutch Cancer Society, project number 10602/2016-2.

OFP-06-003

Prognostic value of tumour deposits for disease-free survival in patients with stage III colon cancer: a post hoc analysis of the idea France phase III trial (prodige-gercor)

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Background & objectives: Tumour deposits (TD) seem to impact the prognosis of patients with colon cancer (CC). In the
TNM7 CC staging, their presence is only considered in the absence of lymph node metastases
(LNM). In the era of personalized duration of histopathological criteria-based adjuvant therapy, this could potential lead to a loss of the prognosis prediction accuracy.
Methods: A post hoc analysis of all pathological reports from stage III CC patients included in the IDEA
France phase III study (NCT00958737) investigating the duration of adjuvant FOLFOX or CAPOX therapy (3 vs 6 months) was performed. The primary objective was to determine the prognostic impact of TD on disease-free survival (DFS). The effect of the addition of TD to LNM count on pN restaging was also evaluated. A multivariable analysis was performed to establish the association between TD and DFS.
Results: Of 1942 patients, 184 (9.5%) had TD. The pN1a/b and pN1c populations showed similar DFS. TD-positive patients had worse prognosis compared with TD-negative patients, with the 3-year DFS rate of

65.6% (95% CI 58.0 to 72.1) and 74.7% (95% CI 72.6 to 76.7; P=.0079). On multivariable analysis, TD were associated with the higher risk of recurrence or death (HR=1.36; P=.0201). Other pejorative factors included pT4 and/or pN2 (HR=2.21; P<.001), the 3-month adjuvant treatment (HR=1.29, P=.0029), obstruction (HR=1.28; P=.0233), and male gender (HR=1.24; P=.0151). pN2-restaged patients (n=35, 2.3%) had similar DFS than those initially classified as pN2

Conclusion: TD is an independent prognostic factor for DFS in stage III CC patients. The addition of TD to LNM may help to better define the duration of adjuvant therapy.

OFP-06-004

Deep neural networks and supervised machine learning for the screening and classification of dysplasia in inflammatory bowel disease

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Background & objectives: Algorithms based on deep neural networks (DNN) have been shown to outperform humans in specialized tasks in pathology. Here we assess the performance of a pathologist-trained algorithm in the search for and grading of dysplasia in inflammatory bowel disease (IBD).

Methods: HE-slides from a cohort of 391 IBD patients were used. A training set of 50 slides was annotated by a pathologist, subsequently used to train a DNN using the Aiforia® cloud platform. The resulting algorithm was applied to a validation set of 250 slides and results were compared to pathologist performance. Discrepant results were reviewed by an expert panel.

Results: The algorithm was consistently able to find areas suspicious for dysplasia. The algorithm could also differentiate between the classes 'indefinite for dysplasia', 'LG dysplasia', 'HG dysplasia' and 'Carcinoma budding', with the diagnosis for carcinoma being aided by the immediate vicinity of a class for 'reactive stroma'. Review of the discrepant diagnoses revealed the inconsistencies of human performance on the one hand and limitations of the trained algorithm on other hand. In a speed test with 100 random IBD slides, the algorithm was able to outperform a pathologist using a conventional microscope, finishing within 1/3 of the time needed by the pathologist.

Conclusion: Our algorithm outperforms pathologists in both speed and consistency, but is limited in scope, and requires a pathologist to make the definitive diagnosis for carcinoma. Nevertheless, with the number of samples continuing to grow, it provides a useful tool for the screening and classification of dysplasia in IBD. With such tools, training pathologists to become 'diagnostic machines' is questionable as a vision for the future of pathology.

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OFP-06-005

Markers of epithelial-mesenchymal transition in early colorectal carcinoma compared to adenoma and adenoma with pseudoinvasion

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Background & objectives: Distinguishing malignant adenoma/early colorectal carcinoma (CRC) from adenoma with pseudoinvasion can be challenging. Our aim was to investigate the expression of markers of epithelial-mesenchymal transition (EMT) in malignant adenoma/early CRC compared to adenoma and adenoma with pseudoinvasion.

Methods: Thirty-two cases of formalin-fixed paraffin-embedded tissue were included (10 adenomas, 10 malignant adenomas/early carcinomas and 12 adenomas with pseudoinvasion). We analysed the expression of miR-200 family and their target genes CDKN1B, ONECUT2, PTPN13, RND3, SOX2, TGFB2 and ZEB2 using qPCR.

Results: We found statistically significant down-regulation of miR-141, miR-429 and PTPN13 and up-regulation of CDKN1B in malignant adenomas/early carcinomas compared to adenomas with pseudoinvasion. We also observed down-regulation of miR-200c and miR-429, and up-regulation of CDKN1B and RND3 in malignant adenomas/early carcinomas compared to adenomas, and down-regulation of TGFB2 and up-regulation of RND3 and CDKN1B in adenomas with pseudoinvasion compared to adenoma.

Conclusion: Down-regulation of the miR-200 family and PTPN13, and up-regulation of CDKN1B in malignant adenomas/early carcinomas compared to adenomas and adenomas with pseudoinvasion is consistent with the postulated role of EMT in the progression of adenoma to early CRC.

OFP-06-006

Inhibition of LPS-mediated TLR4 activation abrogates gastric adenocarcinoma-associated peritoneal metastasis

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Background & objectives: Curative-intent-surgery remains the most beneficial treatment-option for localized gastric-adenocarcinoma(GC),the majority of patients experience cancer recurrence, with peritoneum as the most common site. Clinically, there is an observed link between post-operative infection and metastasis of primary(GC)to the peritoneum, however the mechanisms behind are poorly-understood.

Methods: We aimed to show the effects and mechanisms of LPS-induced TLR4-signaling on peritoneal metastasis of gastric adenocarcinoma, as a proposed mechanism for post-surgical infection induced cancer recurrence. in vitro, ex vivo and in vivo activation of TLR4 by LPS or heat inactivated E. coli using both murine- and human-derived gastric cancer cell lines to human peritoneal mesothelial cells(HPMCs) were done.

Results: Up to a six-fold significant increase was seen in the LPS and E. coli conditions compared to control ($P<0.05$). Use of neutralizing TLR4 antibody and TLR4 signal cascade blockades, notably TAK1 and MEK1/2 blockades, significantly abrogated adhesion ($P<0.05$). A similar effect was seen using a novel ex vivo model of peritoneal metastasis employing peritoneal surface harvested from both C57BL/6 wild type and TLR4–/– knockout mice. In vivo LPS infection potentiates the development of gross metastases in NSG mice after intraperitoneal injection with MKN-45 human gastric cancer cells. Furthermore, murine peritoneal carcinomatosis index (PCI) scores are highest in mice that received LPS injection with MKN-45 cells LPS stimulation.

Conclusion: These studies have shown the relevance of TLR4 and the TLR4 signalling cascade in potentiating metastatic adhesion and spread to the peritoneum upon activation.

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OFP-06-007

Integrated clinicopathologic and immunohistochemical analysis of α-foetoprotein-producing gastric carcinoma: an exploration of histogenesis, molecular features and prognostic markers

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Background & objectives: Typical a-fetoprotein–producing gastric cancer (AFPGC), which is characterized by histological resemblance to hepatocellular carcinoma and a poor prognosis. The aim of this study is to elucidate the clinicopathological, histogenesis and molecular characteristics as well as prognostic markers of AFPGC.

Methods: Fifty-five patients with AFPGC were screened out by morphological features for hepatoid adenocarcinoma (HAC), gastric cancer with enteroblastic differentiation (GCED) and common tubular/papillary adenocarcinoma (COM). The immunohistochemical diagnostic markers

including AFP, GPC3 and SALL4, mucin phenotypes, molecular features and Immunoscore were assessed. Finally, the relationships between each factor and clinicopathologic features as well as the overall survival time were analysed.

Results: In 55 patients, mixtures of 3 types (COM+GCED+HAC) were most commonly observed. The transition between COM and GCED, GCED and HAC, and sometimes transition between COM and HAC were could frequently see. Hyaline globule and pink amorphous substance were often present. Of the three diagnostic indictors, SALL4 was the most sensitive marker (90.9%). AFPGC showed relatively frequent expressions of HER2 (38.2%). Besides, 38 patients (69.1%) showed pure intestinal phenotype and the remained 17 patients were mixed gastric/intestinal phenotype. Cases with prominent hyaline globules had a significantly poor prognosis. SALL4, HER2 and Immunoscore had an independent influence on OS. In addition, HER2low + SALL4low+ Immunoscore high group have the best prognosis.

Conclusion: AFPGC is a genetically heterogenous group. It might be developed from intestinal type gastric adenocarcinoma and progress to GCED, finally HAC. CIN/GS subtypes could be where they belong. SALL4, HER2 and Immunoscore are independent influence on OS of AFPGCs.

OFP-06-008

A pathological risk score based on poorly differentiated clusters, tumour budding and number of harvested loco-regional lymph nodes predicts prognosis in stage II colorectal cancer

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Background & objectives: Use of adjuvant chemotherapy is controversial in patients with stage II colorectal carcinoma (CRC), because of good overall prognosis. This study aims to investigate the prognostic value of several clinical-pathological variables in stage II CRC.

Methods: A cohort of 149 surgically resected stage II CRC patients who did not receive neoadjuvant or adjuvant treatment was selected. Data on cancer specific survival (CSS) was available in all cases. All cases were revised to assess histological grading, tumour budding (TB) grade, poorly differentiated clusters (PDC) count, lymphovascular/perineural invasion and tumour border configuration.

Results: Multivariate logistic regression analysis showed that high TB grade (Bd3), presence of PDC and a number of lymph nodes <12 were significant and independent variables for prediction of cancer related death. A risk score, by assigning 1 point to the presence and 0 points to the absence of each of these variables was formulated. A risk score ≥ 1 was significantly and independently prognostic of shorter CSS.

Conclusion: Examination of an inadequate number of locoregional lymph nodes, high TB grade and presence of PDC were associated with shorter CSS and cancer-related death in patients with stage II CRC. These features may be helpful to select high risk patients who could benefit from adjuvant chemotherapy.

OFP-06-009

Mucinous appendiceal neoplasms: a 10 year review with reclassification and outcomes

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Background & objectives: Appendiceal mucinous neoplasms (AMN) tend to occur in adults in the sixth decade, and usually present with features of appendicitis. In recent classifications two new concepts for AMN were introduced: LAMN (Low-grade AMN) and HAMN (High-grade AMN).

Methods: Retrospective study, in a 10-year period, of 29 cases of AMN. The cases were analysed for gender, age, initial symptoms, TNM classification when applicable, surgical approach, complications, survival rate and recurrence.

Histologic review of all cases was made, to demonstrate how many would now fulfil the criteria for LAMN or HAMN, and how it could have changed treatment and/or prognosis.

Results: 15 were initially diagnosed as mucinous cystadenoma [after review 12 were reclassified as LAMN (80%), 2 as HAMN (13,3%) and 1 as sessile serrated lesion]; 5 were LAMN, 2 HAMN and 5 mucinous adenocarcinomas [no change after review].

Global 2-year survival rate was 95% [LAMN 100%; HAMN 100%] and 5-year survival rate was 66% [LAMN 81%; HAMN 100%]; global recurrence index was 11,1% [LAMN 6,2%; HAMN 0%] and the global rate of disease progression was 14,8% [LAMN 5,8%; HAMN 0%].

Conclusion: In reclassified cases there was no significant change in both prognosis and disease-free survival (despite pT stating), however follow-up is short.

Most LAMN and all HAMN have a 2-year to 5-year follow-up free of disease or signs of recurrence.

Those with adenocarcinoma, as described in the literature, had worse prognosis.

OFP-06-010

p53 and p16 combined immunohistochemistry for the prognostic stratification of adenocarcinomas of cardias and gastroesophageal junction: A multicentric study

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Background & objectives: Adenocarcinoma of the gastroesophageal junction (AdGEJ) is rare and aggressive, and still lacks of biopathological prognostic markers. Aim of the present study was to establish the usefulness of p53 and p16 immunohistochemistry (IHC) in AdGEJ prognosis.

Methods: Eighty-three patients resected for non-treated AdGEJ were enrolled in 5 European centres. Histological variables included: tumour classification according to WHO and Lauren, concomitant intestinal metaplasia, tumour stage, vascular invasion.

IHC was performed for Cytokeratin 7 and 20 and CDX2 for diagnosis and tumour classification, as well as for p53 and p16. p53 mutational status was confirmed by NGS.

Results: p53 was hyperexpressed in 46 (55.4%) cases, and completely null in 5 (6.0%), for a total of 51 p53-mutated cases (p53+), normoexpressed in the remaining cases (p53wt). p16 was hyperexpressed in 42 (50.6%) cases (p16+), applying a cut-off of 7.5% of p16-positive cells, calculated by ROC curve.

Patients were sorted in: p53wt/p16- (N=11), p53+/p16- (N=30), p53wt/p16+ (N=21) and p53+/p16+ cases (N=21). Kaplan-Meier curves of the 4 patients groups showed a significantly different cancer-specific survival (p=0.032): in particular, 90% of patients with p53wt/p16- AdGEJ were alive after 80 months of follow-up, versus 20% of cancer-specific survival recorded among patients with p53+/p16+ AdGEJ. Patients with p53+/p16- and p53wt/p16+ AdGEJ showed intermediate survivals.

Conclusion: IHC for p53 and p16 seems to be an independent prognostic factor in patients with AdGEJ, and it could be proposed in the pathological report.

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OFP-07 Joint Oral Free Paper Session: Dermatopathology / Soft Tissue & Bone Pathology

OFP-07-001

Data mining on transcriptomic data unmasks AXL, TYRO3 and MERTK receptors as new potential prognostic markers for advanced cutaneous melanoma: an ongoing project

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Background & objectives: TAM receptor (TAMr) tyrosine-kinase family plays a significant role in oncogenesis and in immune-modulation, but their role in melanoma is largely unknown. TAMr prognostic relevance and correlation with CD8+ T-cells infiltration (Tils8) was assessed in melanoma patients.
Methods: AXL, TYRO3 and MERTK gene expression profiles regarding 235 primary melanomas along with clinico-pathological and follow-up records were downloaded from TCGA repository. Overall and disease-free survival analyses were performed considering clinico-pathological data, TAMr gene expression and Tils8. Tils8 was estimated by a consensus ranking obtained with TIMER and CIBERSORT tools. P-values<0.05 were considered for statistical significance.
Results: After stepwise selection based on Akaike Information Criterion, low AXL and TYRO3 expressions resulted significantly correlated with worse disease-free survival, while low AXL and high MERTK expressions significantly decrease overall survival in patients with high tumour stage. Significant positive Spearman correlation was observed between AXL and Tils8 score ($p<0.001$).
Conclusion: TAMr are promising prognostic markers for advanced melanoma. To assess our results, we are validating AXL, TYRO3 and MERTK expression by immunohistochemistry in a large cohort of patients with III-IV stage melanoma. Moreover, studies reported the molecule UNC2025 as a specific MerTK inhibitor, suggesting that MerTK receptor could also represent a potential therapeutic target for advanced melanoma.

OFP-07-002

T-cell receptor expression in cutaneous benign and malignant lymphoid infiltrates in comparison with T-cell receptor gene rearrangement and its diagnostic utility in borderline cases

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Background & objectives: Cutaneous T-cell lymphoid infiltrates can represent benign lesion or an infiltration with T-cell lymphoma. Histopathological appearance can overlap and T-cell receptor gene rearrangement evaluation is not always accessible. Expression of different TCR antibodies is studied in cutaneous lymphoid infiltrates.
Methods: Representative cases of reactive and malignant lymphoproliferations were collected. Separate group of lesions with borderline morphology was selected for comparison. Immunohistochemical expression of TCR-beta-F1 (TCR-BF1), TCR-C-beta1 (TCR Jovi.1), TCR gamma/delta (TCRg/d) and TCR delta (TCRd) was performed in all cases. TCR gene rearrangement evaluation was performed in all cases using PCR BIOMED-2 assay.
Results: Benign lymphoid infiltrates were all negative in TCRd and TCRg/d, expression of TCR-BF1 in one. T-cell lymphomas were positive for TCR-BF1 and TCRg/d in 60% and 30% of cases, respectively. TCR gene rearrangement was confirmed in 90% of lymphoma cases. All benign lesions were polyclonal. Borderline lesions showed expression of TCR-BF1 in 6/10 cases and TCR gene rearrangement in 4/10 cases.
Conclusion: Expression of TCR-BF1 and TCR-gene rearrangement was significantly associated with malignant infiltrates. Re-evaluation of the cases and clinical correlation led to the change of the diagnosis and confirmation of T-cell lymphoma in 4/10 of borderline cases. TCR-BF1 positivity in borderline cutaneous lymphoproliferations can raise or support the suspicion of malignancy, nevertheless, confirmation by TCR gene rearrangement and careful clinical correlation is still advisable.
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OFP-07-003

ROCK1 and ROCK2 expression is decreased in late-stage skin melanomas

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Background & objectives: Rho-associated coiled-coil kinases (ROCK) 1 and 2 are controllers of cytoskeleton dynamics and are implicated in several features of carcinogenesis, e.g. adhesion, invasiveness, migration or proliferation. We aimed to determine clinicopathological significance of ROCK1 and 2 expression in skin melanoma.
Methods: ROCK1 and ROCK2 expression was assessed in immunohistochemically stained sections of 129 primary skin melanomas. Obtained results were statistically analysed together with other clinicopathological characteristics.
Results: We found negative correlations between melanocytic expression of either ROCK kinase and Breslow thickness, Clark level, AJCC stage as well as mitotic rate. Moreover, there was a predilection for low ROCK1 and 2 reactivity in ulcerated tumours and nodular melanomas. Decreased ROCK2 immunoexpression in melanoma cells was associated with shorter melanoma-specific and melanoma-free survival in Kaplan-Meier analysis, but did not independently predict prognosis in a multivariable model.
Conclusion: Our results indicate that ROCK signalling may be involved in the pathogenesis of melanoma and that ROCK1 and 2 are downregulated in aggressive and late-stage tumours, which is contrary to most reports concerning other cancers. Therapeutic inhibition of ROCK kinases in skin melanoma may thus be ineffective.
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OFP-07-004

Clinical relevance of tumoral indoleamine 2,3-dioxygenase 1 and PD-L1 co-expression in Merkel cell carcinomas

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Background & objectives: The prognostic role of combined tumoral indoleamine 2,3-dioxygenase 1 (IDO1) and PD-L1 expression in Merkel cell carcinomas (MCCs) has not been studied in a large cohort of patients.
Methods: IDO1 and PD-L1 immunostains were performed on tissue microarrays constructed from paraffin-embedded tissues of 132 MCCs. PD-L1 expression >1% was considered positive. The cytoplasmic IDO1 staining was done using the H-score. We correlated IDO1 and PD-L1 expression with clinicopathologic variables and patient outcomes.

Results: High tumoral IDO1 expression was observed in 48,5% of cases and PD-L1 expression >1% in 48% of cases. There was co-expression of IDO1 and PD-L1 in 25% of cases. By Fisher's exact tests, combined high tumoral IDO1 expression and tumoral PD-L1 expression >1% significantly correlated with favourable survival status (p=0.0002). By univariate analysis, combined high tumoral IDO1 and tumoral PD-L1 >1% expression revealed a trend with improved overall survival (p=0.057).
Conclusion: The co-expression of IDO1 and PD-L1 in MCC suggests a potential therapeutic role of combined IDO1 inhibitor and PD1/PD-L1 inhibitor. Understanding the clinical and pathologic features associated with IDO1/PD-L1 co-expression in MCC may provide insights into effective strategies for therapy.

OFP-07-005
Systems biomarker discovery implicates TEAD3 in cutaneous squamous cell carcinoma perineural invasion
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Background & objectives: Cutaneous squamous cell carcinoma (cSCC) is the second most common primary skin malignancy. Although resection/radiation is generally curative, a significant minority of patients develop recurrence. Perineural invasion (PNI) is a significant risk factor for recurrence, however detection can be limited.
Methods: We apply Weighted Gene Coexpression Network Analysis (WGCNA) to 24 human cSCC transcriptomes (GSE86544) to identify gene clusters associated with PNI. Clusters are ranked by their correlation with PNI, and candidate biomarkers in top clusters are identified based on intracluster centrality, differential expression between tumours with and without PNI, and expression in normal tissues from the Genotype-Tissue Expression (GTEx) project.
Results: We identify 56 gene clusters ranging in size from 31 to 4166 genes. Sixteen clusters show significant correlation with PNI ($p < 0.05$). These clusters are enriched for genes involved in transcriptional regulation, epithelial-mesenchymal transition (EMT), and extracellular matrix (ECM) remodelling ($p < 0.05$). The transcription factor TEAD3 has high network centrality in a gene cluster enriched for transcriptional regulators ($p < 0.05$), is significantly upregulated in cSCC with PNI (fold change = 4.57, $p < 0.05$), and is preferentially expressed in skin compared to nerve, adipose, and salivary gland tissue. TEAD3 expression significantly correlates with expression of the EMT/ECM gene cluster ($p < 0.05$).
Conclusion: Our work suggests TEAD3 contributes to transcriptional regulation of cSCC invasiveness, and TEAD3 expression may be useful in identifying high-risk lesions. Further work must be done to characterize TEAD3 protein expression in cSCC.

OFP-07-006
Secondary syphilis: three-case with different clinico-pathological presentations
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Background & objectives: Syphilis, the old friend, continues in re-emerging with heterogenous presentations which represents a diagnostic dilemma to dermatologist and dermatopathologists. The UK was one of five countries that shows more than double the number of cases over the last 10 years.
Methods: This study aims to highlight the increasing challenge in the diagnosis of secondary syphilis by presenting three cases with different presentations
Results: The first case was a 56-year-old gentleman complaining of fever, chest pain and hearing loss. Followed by the eruption of extensive papular rash over the trunk, palms and soles. Pulmonary scan showed bilateral lung nodules. Histology showed localised granulomatous inflammation with plasma cells and few eosinophils.
The second case was a 43-year-old lady presented with scaly sarcoidal-like nodular lesions on face and chest without mucous membrane involvement. Biopsy showed non-specific perifollicular granulomatous lympho-histiocytic infiltrate with plasma cells.
The third case was a 32-year-old homosexual man developed oral thrush and juicy scaly nodular rash on trunk sparing palms and soles with generalized lymphadenopathy. HIV test was negative and histopathology was non-specific.
Conclusion: Secondary Syphilis can present with non-specific clinical and histological features. Clinical, histological and serological correlation is pivotal for early diagnosis.

OFP-07-007
Indolent cutaneous T-cell lymphoid proliferations of the nose region - a novel diagnostic algorithm and molecular description
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Background & objectives: Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (pc-CD4+TCLPD) and primary cutaneous acral CD8+ T-cell lymphoma (pc-acral-CD8+TCL) are indistinguishable morphologically and could pose a challenge on histopathological and immunohistochemical examination. The study presents a novel diagnostic approach for these rare entities.
Methods: Two patients (p1, p2) present solitary nasal skin lesions. Skin punch biopsies were obtained with histopathological and immunohistochemical evaluation, which were inconclusive. Subsequently fine-needle biopsies (FNB) of the lesions were performed and flow cytometry (FCM) analysis of immunophenotype and T-cell clonality (IO Test Beta Mark) were done. Finally, both lesions underwent next-generation sequencing (NGS) molecular testing (Archer® FusionPlex Lymphoma panel).
Results: Histopathologically, both cases were characterized by a diffuse focal-epidermotropic dermal proliferation of small to medium-sized lymphocytes. Immunohistochemically neoplastic cells were: CD3(+)/CD4(+)/CD8(-)/CD7(-/+)weaker/CD20(-) (p1) and CD4(+/-)/ CD8(+)/CD7(-)/CD30(-)/granzymeB(+)/perforin(-) (p2).
Subsequent FCM showed distinct origin of pathological lymphocytes. Memory CD4(+): CD45RO(+)/CD45RA(-)/CD4(+)/CD27(+)moderate-high/ CD26(+)low/CD7(-)/CD8(-) (p1) and naive CD8(+): CD45RO(-)/CD45RA(+)/CD8(+)/CD27(-)/CD26(+)/CD7(-/+) /CD4(-) (p2). The monoclonal nature of the pathologic T-lymphocyte population was confirmed by demonstrating the lack of clonality of TCR Vbeta on their surface in both cases. The diagnosis of pc-CD4+TCLPD (p1) and pc-acral-CD8+TCL (p2) was made. Next-generation sequencing analysis revealed the EIF4E3[7]-FOXP1[3] fusion in pc-acral-CD8+TCL sample.
Conclusion: FNB/FCM analysis of immunophenotype and clonality are useful in the final diagnosis of cutaneous T-cell lymphoid proliferations. Study presents the first molecular description of pc-CD4+TCLPD and pc-acral-CD8+TCL. We report a novel FOXP1 fusion, which requires confirmation in a larger study.

OFP-07-009

Use of pan-TRK immunohistochemistry for identification of NTRK fusions in mesenchymal neoplasms – real life experience

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Background & objectives: Fusions involving NTRK1-3 are oncogenic drivers occurring in a spectrum of mesenchymal neoplasms. To get further insights into the staining profile with the pan-TRK antibody we performed immunohistochemistry on various soft tissue sarcomas and correlated our results with molecular testing.
Methods: We retrospectively reviewed soft tissue sarcomas diagnosed from 1999 until 2019 at the Institute of Pathology, Medical University of Graz retrieved from the surgical pathology files and consultation cases of one of the authors. Tissue micro arrays from 409 cases were performed and analysed immunohistochemically with pan-Trk rabbit monoclonal antibody (clone EPR17341, Roche/Ventana). Positive cases underwent next generation sequencing (NGS).
Results: Immunohistochemical staining was observed in 18 (4.4%) cases. Five cases showed diffuse nuclear and/or cytoplasmatic staining and each harboured an NTRK-fusion (LMNA-NTRK1, IRF2BP2 - NTRK1, TMB3-NTRK1, ETV6-NTRK3, RBPMS - NTRK3). Thirteen cases (3/31 (9,7%) synovial sarcomas, 2/73 (2,7%) leiomyosarcomas, 2/2 (100%) extraskeletal myxoid chondrosarcomas, 2/116 (0,2%) myxofibrosarcomas, 1/34 (0,3%) atypical lipomatous tumour, 1/33 (0,3%) dedifferentiated liposarcoma) showed weak cytoplasmic/membranous staining and harboured no NTRK Fusion.
Pan-TRK (clone EPR17341, Roche/Ventana) immunohistochemistry is a reliable, highly sensitive but less specific diagnostic marker that can be expressed in non-NTRK-rearranged mesenchymal neoplasms.
Conclusion: Pan-TRK (clone EPR17341, Roche/Ventana) can be used as a surrogate marker for an identification of NTRK fusion, nevertheless, an RNA-based NGS for detection of the specific fusion should be performed to confirm the rearrangement if patients are undergoing targeted therapy.

OFP-07-010

Human sarcoma nude mice xenografts

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Background & objectives: Biological and molecular studies of human sarcomas require fresh tumour tissue. Nude mice xenografts offer a valuable method to maintain tumours, retaining the histological and genetic characteristics. Since 1990 we have produced a tissue bank of 438 xenografted human tumours.
Methods: Tumour tissue is inoculated subcutaneously in the back of the animal, under sterile conditions (1–2 mm3 of tumour tissue). Nude mice are kept in germ-free conditions (complying with all ethical regulations). The tumour is followed until it reaches 1–2 cm in diameter, and then transferred to new animals. Material obtained is kept for histology, cell culture, EM, and frozen.
Results: Positive grafts (Average 40%, Range 27-60%). By histology and frequency: Osteosarcoma and Chondrosarcoma (44/100), Es/PNET (30/80), MFH (18/48), Rhabdo-Leiomyosarcomas (18/41), Synovial sarcomas (17/28), Liposarcomas (12/39), Fibrosarcomas (4/11), GIST (6/22), Vascular sarcomas (5/8) and miscellaneous tumours (22/61). Total 176 positive grafts out of 438 xenografts (40%). Several cell lines in vitro have been established. Frozen tissue and PFETB are available in most cases.
Conclusion: Sarcoma xenografts in nude mice provide a suitable model for the study of tumour morphology, biology and molecular genetics.

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OFP-07-011

Primary and metastatic dedifferentiated malignant melanoma is significantly under-recognized: analysis of 22 cases

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Background & objectives: Dedifferentiated melanoma (primary or metastatic) lacks histological and immunophenotypic melanocytic features; hence cannot be confirmed as melanoma by these conventional tools alone. To date, 38 cases have been reported. We describe 22 cases expanding their phenotypic and genotypic spectrum.
Methods: Cases were identified in our pathology (n=2) and consultation files (n=20). Histological and immunophenotypic findings were reviewed. All cases were negative for melanocytic markers we use routinely (SOX10, S100, pan-melanoma, Melan A, HMB45) except for minimal foci (<5%) of differentiation or immunoreactivity observed in a few cases. Molecular testing was performed (TST15 gene panel; Illumina® Inc., San Diego, CA, USA).
Results: Age range was 31-86 years (median, 62). Fourteen patients were males. Twenty tumours were metastases and two were primary (subungual, anorectal). Initial diagnosis was undifferentiated pleomorphic sarcoma (10), unclassified malignancy (5), other sarcomas (2), metastatic melanoma (2) and reactive (1). In only two cases was dedifferentiated melanoma mentioned. History of melanoma was positive in 13 cases. Sites of metastases were axilla, inguinal, shoulder, gastrointestinal, bone, neck, lung/pleura. Histology was predominantly undifferentiated pleomorphic sarcoma (11). Unusual patterns include osteochondroblastic, tenosynovial giant cell tumour-like and low-grade fibromyxoid sarcoma-like. Melanoma-typical mutations were detected in 17/21 (81%) cases (NRAS=8, BRAF=8 and KIT=1). Of 4 wild type tumours, one showed NF1 mutation by extended testing.
Conclusion: This extended follow-up study highlights the phenotypic plasticity of dedifferentiated malignant melanoma and indicates significant underrecognition of this aggressive disease among general surgical pathologists. UPS and other unclassified high-grade sarcomas occurring at unusual sites such as the axilla, inguinal area and the lateral neck should alert to the possibility of dedifferentiated melanoma, even in the absence of positive clinical history. Genotyping represents a valuable adjunct to confirm diagnosis.

OFP-07-012

Atypical pleomorphic lipomatous tumours: a clinicopathologic analysis of 55 cases

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Background & objectives: Atypical pleomorphic lipomatous tumour is a recently described adipocytic neoplasm. Diagnosis and distinction from pleomorphic liposarcoma can be challenging due to its wide-ranging morphology. We present the clinicopathological features of a large case series to further characterise this emerging entity.
Methods: 55 cases were identified from the consultation files. Clinical and follow up information were obtained from referring institutions. Immunohistochemistry for MDM2, CDK4, CD34, Rb, S100 and desmin was performed in cases with available material.
Results: Patients were 20 women and 35 men; median age was 59 years (range: 20-89). Tumours arose in upper limb (33%), trunk (31%), lower limb (29%), head and neck (7%) with size range 2.3-11.5 cm (median: 5.9). Tumours were variably composed of atypical and pleomorphic cells,

adipocytes, and lipoblasts, often showing infiltrative growth, myxoid or collagenous stroma, and multinucleated floret cells. Mitoses were infrequent. Tumours expressed CD34 (65%), S100 (64%), and desmin (30%). 86% (38/44) showed Rb loss. Rare cases expressed MDM2 (2%) or CDK4 (13%); FISH for MDM2 amplification was negative (0/11). Follow up in 15 patients so far (median: 33 months) revealed no local recurrences or metastases.
Conclusion: Despite its frequently infiltrative growth, nuclear pleomorphism, and hypercellularity which can mimic sarcoma, atypical pleomorphic lipomatous tumour behaves in an indolent fashion. Immunohistochemistry for CD34, S100, desmin and Rb (demonstrating loss) can support the diagnosis.

OFP-08 Joint Oral Free Paper Session: Endocrine Pathology / Head and Neck Pathology

OFP-08-001
Diagnostic findings and clinical behaviour of non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) in a large Iberian retrospective series

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Background & objectives: Providing diagnostic and clinical data about the challenging entity Non-invasive Follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) is of interest.
Objective: To record the diagnostic, management and follow-up data of NIFTP in a large multi-centre Iberian retrospective series.
Methods: Surgical cases of Papillary Thyroid Carcinoma (PTC) and tumours of Uncertain Malignant Potential (UMP) over 5 mm (years 2005 to 2015) were recorded from pathological reports of 16 institutions, and slides reviewed if needed. Diagnostic and clinical data from cases finally considered as NIFTP were recorded.
Results: From 3134 PTC and 14 UMP nodules, 175 (5.55%) cases were considered to meet the original criteria of NIFTP (141F/34M, age range 18-78, average 49). Ultrasound report was available in 142, 56 of them with suspicious findings (39.4%). Pre-surgical fine needle (FN) cytology or biopsy was performed in 150 cases (85.7%), being its result the first reason for surgery in 102 (58.3%). Undetermined Bethesda categories were the most prevalent (52.66).Total thyroidectomy was performed initially in 112 (64%), and deferred in 45 (25.7%), receiving radio-iodine therapy 132 (75.4%), with an average dose of 96.7 mCi. Follow-up disclosed 10 patients with biochemical +/- structural persistence, but no recurrences.
Conclusion: In our series of NIFTP prevailed non-suspicious ultrasonography (60.6%), undetermined Bethesda categories (52.6%) total thyroidectomy procedure (89.7%), and radioiodine therapy (75.4%). No recurrence was identified.

OFP-08-002
Incidence and clinicopathological features of non-invasive follicular neoplasm with papillary-like nuclear features (NIFTP) in a large Iberian retrospective series

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Background & objectives: Incidence of Non-invasive Follicular Neoplasm with papillary-like nuclear features (NIFTP) varies between countries. Furthermore, histological diagnostic criteria have changed recently.
Objective: To determine the incidence and histological features of NIFTP in Iberian countries applying the original and new diagnostic criteria.
Methods: Sixteen institutions from Spain and Portugal joined the study. Surgical cases of Papillary Thyroid Carcinoma (PTC) and tumours of Uncertain Malignant Potential (UMP) over 5 mm (years 2005 to 2015) were recorded from pathological reports, and slides reviewed if needed. Incidence and histopathological findings of cases considered finally as NIFTP following the original and the new diagnostic criteria were recorded.
Results: From 3134 PTC and 14 UMP lesions, 175 (5.55%) cases were considered to meet the original criteria of NIFTP. Overall incidence among PTC was 4.67% (range: 0-12.12% depending of the institution), and 50% among tumours of UMP. Thirty-five cases measured between 5 and 10 mm. Average size was 21.8 mm (range 5-100 mm). In 95 cases the whole lesion was studied, and in 97 the whole nodular margin. If new diagnostic criteria were applied, 39 cases (22.28%) must be removed (38 with papillae, 1 BRAF V600E mutated), with a final incidence of NIFTP of 4.32%. There were no significant differences regarding the nuclear features when applying the different diagnostic criteria.
Conclusion: In our Iberian retrospective series, incidence of NIFTP was low (5.55%), with moderate variability among institutions. The lesion was studied completely in more than half of the cases. Applying the new diagnostic criteria, 22.28% of them had to be excluded from the series, with a final incidence of 4.32%. Although that, no differences in nuclear features were observed.

OFP-08-003
Chromophobe renal cell carcinoma-like thyroid carcinoma – expanding spectrum of thyroid cancer with a distinct entity

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Background & objectives: Chromophobe renal cell carcinoma (cRCC)-like thyroid carcinoma was first described in 2017 as a distinctive clinicopathological entity of thyroid carcinoma. However, there have been no additional cases reported so far.
Methods: We retrieved four cases of primary thyroid tumours with cRCC-like appearance from the files of Ito Hospital, Tokyo, a large-volume thyroid centre.
Results: There were 3 males and 1 female (mean age 46 years) without history of genetic disorders. Two cases were initially diagnosed as invasive HTT, one as PTC, solid variant, and one as PDTC. All tumours were invasive and showed trabecular/alveolar pattern. IHC revealed TTF1+, PAX8+, Tg-, CD117-, and low Ki67 index. Histochemistry showed weak cytoplasmic colloidal iron staining. One patient developed locoregional recurrences and probable lung metastasis (late after surgery).
Conclusion: cRCC-like thyroid carcinoma revealed to be distinctive in histology and could be misdiagnosed as Hurthle cell carcinoma, HTT, and metastatic carcinoma in thyroid tumour pathology. Our cases were not in association with any finding of tuberous sclerosis complex. Further characterization by immunohistochemistry and genetic analysis in this rare tumour is required to define its position in the histopathological classification.

OFP-08-004
Distinct morphological and immunophenotypical features of cribriform-morular tumour of thyroid: towards a separate entity

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Background & objectives: Cribriform-morular variant of papillary thyroid carcinoma (CMv-PTC) is an extremely rare variant of PTC with

cribriform architecture and squamoid morules. In this study, we investigated morphology, immunoprofile and genetics of these tumours to further our understanding of this biologic entity.
Methods: We reviewed twenty-three CMv-PTC cases in this study. Representative blocks from these cases were subjected to immunohistochemical studies using antibodies against B-Catenin, BRAF, HBME1, TTF-1, p63, CD5 and CK5. Molecular studies to identify APC variants were performed in certain cases.
Results: All patients with CMv-PTC were female and ranged in age from 18 to 59 (n=23).
All cases showed strong nuclear and cytoplasmic staining of B-Catenin (23/23+).
Molecular studies revealed pathogenic APC variants (12/12+).
HBME1 (15/15-) and BRAF (4/4-) showed negative staining.
TTF-1 showed positive staining in cribriform areas and negative staining in morules (n=2).
CD5 (8/8+) and CK5 (5/5+) staining highlighted the morules, and the cribriform areas were negative. Morules were negative for p63 (2/2-).
Conclusion: Nuclear B-Catenin positivity and APC mutations are characteristic features of CMv-PTC.
Negative HBME-1 and BRAF staining, TTF-1 staining pattern suggest a different pathogenesis than classical PTC.
The morules are positive for CK5 and CD5, and negative for p63. These findings suggest a different biological pathway for morule formation and can be used to aid diagnosis of this tumour.
Further immunohistochemical and genetic studies would increase our understanding of this tumour leading to reclassification as a separate entity as cribriform-morular tumour of thyroid.

OFP-08-005
Invasion matters also in encapsulated conventional papillary thyroid carcinoma
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Background & objectives: We aimed to investigate the histopathological features and BRAF status of understudied encapsulated (conventional) papillary thyroid carcinoma (EC-PTC).
Methods: Among 823 PTC cases diagnosed at our institution between 2015-2018, 121 tumours in 105 patients(12,75%) were reclassified as EC-PTC. Size, localization, cystic changes, background thyroiditis, presence/amount of psammoma bodies(PB), cervical lymph node metastasis(LNM), capsular/lymphovascular invasion(CI/LVI), immunohistochemical BRAF-VE1 expression were evaluated. 92 non-encapsulated conventional PTC cases were chosen as control group. Pearson chi-square and Fischer's exact tests were performed for analyses.
Results: EC-PTC cases were predominantly women(73,3%), 47% were microcarcinomas, 97,5% had cystic changes, and LNM was positive in 55,2%. 20.7% of the tumours showed total encapsulation, whereas, CI was detected in 79,3%(partial:57,9%, extensive:21,5%). LVI was rare(5,8%). Thyroiditis(48.8%) and PB (52.9%) were detected in nearly half of cases. Relationship between LNM and CI was statistically significant (p=0.008) and was more prominent in cases with extensive CI(p=0.011). PB positive cases showed a higher rate of LNM(p=0.009). BRAF was positive in 81,1% of EC-PTC and 85,7% of nonencapsulated PTC. In nonencapsulated cases, patients older than 40 showed more BRAF positivity (p=0.016), whereas in EC-PTC, there was no difference in terms of age and BRAF(p=0.15).
Conclusion: As in encapsulated follicular-variant PTC, invasion status is important in EC-PTC in predicting clinical behaviour, such as LNM.
Cystic changes are very common, deserves mentioning in morphological characteristics of EC-PTC.
BRAFV600E mutation determined by immunohistochemistry isn't different than non-encapsulated PTC.

OFP-08-006
The enigmatic mixed medullary-follicular carcinoma of the thyroid: a comparison of 2 cases and a review of the literature
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Background & objectives: Mixed medullary-follicular thyroid carcinomas(MMFTC) comprise a partially understood group, including collision tumours, synchronous/metachronous follicular and medullary carcinomas and "true" MMFTC.There are many theories of possible origins of MMFTC, none indisputably proved.
We relate two cases followed at our institute, while reviewing the literature.
Methods: A 65year-old female and 60year-old male patients were followed at our institute since 2011 and 2019 for thyroid nodules. Analytically, only calcitonin levels were increased (1949pg/mL and 428,5pg/mL, respectively). Total thyroidectomy and cervical lymph node dissection were performed in both cases.
Results: Histology showed predominantly medullary carcinomas(calcitonin+, neuroendocrine+).In the first case, there was a slightly juxtaposed population of morphologically-papillary features(thyroglobulin+); the second case had also a confirmed papillary component, deeply intermingled. Both lymph node metastasis had a mixture of papillary and medullary-like features. The final report diagnosis was collision tumour(pT1bN1b) and "true" MMFTC(pT2(m)N1b) respectively, both patients being alive and without evidence of the disease.
Conclusion: While some authors defend a common origin for the components of MMFTC using a "stem cell" or a "divergent differentiation" theory, others suggested a "field effect", a "collision effect" or a "hostage" theory based on a dual origin. It has been recently questioned whether C-cells are endodermal-derived rather than neural-crest-derived, suggesting the ultimobranchial stem-cell as a possible common cell lineage for MMFTC.
We report two cases, one of which was considered a collision tumour and other one a "true" MMFTC. The etiopathogenesis remains uncertain.

OFP-08-007
Prognostic significance of oral dysplasia features – analysis of a preliminary cohort
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Background & objectives: Grading of oral epithelial dysplasia (OED) remains the gold standard for malignant change prediction. However, little is known about the prognostic significance of individual histological features. This study aims to determine the prognostic significance of OED features in a preliminary cohort.
Methods: OED cases with varying grades (n=51) were identified (2005-2013) from the local tissue archive after ethical approval. New H&E sections were obtained, and five-year clinical follow-up data collected. Blind histological examination was undertaken to review the original diagnosis and identify the most prominent features from the WHO Classification for each case. The prognostic significance of specific histological features was measured.
Results: 17/51 (33%) lesions showed malignant progression; 10 (59%) of these were originally graded as moderate dysplasia and 7 (41%) as severe dysplasia. The most significant features predictive of malignant transformation were: loss of epithelial cohesion/acantholysis (RR 3.9, CI 1.4-10.4, p=0.0057), hyperchromatism (RR 4.0, CI 1.6-9.6, p=0.0018), irregular and/or verruciform surface keratination (RR 0.44, CI 0.2-0.9, p=0.0282), dyskeratosis/individual cell keratinisation (RR 4.4, CI 1.1-17.3, p=0.0316) and presence of suprabasal mitotic figures (RR 7.8, CI 1.9-30.6, p=0.0033).

Conclusion: Our preliminary findings reveal feature-specific risk of malignant progression in OED for the first time. These findings need to be explored on bigger cohorts to establish their true significance and provide useful prognostic information to aid management.

OFP-08-008

Head and neck squamous cell carcinoma of never-smokers and never-drinkers show frequent PD-L1 expression and association of tumour infiltrating lymphocytes with favourable survival

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Background & objectives: PD-L1 expression is a predictive biomarker for immunotherapy in head and neck squamous cell carcinoma (HNSCC). Our objective was to assess if PD-L1/2 expression and tumour infiltrating lymphocytes (TILs) in HNSCC of non-smokers and non-drinkers (NSND) have prognostic value.
Methods: Clinical data and tumours of 114 NSND HNSCC patients were collected retrospectively. Immunohistochemistry was performed for PD-L1, PD-L2, and lymphocyte markers PD-1, CD45, and CD8 on Tissue MicroArrays. Difference in 5-year survival of patients with and without expression of these biomarkers was determined using Kaplan-Meier and log rank analysis.
Results: The patients were on average 71.6 years old and predominantly women (77%) with a tumour of the oral cavity (78%). PD-L1 (tumour proportion score ≥1% and ≥50%) and PD-L2 (≥1%) expression was detected in 70%, 18%, and 10% of the tumours, respectively. A high number of CD45 and CD8-positive TILs (≥150/mm2) was a predictor for a significantly better 5-year disease free (HRCD45=.50, p=.010; HRCD8=.51, p=.013) and overall survival (HRCD45=.40, p=.001; HRCD8=.50, p=.014). This significant difference persisted, regardless of which cut-off value for TILs/mm2 was applied.
Conclusion: PD-L1 expression is present in a large percentage of HNSCC in NSND. This might have implications for the application of immunotherapy in this patient group. A high number of CD45 and CD8-positive TILs is predictive for a better disease free and overall 5-year survival.

OFP-08-009

A subgroup of oropharyngeal squamous cell carcinoma with unfavourable prognosis shows oxidative stress signatures and a mesenchymal-like phenotype

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Background & objectives: A subgroup of oropharyngeal squamous cell carcinoma (OPSCC) with integrated HPV 16 shows oxidative stress signatures and an unfavourable prognosis. The objective was to further investigate these oxidative stress signatures and their possible relation to a mesenchymal like (EMT) phenotype.
Methods: 51 OPSCCs including 28 HPV-positive cases (FFPE and frozen tissue) were available. Expression of EMT, retinoic acid and oxidative stress pathway components including NRF2, AKR1C1/3, ALDH1A2, Frizzled 10, b-Catenin, E-Cadherin, Vimentin, miR-9 and miR-16-2 were assessed by immunohistochemistry, RT-qPCR and/or in-situ hybridization. The impact of viral oncogenes on EMT-relevant components was addressed in primary human keratinocytes overexpressing HPV16-E6 and/or -E7.
Results: Expression analysis revealed that subgroups of OPSCC predominantly related to HPV-infection exhibit an increased oxidative stress response (NRF2, AKR1C1/3) as well as activating EMT pathway signatures (Frizzled 10, b-Catenin, E-Cadherin, Vimentin, miR-9 and miR-16-2), frequent metastasis, and downregulated retinoic acid synthesis (ALDH1A2). Moreover, in vitro experiments showed that HPV16-E6 expression results in induction of miR-9, miR-16-2 and b-Catenin expression.
Conclusion: Our data show, that OPSCC presenting with upregulation of oxidative stress response signatures have a higher tendency to undergo EMT. Frizzled 10 expression known to be regulated by retinoic acid was highly correlated to ALDH1A2 expression and inversely correlated to EMT and oxidative stress. Our data implicate that subgroups of tumours might benefit from adjuvant treatment with retinoids, which should be further studied.

OFP-08-010

Secretory carcinoma of the parotid gland a new entity: a case series

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Background & objectives: Secretory carcinoma, first described in 2010 by Skálová et al, is a low-grade salivary gland carcinoma characterized by sharing morphological features with mammary secretory carcinoma. It harbours a recurrent translocation t(12;15)(p13;q25) which causes ETV6-NTRK3 fusion.
Methods: It activates RAS-PI3K-AKT pathway, promoting cell proliferation and survival. Moreover, it's also known that first generation TRK inhibitor can be used as a treatment.
We report three patients diagnosed with secretory carcinoma at the Vall d´Hebron University Hospital Pathology department from 2017 to 2020.
Results: In our series, two patients were female with a median age of 43 years (range 32-62).The tumour was located in parotid gland. All cases were treated with parotidectomy. Histologically the tumour showed solid, tubular and microcystic structures with abundant eosinophilic bubbly secretion. Neoplastic cells had eosinophilic vacuolated cytoplasm, occasionally with condensed material (mucin) and uniform, round nuclei with small nucleoli. Immunohistochemical stains were performed, the tumour cells were positive for CK7, mammaglobin and S100. In all the cases pan-NTRK immunohistochemistry was positive. The presence of ETV6-NTRK3 translocation was confirmed by Fluorescent in-situ hybridization (FISH) break-apart for ETV6. In only one patient distant metastases and local recurrence have been reported.
Conclusion: Secretory carcinoma is a recently described tumour with distinctive morphology, immunohistochemistry and genetic profile. It is the only salivary gland tumour related to ETV6-NTRK3 gene fusion. Nowadays, its presence is useful for diagnosis and specific treatment.

OFP-08-011

Revisiting a case series of glomangiopericytomas: reassessing STAT6 value in differential diagnosis

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Background & objectives: Glomangiopericytoma is a rare sinonasal neoplasm. Despite contrary evidence in literature, we came across a STAT6-equivocal and beta-catenin+ glomangiopericytoma. This prompted a thorough review of all published reports and re-evaluation of histology and immunohistochemistry in all cases from our Institute.
Methods: Four cases were retrieved from our pathology archive. All the histological material and corresponding clinical files were re-examined.

New STAT6, beta-catenin and CD34 immunostains were performed on freshly cut formalin-fixed paraffin-embedded sections. Older stains were also reviewed. Furthermore, one case required additional search for mutations of the *CTNNB1* gene by Sanger sequencing. Literature review was conducted using PubMed.
Results: Two patients were male. The age range was 40-79 years. All cases displayed typical cytoarchitectural and immunohistochemical features of glomangiopericytomas, except for one showing moderate STAT6 nuclear positivity, both in tumoral and peritumoral tissues. Being described as consistently negative in glomangiopericytomas and positive in solitary fibrous tumour (SFT), our STAT6 yielded differential diagnosis issues. Nevertheless, our literature review disclosed rare STAT6-equivocal glomangiopericytomas. Furthermore, Ghaffar et al. described non-specific STAT6 positivity in the nasal mucosa of patients with chronic rhinitis, which our patient had. This phenomenon might lead to misdiagnosis. A mutation in exon 3 of the *CTNNB1* gene was found in this last case, confirming the diagnosis of glomangiopericytoma.
Conclusion: Glomangiopericytomas represent a diagnostic challenge. Differential diagnosis especially includes SFT, and STAT6 immunostaining plays a key role in discriminating the two entities. Cautious interpretation of STAT6 in patients with chronic rhinitis is advised.

OFP-08-012
IDH2 R172 mutated sinonasal carcinoma: pathological and molecular assessment of 32 cases
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Background & objectives: IDH2 R172 mutations are present in >80% sinonasal undifferentiated (SNUC) and large-cell neuroendocrine carcinomas (LCNEC), while their presence in olfactory neuroblastoma (ONB) remains controversial. Here, we explored pathological features of a sizable cohort of IDH2 mutated sinonasal carcinomas (SNC).
Methods: Thirty-two primary IDH2 R172 mutated SNC were studied by light microscopy and by immunohistochemistry (IHC) including S-100, cytokeratins, synaptophysin and chromogranin. IDH2 mutation status was assessed by targeted exome sequencing or by IDH2 IHC (clone 11C8B1) in most cases. DNA methylation profiles were analysed by semisupervised hierarchical clustering and IDH2 wild-type sinonasal tumours were used for comparison.
Results: IDH2 variants included R172S (61%), R172T (14%), R172K (14%), R172G (7%) and R172M (4%). All cases were high-grade with a median 21 mitoses/10 high-power-fields, frequent necrosis (85%), apoptosis (100%) and prominent nucleoli (97%). Most (94%) were SNUC or LCNEC. Two cases showed glandular/acinar differentiation. While no tumour had definitive features of ONB, two ethmoid carcinomas focally labelled for S-100 (sustentacular pattern) suggesting the olfactory bulb origin. Surface and/or minor salivary glands involvement was detected in 39% cases supporting the Schneiderian mucosal origin. All cases, irrespective of subtle differences as to their putative cell/tissue of origin, formed one distinct methylation cluster and clearly separated from IDH2 wild-type tumours.
Conclusion: IDH2 R172 mutated SNC are phenotypically, genetically and epigenetically remarkably similar suggesting that their biology and clinical behaviour might be primarily defined by their unique molecular signature. A confirmation of these findings in further studies may impact future (re)classification of the current WHO categories: SNUC, LCNEC and ONB.
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OFP-09 Joint Oral Free Paper Session: Pulmonary Pathology / Thymic and Mediastinal Pathology

OFP-09-001
Clinical significance of ephrin receptors (Ephs) type-a and -b expression in thymic epithelial tumours
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Background & objectives: Ephrin receptors (EPHs) are receptor tyrosine kinases (RTKs) implicated in tissue development and homeostasis and are aberrantly expressed in tumours. Here, immunohistochemical EPHs (type-A and -B) expression in thymic epithelial tumours (TETs) was assessed and correlated with clinicopathological parameters.
Methods: TMAs from 98 FFPE TETs excised in 2009-2019 (55 females, 43 males; aged 29-85; histologic types: 12 A, 22 AB, 49 B, 2 micronodular, 13 carcinomas) were stained for EPH-A1, -A2, -A4 -A6, -B1, -B2, -B4, -B6. The relationship between neoplastic and lymphoid cell immunoreactivity score (IRS), histopathological parameters (Pearson's test) and survival of 35 patients (Mantel-Cox model) was explored.
Results: Epithelial-rich subtypes showed higher EPH-A6 cytoplasmic IRS (B2, B3, carcinoma) ($P<0.001$) and stronger EPH-A4 IRS (B3, carcinoma) ($P=0.011$). The immature T-cells, especially in subtypes AB and B1, had a higher EPH-B6 IRS than carcinoma-associated mature lymphocytes ($P<.001$); carcinomas had a higher lymphocytic EPH-B1 IRS ($P=0.026$). High lymphocytic EPH-A6 IRS was overall rare, but more common in B1 thymomas ($P=0.015$). Higher lymphocytic and lower epithelial EPH-B6 IRS correlated with low Masaoka stages (stages ≤II) ($P=0.043$, $P=0.010$ respectively). All cases showed variable epithelial and lymphocytic EPH-A2 expression, but clinicopathological associations with EPH-A2 were not reached.
Conclusion: Our study confirms the expression of EPHs type-A and -B in TETs, which is associated with established prognostic parameters, i.e. tumour subtype and Masaoka stage, although correlation with patient survival was not reached. Such findings suggest involvement of these RTKs in thymic neoplasia, as well as their potential utility as treatment targets.

OFP-09-002
Primary mediastinal germ cell tumours with high prevalence of somatic malignant transformation: an experience from a single tertiary care cancer centre
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Background & objectives: Primary mediastinal germ tumours(PMGCT) constitutes 3-4 % of all germ cell tumours(GCT).They account for approx. 16% of mediastinal tumours in adults and 19-25% in children as per western literature. There is hardly any large series on PMGCT from India.
Methods: We have retrospective analysed clinic-pathological features of 101 PMGCT cases, diagnosed over a period 10years(2010-2019) from a single tertiary care oncology centre. Metastatic tumours to mediastinum were excluded.
Results: The study group(n=101) comprised predominantly of males(n=95),with mean age=25yrs(range 3months to 57 year).Tumours were predominantly located in anterior mediastinum(n=99).Non-seminomatous germ cell tumours (NSGCT)(composed embryonal, yolk sac tumour(YST) &teratoma) was the most common histological subtype(n=26), followed by seminoma(n=25),mature teratoma(n=21),YST(n=13),immature

teratoma(n=6) , mixed tumours (n=4) and GCT;NOS(n=6).Secondary somatic malignancy was seen in 11 cases and six out of them either died or had progressive disease.
Conclusion: Interestingly, in this series, PMGCT was seen predominantly in young adult males and somatic malignancies was noted in as high as in 10% of cases. Patient with somatic malignancy have aggressive clinical course, hence, extensive sampling and careful histopathological evaluation is recommended for definitive characterization.

OFP-09-003
Clinicopathological correlations of PD-L1 expression in thymic epithelial tumours using two immunohistochemical assays
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Background & objectives: Thymic epithelial tumours (TETs) range from locally aggressive to frankly malignant. In our study, PD-L1 expression in TETs was assessed by two immunohistochemical assays and associations with clinicopathological parameters, as well as the concordance of the two assays were evaluated.
Methods: TMAs from 98 FFPE TETs excised in 2009-2019 (55 females, 43 males; 29-85 years old; histologic types: 12 A, 22 AB, 49 B, 2 micronodular, 13 carcinomas) were stained using SP143 and SP263 assays. The relationship between epithelial PD-L1 expression at 1%, 5%, 10%, 25%, 50% cut-offs, histopathological parameters (Pearson's test) and survival of 35 patients (Mantel-Cox model) was explored.
Results: The percentage of PD-L1+ TETs at ≥1%, ≥5%, ≥10%, ≥25% and ≥50% cut-offs was respectively: 45%, 34%, 29%, 19% and 14% for SP143; 54%, 46%, 40%, 36% and 29% for SP263. PD-L1 expression was more frequent in type B thymomas, especially in the epithelial-rich subtypes B2 (67-78%) and B3 (93-100%) [P<0.001 (all assays and cut-offs)]. A suggestive relationship between PD-L1 ≥50% expression and shorter survival [P=,077 (SP143); P=0,068 (SP263)] was noted. Cohen's agreement (SP143 vs SP263) was: substantial for 5% (k=0.662), 10% (k=0.753) and moderate for 1% (k=0.590), 25% (k=0.575) and 50% (k=0.586) cut-offs.
Conclusion: Epithelial PD-L1 expression in TETs is frequent, variable, significantly associated with histological subtype and less strongly with survival, suggesting a role in TET pathobiology. About half [45% (SP143) vs 54% (SP263)] of TETs are PD-L1 positive (≥1% epithelial expression), therefore potentially eligible for anti-PD-L1 treatment. Discrepant scoring (SP143 vs SP263) is noted and varies with cut-off values. Clinical trials of anti-PDL1/PD1 agents should take into account variability in PD-L1 expression.

OFP-09-004
Utility of methylthioadenosine phosphorylase (MTAP) immunohistochemistry in malignant pleural mesothelioma: correlation with CDKN2A genomic status and inter-assay agreement
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Background & objectives: Deletion of CDKN2A/p16 is one of the hallmark genomic events in the pathogenesis of malignant pleural mesothelioma (MPM). Methylthioadenosine phosphorylase (MTAP) has emerged as a potential cost-effective surrogate marker. Inter-assay agreement and correlation with genomic status however are currently uncertain.
Methods: This is a single-institutional validation study of MTAP IHC for routine diagnostics using whole exome sequencing (WES) and single nucleotide polymorphism (SNP) genotyping as gold standard. Twenty-seven histologically confirmed MPM with matched frozen and FFPE tissue were included. Inter-assay agreement was performed for two commercial clones (EPR6893, Abcam & 2G4, Abnova). Inter-observer agreement was performed between two scorers.
Results: CDKN2A deep deletion was detected in 56% (15/27) of cases. Overall concordance between sequencing and MTAP IHC (EPR6893) was 73%. Focal staining was seen in 22.2% (6/27). By treating focal staining as positive, sensitivity, specificity, positive predictive and negative predictive values were 81.8%, 66.7%, 64.3% and 83.3% respectively, similar to previous studies. No significant difference was observed between the two clones (p=0.180). Inter-observer agreement was good (Cohen's kappa = 0.713).
Conclusion: MTAP IHC showed reasonable concordance with CDKN2A genomic status. Based on available evidence, EPR6893 and 2G4 clones could be used interchangeably and inter-observer agreement was good. Given detection of CDKN2A status is currently hampered by inadequate assay sensitivity (p16 IHC), limited access to assay platforms (PCR, NGS) or high cost (CDKN2A FISH), our findings support MTAP IHC to be used as a reliable surrogate marker. Financial and logistic considerations need to be taken into account prior to local implementation.
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OFP-09-005
Atypical mesothelial proliferation (amp) of the pleura: multidisciplinary approach, prognostic stratification and proposal of minimally invasive malignant pleural mesothelioma
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Background & objectives: Atypical mesothelial proliferation (AMP), along with cases limited by sampling, also likely includes those exhibiting morphological features of malignant pleural mesothelioma (MPM) yet showing insufficient invasion. We reviewed these cases with a view to improve early diagnosis of MPM.
Methods: This is a retrospective study including 131 consecutive cases of histologically confirmed AMP diagnosed at our institution (2005-2019), of which 35 (26.5%) had subsequent biopsies showing definitive MPM. Clinicopathological data were retrieved from an institutional mesothelioma database. Prognostic variables predictive of overall survival (OS) were identified using univariate and multivariate Cox regression analyses. Statistical significance was denoted as p<0.05.
Results: AMP had comparable demographic profile to invasive MPM. Multivariate analysis showed lack of subpleural structure sampling (p=0.010) and severe nuclear atypia (p=0.001) were independent predictors of worse OS. Cases fulfilling the criteria of (i) adequate subpleural sampling either without invasion or invasion limited to fibrous pleura, (ii) no severe nuclear atypia, (iii) no necrosis, were associated with significantly improved median OS compared with those without (24.4 vs 12.8 months, p<0.001).
Conclusion: AMP poses challenges to diagnosis and patient management as it encompasses a spectrum of benign and malignant mesothelial lesions. We propose morphology-based criteria to stratify AMP into high and low risk groups. It is likely the former was the result of insufficient sampling whilst the latter represented minimally invasive MPM. This

allows MPM to be diagnosed earlier in its natural history. Further refinement using BAP1/MTAP immunohistochemistry as part of a multidisciplinary approach is currently being investigated.
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OFP-09-006
Congenital pulmonary airway malformations with K-RAS mutations may have malignant potential
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Background & objectives: Potential malignant degeneration is often argued as a reason to resect asymptomatic congenital pulmonary airway malformations (CPAM). In this study, we analysed immunohistochemical expression patterns and molecular findings of adult lung tumour markers in CPAM.
Methods: CPAM tissue samples were morphologically evaluated, classified, and subsequently analysed by immunohistochemistry using a panel of lineage differentiating (TTF1/CDX2/MUC2/MUC5ac/CC10) and tumour (p16/p53/Dicer1) markers. Intensity of immunohistochemical staining was quantitatively assessed in normal lung tissue, CPAM and mucinous proliferations (MP) in each sample. Next generation sequencing of adult tumour markers (KRAS/BRAF/EGFR/ERBB2) was also performed separately for the aforementioned categories.
Results: We analysed 50 CPAM samples (Types 1 and 2; n=25 each). Irrespective of the type of CPAM, mucinous cell clusters were detected in 11 cases all characterized by a lack of CDX2, MUC2 and to a lesser extent TTF1 expression, whereas MUC5ac was strongly expressed. P16, DICER1 and p53 showed no aberrant expression. All 11 samples with mucinous proliferations harboured a K-RAS mutation. The normal, surrounding lung tissue showed no genetic alternations.
Conclusion: Immunohistochemistry using TTF1 and MUC5ac may help to identify small MP in the pathological assessment of CPAM. These proliferations were found in both CPAM type 1 and 2 and harboured a K-RAS mutation in all cases. These findings support the notion that a subset of CPAMs may be considered potentially pre-malignant lesions.
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OFP-09-007
Can pulmonary sarcoidosis with severe fibrosis be considered as a severe form of lung sarcoidosis?
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Background & objectives: 0,3 - 7,8 % of patient population with lung sarcoidosis (SL) has "malignant course" which leads to the rapid development of honeycomb lung. Target: to study morphological and molecular biological particularities of lung sarcoidosis with severe fibrosis.
Methods: A retrospective clinical and morphological analysis of open transthoracic (46) and transbronchial (10) lung biopsies and autopsy (2 cases) from 58 patients with diagnosed lung sarcoidosis. Serial paraffin sections were stained with hematoxylin and eosin, picrofuchsin Van Gieson. Immunohistochemical analysis was performed with the following markers: MMPs, Dsm, Vim, SMA, Apo-Cas, IGF1, TNF-α, TGF-β, Oct-4, CD 117.
Results: SL with severe fibrosis - 15 cases (16%). were characterized by multiple sarcoid granulomas with apoptosis of epithelial cells, lymphohistiocytic infiltration, vasculitis and sclerotic changes, the destruction of the basement membranes in the bronchioloalveolar transition zone (BATZ) with the replacement of alveolocytes by cells with a myofibroblastic immunophenotype (SMA, Dsm, Oct-4 & CD 117 positive). It differed from SL without fibrosis by increased expression of profibrotic molecular markers in the in the epithelium of bronchioles, myofibroblast foci: and granuloma cells ($p<0,05$).
Conclusion: Pulmonary sarcoidosis with severe fibrosis can be considered as a severe form of lung sarcoidosis according to the differences of molecular profibrogenic activity of granuloma cells.

OFP-09-008
Evaluation of pathologic response and immune microenvironment in "Pancoast tumour" series after induction chemo-radiotherapy
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Background & objectives: The analysis of pathologic response (PR) is crucial for the evaluation of the response to chemo-radiotherapy treatments. The histological analysis of PR is coded for other malignancies in which it seems to play a prognostic role.
Methods: We retrospectively analysed eight consecutive samples of Pancoast tumour surgically resected after induction chemo-radiotherapy. The PR was evaluated according to the last IASCL recommendations [Travis WD, 2020]. Microenvironment assessment included immunostaining for several tumour-infiltrating immune cells (TIICs) (CD3, CD4, CD8, CD68) and PD-L1 expression (tumour proportion score). Radio-metabolic responses and radiomic evaluation were also reported and correlated with our data.
Results: Histologically the tumours were six adenocarcinomas, one squamous cells carcinoma and one non-small-cell lung cancer-not otherwise specified (NSCLC, NOS). Two cases showed a complete pathologic response (CPR) and two other a major pathologic response (MPR); the rate of residual tumoral cells (RTCs) was 10% (median value; from 0 to 60%). No oncogene addiction was detected, PD-L1 was < 1% in all cases. All TIICs had a score >2+, except for CD4+ that scored 1+ in 88%. Tumours with a greater metabolic response showed a higher CD68+ TIICs and lower RTCs ($p=0.020$ and $p=0.042$, respectively). No other statistically significant differences were found.
Conclusion: Based on our data, the histological evaluation of the PR does not correlate with the radiological, metabolic and radiomic findings, highlighting the crucial value of morphological analyses. Data from radiomic analyses require larger case series. A precise immune microenvironment assessment with focus on macrophages (CD68+) could represent a marker to include in the evaluation of PR.

OFP-09-009
Revised MET-FISH evaluation algorithm: a simplified method
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Background & objectives: MET is altered in ~5 % of non-small-cell lung cancer (NSCLC) and according to the newest NCCN guideline, evaluation of MET should be performed for every advanced-stage NSCLC. FISH-analysis reliably identifies MET-amplified tumours. With a steadily increasing number of cases, currently applied FISH-criteria can be time-consuming for the evaluating pathologist.
Objectives: to propose a faster and equally reliable MET-FISH evaluation algorithm.
Methods: In the present two-centred study, we re-evaluated the MET-amplification status obtained by FISH of n=497 NSCLC. For each case, after counting the first 20 cells, the possible results (negative/low-/intermediate-/high-level amplification as previously defined by us) were compared to the original results based on 60 cells.

Results: Of all 497 cases, 471 (94%) showed identical results when counting 20 or 60 cells. Only 26 cases (5%) showed discrepancy: n=19 (4%) would have been upgraded in a higher diagnostic category when counting 20 cells only and n=6 (1%) would have been downgraded. Most importantly, all high-level amplified and negative cases remained the same. To prevent scoring-errors, we propose the following evaluation algorithm: After thorough examination of the tumour, 20 continuous nuclei are counted in the area with most MET-signals. If the case is negative or high-level amplified, it can be signed out. If it fulfils the criteria for low- or intermediate-level amplification, another 40 cells in two different areas must be counted to reach a total of 60 cells.
Conclusion: We propose a modified FISH-evaluation algorithm for MET-amplification in NSCLC that provides a much faster, yet equally reliable method.

OFP-09-010

Overexpression of p14/ARF in PD-L1 positive malignant epithelioid pleural mesotheliomas with high nuclear grade

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Background & objectives: CDKN2A gene plays a central role in the pathogenesis of malignant pleural mesothelioma (MPM). It encodes for two tumour suppressor proteins, p16/INK4A and p14/ARF. We aimed to determine the correlation between p14, morphology and immune microenvironment, to date still unknown.
Methods: Diagnostic biopsies from 76 chemonaive MPM (54 epithelioid, 18 biphasic, 4 sarcomatoid) were evaluated. Pathological assessment of histotype, necrosis, inflammation, grading, and mitosis was performed. p14/ARF positivity (nuclear and cytoplasmic), PD-L1 (tumour proportion score), Ki-67 (percentage) were evaluated by immunohistochemistry. Inflammatory cells (CD3, CD4, CD8 T lymphocytes; CD20 B-lymphocytes; CD68 macrophages) were quantified as percentage distinguishing intratumoral and peritumoral areas.
Results: P14/ARF was evaluable in 68 patients that showed a sufficient number of tumour cells. A strong nuclear and cytoplasmic positivity was detected in 14 patients (21%) (11 epithelioid and 3 biphasic MPMs). P14/ARF positive epithelioid MPMs showed higher nuclear grade (G3) (p=0.002), higher peritumoral CD4 positive T-lymphocyte percentage (p=0.04) and PD-L1>1% (p=0.04). No other statistically significant differences with morphological findings were found.
Conclusion: p14ARF positive epithelioid MPMs seem to mark a more aggressive histological phenotype, being related to a higher nuclear grade and PD-L1 expression. Larger case series are mandatory to validate our preliminary results thus carrying out more complete statistical tests also with clinical data.

OFP-09-011

Revised usual interstitial pneumonia/idiopathic pulmonary fibrosis diagnoses after the 2018 International Guideline: a 17-year bicentric experience

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Background & objectives: Improved knowledge has highlighted the importance of additional histological and clinico/radiological features for the diagnosis of non-Idiopathic Pulmonary Fibrosis (IPF)/Usual Interstitial Pneumonia (UIP) patients. We present findings of bicentric revised UIP/IPF cases after multidisciplinary discussions(MDDs) according to the 2018 ATS/ERS/JRS/ALAT Guideline.
Methods: Histological and radiological review were performed, categorizing cases as "UIP", "Probable UIP", "Indeterminate for UIP", "Alternative diagnosis" following the guideline. Experienced pathologists reviewed all cases considering also additional morphological features suggestive of connective tissue diseases (CTD):germinal centres,>4 lymphoid follicles/cm2, lymphocyte/plasma-cell ratio≥1, lymphocytic pleuritis, vessel remodelling and of chronic hypersensitivity pneumonitis (CHP): bridging fibrosis, peribronchial metaplasia, centrolobular fibroblastic foci, granulomas/giant-cells. Cinical data were also reviewed.
Results: All 2002-2018 cases with diagnosis of IPF, complete clinical information and available HRCT images (101 patients: 81 explanted lungs and 20 VATS) were independently evaluated by pathologists, radiologists and clinicians; they were then re-categorized after MDDs. In 44% of patients the final diagnosis was IPF, in the remaining 56% it was not a "high-confidence" IPF diagnosis: 16% IPF likely, 10% indeterminate for IPF, 8% IPF likely/non-IPF and 22% non-IPF. After MDDs, 62% of cases were finally categorized as IPF, 13% as CHP, 7% as CTD, 12% as other diseases and 6% remained unclassifiable. Pathological diagnosis of "UIP" showed the best performance in term of sensitivity and specificity than radiological assessment (67%-92% vs 40%-97%).
Conclusion: In conclusion, the rate of IPF diagnoses appears to have been overestimated in the last decade. The current knowledge and good practice of MDDs have significantly improved the diagnostic accuracy. In MDDs, experienced pathologists play a key role to establish a final diagnosis.

OFP-09-012

Association of genetic variants of glutathione S-transferase with P53 phenotype and DNA damage in non-small cell lung carcinoma

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Background & objectives: Glutathione S-transferases (GSTs), including GSTM1, GSTT1 and GSTP1 are phase II metabolic enzymes which regulate cell signalling and cell death. They may enhance occurrence of mutations in critical tumour suppressors, such as p53 increasing risk of Non-Small Cell Lung cancer(NSCLC).
Methods: A case series of histologically diagnosed NSCLC (n=74) were tested for GSTM1 (Fuc./Del.),GSTTI(Fuc./Del.) and GSTP1 (Ile 105 Val) variants using polymerase chain reaction(PCR) followed by restriction digestion. P53 phenotype was categorized as mutant type with >50% 2-3+ intensity in IHC. DNA damage (n=48) in lymphocytes was assessed by comet assay. Statistical analyses were performed with SPSS version 16 (Chicago, USA).
Results: Age was 54.4±11.4; male:female ratio was 2.36; Study sample included 91.8% adenocarcinoma, and 8.1% squamous cell carcinoma. Mutant type P53 was seen in 62.2 % NSCLC and was significantly associated with GSTM1 del genotype RR1.97(p=0.002) and GSTP1 Val/Val genotype RR1.98(p=0.03). GSTT1 genotype showed insignificant RR1.03(p=1.0), Lymphocyte DNA damage was significantly associated with GSTM1 (Fuc/Del) (Mean±SD 5.50±1.62/8.74 ±3.46;p=0.001) and GSTT1(Fuc/Del) genotype (Mean±SD 5.60±2.09/ 8.76±3.20; p=0.001); and with GSTP1 Val/Val genotype (Mean±SD 7.24±2.81;p 0.001).
Conclusion: GSTM1 and GSTP1 genes could play a role in carcinogenesis in NSCLC, possibly through increased frequency of mutations in p53 independently or through known mechanisms of decreased detoxification of carcinogens including tobacco smoke. Mutant type GSTs genotype are associated with increased post chemotherapy DNA damage evidenced in circulating lymphocytes possibly affecting susceptibility of tumour to chemotherapy. Association between mutant p53 phenotype and DNA damage was not seen.

OFP-10 Joint Oral Free Paper Session: IT in Pathology / Autopsy Pathology / Pathology in Favour of Developing Countries / Cardiovascular Pathology / History of Pathology / Electron Microscopy / Other Topics

OFP-10-001
Deep learning artificial intelligence-based image analysis algorithm for Ki-67

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Background & objectives: Analysing of immunohistochemical stains is often time consuming, non-reproducible, and prone to subjectivity. The aim of this study was to determine, how a deep learning artificial intelligence (AI)-based image analysis algorithm performs in analysing Ki-67 labelled pulmonary carcinoid tumour samples.
Methods: Study material consisted of 127 pulmonary carcinoid tumours labelled with Ki-67. AI was trained to recognize diaminobenzidine stained Ki-67 positive cells as well as all cells negative for Ki-67. The results retrieved from AI's Ki-67 algorithm were compared with a conventional area-based image analysis software as well as with the analysis of the pathologist that served as the ground truth.
Results: Altogether 11 658 tumour cells positive or negative for Ki-67 were annotated to train the algorithm. After training, the specificity of the algorithm was 96.8% and sensitivity 96.1%. F1-score was 96.4%. The correlation between the AI model and manual analysis performed by the pathologist was 0.94 (P=0.0001). The correlation between the AI model and the conventional image analysis software was 0.66.
Conclusion: This study showed that AI-based image analysis algorithm yields similar results compared with a human observer. It was superior compared with a conventional image analysis software. Thus, AI-based Ki-67 algorithm can assist pathologists to perform Ki-67 analysis in PC tumours.
Funding by: Finnish Cancer Foundation and Helsinki University Hospital Research Fund

OFP-10-002
Development of semi-automatic interactive algorithm for annotating histological images of colon epithelial neoplasms

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Background & objectives: Complete manual labelling is extremely time-consuming process which limits possibility of developing deep learning algorithms for histological images analysis (e.g. the problem of segmentation of mucous glands). Development of semi-automatic interactive annotation tools helps a lot to solve this problem.
Methods: The proposed algorithm for semi-automatic image segmentation works with scribble annotations and is based on a graph model with 2-stage label propagation. The weights of graph edges are predicted with a CNN, that was trained on a fully labelled dataset.
Results: The developed algorithm was trained and tested on the Warwick-QU dataset as well as PATH-DT-MSU dataset (https://imaging.cs.msu.ru/en/research/histology/path-dt-msu) containing 80 full-size annotated images of colon epithelial neoplasms. The proposed algorithm works in real time and allows to add new scribbles during the annotation which makes the labelling process interactive. Despite the high accuracy of the proposed algorithm we also offer a "classical" set of manual annotating tools to postprocess the results of the algorithm thus allowing annotator to finalize the annotation down to the smallest details. The developed algorithm allows to perform interactive labelling with scribbles and reduce the annotation time of one image from 150 minutes to 25-30 minutes.
Conclusion: Using this semi-automatic interactive tool will significantly increase the number of fully annotated images of colon epithelial neoplasms in PATH-DT-MSU which is necessary for the development of real diagnostic algorithms. The work was supported by RFBR grant 19-57-80014 (BRICS2019-394).

OFP-10-004
Giant cell interstitial pneumonia: value of scanning electron microscopy coupled with energy dispersive X-ray spectroscopy analysis

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Background & objectives: Hard metal lung disease (HMLD) is an occupational disease caused by exposure to hard metal particles histologically characterized by giant cell interstitial pneumonia (GIP). We present a case series of HMLD studied by histology and scanning electron microscopy with microanalysis.
Methods: Surgical pathology files from 2006 to 2019 were searched for lung biopsies and explanted lungs with morphological diagnosis of GIP. A detailed clinical history was collected in all cases. Sections from formalin-fixed paraffin-embedded (FFPE) of two transbronchial biopsies, one cytoblock of bronchoalveolar lavage and from native lung tissue were analysed at Scanning Electron Microscopy and Energy Dispersive X-ray spectroscopy (SEM/EDX).
Results: All patients had clinical history of occupational exposure (metal workers, miner, railway maintenance worker), none reported a clear-cut hard metal exposure (tungsten carbide or cobalt). At histology all lung samples showed features of GIP with multinucleated giant cells of both alveolar macrophage and type II pneumocytes. SEM/EDX analysis was successfully performed also in small transbronchial biopsies and cytoblock. Only one patient (with both biopsy and cytology) had detectable tungsten level. Other metals and inorganic chemical compound were detected in the remaining cases.
Conclusion: SEM coupled with microanalysis, the gold standard tool for the detection of environmental dusts, may be performed also in FFPE tissue of small samples or cytology. SEM/EDX is ongoing on additional FFPE fragments of explanted lung and the final data will be presented at the next ECP-IAP congress.

OFP-10-005
Evolution of pathology repositories – from kunstkammer to digital pathology

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Background & objectives: Description how collections of anatomy/pathology specimens changed in time. Serving at the beginning multiple purposes like art or medicine, slowly became didactic aid. Nowadays we face the computer revolution on massive scale and pathology also entered the digital world.
Methods: We analyse early anatomical drawings and models accompanied by digital collections of microscopic slides of contemporary and ancient tissue samples. Through evolution of recreating nature, we move to collections of specimens in new dimension. We present the consecutive steps to contemporary microscopy supported by digital equipment with efficient and accurate representation of specimen collections from everyday work to ancient research.

Results: We present the evolution of pathology representations. From collections of objects showing gross pathology, through the world of art to science, with specimens as didactic help. Presented in special cabinets, then dedicated rooms and museums. Those collections started with basic figurative sculptures presenting anatomy and pathology, through drawings to spatial models. At the beginning made of wood, bone up to wax resembling human tissues. It was necessary when preserving real tissue was impossible. The invention of fixatives let show real-life pathology. Development of microscopes let observe the cellular pathology and stained microscopic slides could also be stored. Development of collections with consecutive evolution to digital pathology and scanned image databases.
Conclusion: Analysing the timeline we observe that the quality and amount of information carried by the collection's changes accordingly to the of development of science, including all aspects of presentation. From organized rooms and buildings, we move into digital realm not limited by any physical boundaries. We go through macroscale to microscopy, augmented by 3D representation, even on the cellular level, but also to virtual images of anatomopathological collections.

OFP-10-006
Encephalitis lethargica from the autopsy reports of the University of Turin: a brief history full of doubts
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Background & objectives: Since the greatest virulence of Encephalitis lethargica was during the Spanish flu pandemic, an archive search was carried out on the old autopsy reports to investigate the relationship between Encephalitis lethargica and Spanish flu in Turin.
Methods: The cases were selected based on the diagnosis of "Encephalitis lethargica" which was clearly indicated on all the selected reports. The time period considered was that of the spread of Encephalitis lethargica, between the years1915 and 1926 according to the spread of the pandemic.
Results: The first case of Encephalitis lethargica in Turin dates back to 20th January 1920. The autopsy was performed on a 30-years-old male who died at St. John Hospital. No special autopsy findings were reported except a red colour of the meninges. There were a total of 14 cases all in the year 1920. None of them were affirmed by the pathologists of Turin. Indeed, many question marks were written near the diagnosis.
Conclusion: The autopsy reports show the presence of the Encephalitis lethargica in Turin at the end of the pandemic of Spanish flu. A big doubt seems to emerge from these reports due to the scepticism of the pathologists.

OFP-10-007
Comparison of antemortem clinical diagnosis and post-mortem findings in intensive care unit patients
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Background & objectives: The autopsy is an important tool to advance medical knowledge and an excellent assurance indicator of patient management.
The objective is to analyse the discrepancies between premortem clinical and post-mortem pathology findings in adult patients deceased in Intensive Care Unit(ICU).
Methods: We retrieved the clinical and post-mortem findings of all patients who died in the ICU of Erasme University Hospital, Belgium from January 1st 2016 to December 31st 2018 and underwent autopsy. Afterwards the comparisons between clinical and histological findings were classified in five classes according to the classification proposed by *Goldman et al*.
Results: The 2016' series included 141 complete autopsies. Post-mortem examinations revealed unexpected findings in 63 cases (47%), of whom 20 (14.2%) were classified as major discrepancies. The first two major misdiagnosis were malignancy/metastasis (9 [6.4%]) and pulmonary embolism (4 [2.84]). There is no statistical difference between major-minor discrepancies and the ICU stay and age respectively. Compared to the study conducted by *C. Maris et al.* in 2007, a discrete decrease of the frequency of major discrepancies was observed (14% vs 19%) and the absence of statistical difference in discrepancies with regard to length of stay in the ICU was observed (p=0.21 vs p=0.008).
Conclusion: Although the incidence of major discrepancies identified is low and in discrete decrease compared to our previous study, autopsy remains a valuable tool to asses the causes leading to death, to assess the accuracy of clinical diagnosis and for training.

OFP-10-008
Cardiac amyloidosis in the elderly is not related to Alzheimer's disease or cerebral amyloid angiopathy
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Background & objectives: Cerebral amyloid angiopathy (CAA), Alzheimer's disease (AD) and cardiac amyloidosis due to transthyretin are all age-related diseases characterized by amyloid deposition. In this study, the relationship between cardiac amyloidosis and AD/CAA was investigated in autopsies of elderly patients.
Methods: Autopsies with cardiac amyloidosis in patients 80 years old or older were matched with control patients without cardiac amyloidosis based on age and gender. Patients with AL amyloidosis were excluded. The association between cardiac amyloidosis and CAA or severe AD (Braak stage V or VI) was assessed by Fisher test. P values less than 0.05 were considered significant.
Results: Sixty-five patients with cardiac amyloidosis met the study criteria and were matched with 65 control patients without cardiac amyloidosis. CAA was present in 17 (26%) of the cardiac amyloidosis cases and in 13 (20%) of the controls (p=0.53). Severe AD was present in 11 (17%) of the cardiac amyloidosis cases and in 14 (22%) of the controls (p=0.66). The amyloid stained positively for transthyretin by immunohistochemistry or immunofluorescence.
Conclusion: Some recent studies have suggested a relationship between AD and cardiac amyloidosis in the elderly, potentially resulting from the release of amyloidogenic peptides from the brain into the bloodstream in AD. However, in this series of patients, there is no significant association between cardiac amyloidosis in the elderly and severe AD or CAA. The cardiac amyloid in these elderly patients is derived from transthyretin.

OFP-10-009
Implementation of a cardiac proforma to autopsy practice
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Background & objectives: There is considerable variation in the way in which pathologists approach heart dissection. To improve the quality of reporting, a proforma was introduced. A subsequent audit was conducted to see if there was improvement in the recording of heart measurements.
Methods: Training was given on how to use the cardiac proforma, specifically on how to undertake the measurements required. Following this, the proforma was introduced. We subsequently extracted specific data items from our departmental post-mortem reports before and after the introduction of the cardiac proforma.

Results: Undertaking heart examination in a systematic way with reproducible results helps to inform clinico-pathological correlation and the need for genetic testing. Since introducing the proforma, septal wall thickness measurement increased by 30%, left ventricular wall thickness by 12% and right ventricle wall thickness by 10%. The ventricular diameters measurements increased by 8% and 10% more cases commented upon the pattern of ventricular hypertrophy. Measurement of aortic valve circumference/leaflet number rose by 53%.
Conclusion: Following the introduction of the proforma, there was an improvement in the number of measurements recorded when examining the heart during autopsy. User satisfaction has also increased. We recommend the use of cardiac proforma in the autopsy setting.

OFP-10-010
Valid diagnostics from autopsy samples: proteomical analysis of the post-mortem interval-dependent human tissue degradation
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Background & objectives: Comprehensive analyses of changes in the composition of proteins using high resolution mass spectrometry-based proteomics might provide insight into post-mortem decomposition processes. Here we characterize the dynamics of protein degradation in human autopsy samples of the liver, kidney and lung.
Methods: Snap-frozen tissue samples were processed for liquid chromatography-tandem mass spectrometry with label-free quantification. Representation pattern of the proteins in the mass-composition were identified by comparative analysis of co-expression networks of the targeted tissues. Stable and unstable proteins were coupled with the Gene Ontology (GO) database and analysed according to molecular functions.
Results: Patients were included with predefined exact post-mortem time intervals (6-12-18-24-48-96 hours; 78 tissue specimens of 26 patients). Dynamic changes in representation of proteins in the mass-composition were different in the investigated organs. The kidney tissue cytoskeletal proteins remained stable by the increasing time intervals whereas proteins of the mitochondrial respiratory chain complex became underrepresented. In the liver, proteins of the lipid metabolism became underrepresented while pigment storage-related proteins accumulated by the time. Contrary to the liver and kidney, proportion of the lung cytoskeletal proteins decreased while proteins involved in activation of neutrophil granulocytes and lipid metabolism increased by the time in the mass-composition.
Conclusion: Protein degradation is one of the major processes in tissue decomposition after death. Understanding the biology behind the post-mortem interval-dependent changes of the mass-composition offers breath-taking opportunities for diagnostic and therapeutic improvements and paves the way for proteomic quality analyses of snap-frozen and formalin fixed-paraffin embedded tissue specimens.
This study was supported by the Start-up Grant of Semmelweis University (11722).

OFP-10-011
Review of water-related deaths in Oxfordshire over the last 22 years
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Background & objectives: The UK National Water Safety Forum reported 585 water-related deaths in 2018. Most water-related deaths are presumed to be accidental drownings. Autopsy reports on water-related deaths in Oxfordshire over 22 years was reviewed to identify factors contributing to these deaths.
Methods: Water-related deaths (n=194) in Oxfordshire (1997-2019) were identified by search of the electronic adult post-mortem database and the Coroner's autopsy reports were reviewed.
Results: The mean age of individuals dying in water was 57 years (range 15-96 years). 70% of the deaths occurred in men. The month of August witnessed the most deaths. Water-related deaths were more likely to occur in the summer for individuals under 30 years-old and in the winter for those above 60. 71% were deaths due to drowning of which 32% were directly contributed to by medical conditions. Toxicology results were available for 107 autopsies; 28% of deaths due to drowning were associated with alcohol and/or drug intoxication. 22% of individuals had a history of psychiatric illness; 10% of deaths were attributed to suicide and occurred mostly in the spring.
Conclusion: A majority of water-related deaths occurred in men and the most common cause of death was drowning. Alcohol/drug intoxication and pre-existing medical conditions frequently contributed to drowning.

OFP-10-012
Implementing digital pathology in a large-scale laboratory in Brazil: one year of experience
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Background & objectives: The implementation of digital pathology in Brazil is an opportunity to provide diagnostics to a larger number of people. It has the potential to overcome some of the urgent demands of serving a population of 210 million and 3,500 pathologists.
Methods: DCP was implemented at the main laboratory that processes 50% of the cases. Five Philips UFS scanners were installed and operate 24/7. Eighteen pathologists sign out using glass slides and 14 pathologists report 100% digitally from distant locations.
Results: 260,000 cases were reported digitally in 2019, which represents >65% of the case volume of the main laboratory. The cases have been signed out by pathologists in 8 different cities from 6 different states.
Conclusion: The implementation of digital pathology in large scale is technically challenging and costly. The adaptation of the laboratory, pathologists and technical staff is a complex process. DP implementation allowed the reference lab to greater a network of specialized pathologists.

OFP-10-013
How does it feel to be a pathologist? Results of a nation-wide survey on job satisfaction of pathologists in Turkey and comparison with Minnesota satisfaction questionnaire
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Background & objectives: Job satisfaction has a direct impact on workplace performance and there is limited research regarding pathologists' job satisfaction.
Methods: We conducted a 59-item web-based survey questioning respondents' institutional background, history of training (HT), workplace (technical and physical) conditions (WPC), professional well-being (PWB) and job satisfaction level. Likert-type and open/close ended questions were asked and cored. The participants were also asked to complete Minnesota Satisfaction Questionnaire-Short Form (MSQ).
Results: Of the 321 participants, 75% were female and median age was 41±8.82 (range 28-71 y.o.). The respondents' experience as a pathologist ranged between 0.12 years and 44 years (mean 11.4±9.16 years). Academic pathologists had significantly higher scores of MSQ, HT, WPC and PWB. Senior pathologists working at larger laboratories were significantly more satisfied of their WPC, with higher scores of MSQ and HT. Overall, 83% of participants were happy to have chosen pathology, but 45% reported to experience the feeling of burnt out. Most (98.4%)

agreed that pathologists have a critical impact on patient management, but 92% thought that patients barely know pathologists' importance.
Conclusion: Our findings suggest that pathologist's job satisfaction increases with years of experience, physical and technical quality of the pathology laboratory/institution, and professional well-being, i.e., to maintain work/life balance. Pathologists seem to be aware of their important role in patient management although pathology remains to be invisible to the patients.

OFP-10-015
Evaluation of two-photon fluorescence microscopy for sectioning-free virtual H&E imaging of different tissues
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Background & objectives: The pathology workflow relies on preparing paraffin sections with a thickness of one cell layer. We develop a two-photon fluorescence microscope based on optical fibre lasers to create H&E images from bulk tissue samples without sectioning in less than 1h.
Methods: A bulk tissue sample is stained with acridine orange (AO) and sulforhodamine 101 (SR) for <10min. The two-photon fluorescence microscope creates an image of the sample within ~20 min/cm2. The obtained data is transformed to a virtual H&E image in 10min. Two-photon fluorescence can be used to scan a section or a 3D volume of a bulk tissue sample.
Results: We measured a set of different tissues with our self-built two-photon fluorescence microscope to show a proof of concept for a digital and fast sectioning-free H&E imaging technique with similar quality to paraffin sectioning. It allows staining with AO&SR as well as H&E. By improving the microscope scanner and data processing, we expect to increase the speed of our two-photon fluorescence microscope to a few minutes per square centimetre.
Conclusion: Virtual H&E imaging provides an alternative to conventional bright field microscopy of stained paraffin sections in a fraction of time. We will further investigate the usage of fluorescent immunostains and potential combination with other imaging modalities (e.g. Two-photon fluorescence lifetime imaging) for in vivo application.
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OFP-11 Joint Oral Free Paper Session: Cytopathology / Neuropathology / Ophthalmic Pathology

OFP-11-001
Primary sarcomas of the orbit: 15-year experience from the Queen Elizabeth University Hospital, Glasgow
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Background & objectives: In adults, primary orbital sarcomas are rare, limited to individual case reports and small case series in the literature. Here we review our experience with these tumours at the Department of Pathology, Queen Elizabeth University Hospital, Glasgow.
Methods: Seven cases were identified from the institutional database. Three were classified as post-radiation sarcoma (PRS) using the following diagnostic criteria: 1. the sarcoma arose in a previously irradiated field; 2. it was histologically distinct from the original neoplasm; 3. it was not present at the time of radiotherapy; and 4. there was a latency period of at least 2 years.
Results: A variety of histological types were encountered, including malignant peripheral nerve sheath tumour (MPNST) (2); atypical lipomatous tumour/well-differentiated liposarcoma (ALT/WDLS) (2); malignant solitary fibrous tumour (SFT) (1); rhabdomyosarcoma (1); osteosarcoma (1); and low-grade sarcoma of uncertain histogenesis (1). PRS accounted for 43% of cases, with an average age at diagnosis of 40 years and a median latency period of 15 years (range 12-45).
Conclusion: This review represents one of the largest series to date, with seven cases identified over a 15-year period between January 2005 and January 2020. Primary orbital sarcomas are rare and difficult to treat. Whereas in children embryonal rhabdomyosarcoma predominates, in adults they comprise a variety of histological types. Irradiation is a significant risk factor and patients who receive radical radiotherapy require long-term follow-up.

OFP-11-002
The genetic background of conjunctival melanoma and correlation with recurrences and metastasis
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Background & objectives: Conjunctival melanoma have limited treatment options once a lesion has metastasized. The aim of this study is to elucidate the genetic background of conjunctival melanoma within the spectrum of ocular melanoma, correlated with the development of recurrences and metastasis.
Methods: Twenty-eight conjunctival melanoma from the Rotterdam Ocular Melanoma Study group were collected and DNA was isolated from formalin fixed paraffin embedded tissue using lysis buffer and Chelex. DNA from fresh tumour tissue was isolated using the QIAmp DNA-mini kit. Targeted next-generation sequencing was performed using a panel covering GNAQ, GNA11, EIF1AX, BAP1, BRAF, NRAS, c-KIT, PTEN, SF3B1 and TERT.
Results: Preliminary data show recurrences and metastasis in ten (36%) and nine (32%) conjunctival melanoma cases respectively. BRAF mutations were most common, but also NRAS, c-KIT, PTEN, TERT and SF3B1 mutations were observed. No mutations in GNAQ, GNA11 and EIF1AX were found. There was no significant association with the development of recurrences or metastasis.
Conclusion: Conjunctival melanoma and uveal melanoma are both ocular melanomas. Yet, based on molecular characteristics our data suggest a different pathogenesis in conjunctival melanoma compared to uveal melanoma, with involvement of BRAF, NRAS, c-KIT, PTEN, SF3B1 and TERT mutations occurring mainly in conjunctival melanoma and less frequent in uveal melanoma, although there are overlapping gene mutations. In our study no association was found between specific mutations and recurrences or metastasis.
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OFP-11-003
Morphological study of perivascular interstitial cells in glioblastoma
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Background & objectives: Telocytes (Tcs) and pericytes (Pcs) are two types of perivascular interstitial cell known to be widespread in various organs and tissues, including the brain. Objective: morphological study of Tc and Pc role in glioblastoma (GBM) neovascularization.
Methods: Samples from 15 GBM, 10 diffuse astrocytomas and 5 tumour-free frontal lobes (control samples) were studied. We used

immunohistochemistry and double immunohistochemical staining with antibodies to GFAP, Ki-67, CD117, NeuroD1, NG2, CD34, SMA, connexin43; confocal laser scanning microscopy of glioma cultures and frozen and paraffin embedded GBM sections. Electron microscopy of GBM was performed in 4 cases.
Results: The presence of Tcs and Pcs was shown in GBM sections and glioma cultures. The Tc immunophenotype was CD117+/CD34+/connexin43+/NeuroD1+. The Pc immunophenotype was SMA+/NG2+/CD13+. The number of Tcs in GBM specimens was 10 times more than in astrocytoma. We also identified CD13/CD117 and CD34/NG2 co-expressing cells in GBM blood vessels.
Conclusion: Four immunophenotypes were found in GBM vessels, corresponding to endotheliocytes, Pcs, Tcs, and a mixed Pc/Tc immunophenotype. Study of these cell types and their roles in brain tumour oncogenesis will likely enable improved targeted therapies.

OFP-11-004
Copy number alterations of chromosome 1p could be helpful to differentiate spindle cell oncocytoma from pituicytoma
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Background & objectives: Spindle cell oncocytoma (SCO) and pituicytoma are tumours of the posterior pituitary with overlapping morphology. They are both classified as grade I, but SCO has higher local invasiveness and more frequent recurrence rate. This study aimed to analyse which histopathological, immunohistochemical and genetic features may be helpful in the differential diagnosis between these two tumours.
Methods: We reviewed the histological and immunohistochemical features of 7 SCOs and 4 pituicytomas. In addition, we analysed the mutational and copy number variation (CNV) profile of all cases using the Oncomine Tumour Mutational Load assay, which covers 409 cancer-related genes, and Fluorescent In Situ Hybridization (FISH) for chromosomes 1p and 1q.
Results: All SCOs, but not pituicytomas, had lymphocytic infiltrate. 3 SCOs and 1 pituicytoma had sufficient DNA for sequencing and had no mutations in any of 409 genes analysed. At CNV or FISH analysis 7/7 SCOs, but none of 4 pituicytomas, had loss or gains of chromosome 1p.
Conclusion: CNV of chromosome 1p could be potentially used in the differential diagnosis between these SCO and pituicytoma.
This study was supported by Research and Mobility 2017 Funding of the University of Messina to MC and VB.

OFP-11-005
Cytokeratin 18-negative somatotroph pituitary neuroendocrine tumours (adenomas) are not clinically distinct tumour subset and often express internexin-alpha
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Background & objectives: Low molecular weight cytokeratin (LMWK: CAM5.2 or cytokeratin 18) expression is used for subclassification of somatotropinomas. A small subset is LMWK immunonegative and these have not been well studied: we decided to explore clinicopathological features of this subgroup.
Methods: 105 somatotroph tumours with known clinical features (tumour size, levels of IGF1, GH, prolactin, TSH) were analysed using antibodies against cytokeratin 18, prolactin, growth hormone, βTSH, Ki67 and p53. E-cadherin, SSTR2 and SSTR5 expression was recorded in form of H-score. In cytokeratin-negative tumours (<10% of immunoreactive cells), additional antibodies (AE1/3, CK8/18, vimentin, neurofilament and internexin-alpha) were used for further characterisation.
Results: In total, 10 tumours (9,52%) stained negatively for CK18. Compared to the rest of tumours (n=95), we observed no difference with respect to the tumour size, biochemical or other pathological features. The results were similar when compared with subgroups of sparsely granulated (SGT, n=39) and non-sparsely granulated (nSGT, n=46) tumours. CK18-negative tumours showed lower E-cadherin expression compared to nSGT but not SGT (p<0,01), while SSTR2 expression was comparable to nSGT group and significantly higher than in SGT (p<0,01). One tumour stained for cytokeratin 8/18 and AE1/3 and 6 tumours stained for internexin-alpha in more than 10% of cells (mean 74% positive cells, SD±26,1%) in morphological patterns similar to LMWK.
Conclusion: Cytokeratin 18-negative somatotroph tumours are not a distinct clinicopathological subgroup. They may show lower E-cadherin expression and majority of these tumours express internexin-alpha, while vimentin and neurofilament light chain are not expressed at all.
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OFP-11-006
Metastatic tumours of the central nervous system and their prognostic outcomes: a clinicopathological evaluation of 221 cases
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Background & objectives: The involvement of the central nervous system (CNS) with metastatic tumours is seen frequently since it has a strong neurovascular network. We aimed to evaluate the histopathological characteristics and the prognostic outcomes of the patients with metastatic tumours of the CNS.
Methods: All patients who had a diagnosis of a CNS tumour between January 2006 and January 2020 were re-evaluated with the help of clinical, morphological, immunohistochemical, radiological and prognostic findings. The age, gender, primary tumour, histopathological diagnosis, survival time of the patients, the duration between the metastasis and the primary tumour, the location and number of metastases in the brain were recorded and analysed.
Results: Of all 936 patients operated with a CNS tumour, 221(23.6%) patients were diagnosed with metastasis.34.8% was female and 65.2% was male. The mean age was 58.3.The most common primary site was the lungs(55.7%) followed by breast(14%) and colon(7.7%). There were multiple metastases in 37.6%.In 50.2%, first diagnosis was made with the metastasis. In patients with a previously known primary tumour, the median interval between the diagnosis of the primary tumour and CNS metastases was 13.2 months. Mean overall survival time was 6.9 months. There wasn't a statistically significant correlation between the primary origin of the metastases and the survival time. The patients with multiple metastases had a significantly worse prognostic outcome (p=0.002).
Conclusion: Clinical symptoms and radiological features can be diagnostic in CNS tumours, however; as our study shows, brain metastasis can be the first onset of previously unknown primary tumour. Histopathological evaluation is crucial if the differential diagnosis includes a primary tumour or unknown primary site.

OFP-11-007

Implementing diagnostic digital cytology into routine clinical practice

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Background & objectives: Adoption of digital cytology into routine pathology workflow is challenging due to technical limitations. There are only few reports on successful implementation available, mainly limited to remote rapid onsite evaluation. Other case uses of digital cytology are largely unexplored.
Methods: Kameda Medical Center with approximately 22.000 cytopathology cases annually served as a model institution. The routine cytologic workflow included two-step screening by cytotechnologists followed by a sign out by pathologist. Available equipment suitable for digital cytology were digital microscope with live video output (Olympus), robotic microscope (Sakura), Panoptiq microscopic digital imaging platform, and slide scanner with Z-stack mode (Motic).
Results: We introduced sign out of cytologic cases using live digital microscope operated by cytotechnologist, which allowed reviewing slides remotely by pathologist via video streaming (1800 cases in 16 months). We also provided cytologic correlation to support the virtual slide-based sign out of histopathological specimens (2560 cases in 32 months). In addition, positive cytology cases are archived for integration into LIS and for prospective AI studies (1300 cases in 32 months).
Conclusion: Since 2017 several case uses of digital cytology, including remote sign out, providing cytologic correlations, and archiving virtual slides are routinely used at our hospital and proved to be successful for practical and educational purposes. This unique experience may serve as a role model for other institutions.

OFP-11-008

Accuracy of pleural and peritoneal effusion cytopathology using the newly-proposed international system for reporting serous fluid cytopathology

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Background & objectives: Serous effusion cytology is an important tool in the evaluation of effusions. Currently, there is no framework for reporting serous effusion cytology. The recently proposed International System for Reporting Serous Fluid Cytopathology (ISRSFC) aims to standardize reporting and increase reproducibility.
Methods: Pleural and peritoneal effusion samples admitted at our institution between 2012-2016 for cytological analysis were reviewed and reclassified according to the five categories proposed by the ISRSFC. Accuracy of serous effusion cytology was measured against histological analysis, imaging, surgical findings and clinical follow-up.
Results: 1496 pleural effusion samples were recategorized: 12(0.8%) non-diagnostic(ND)|944(63.1%) negative for malignancy(NFM)|9(0.6%) atypia of undetermined significance(AUS)|54(3.6%) suspicious of malignancy(SFM)|477(31.9%) malignant(M). 763 peritoneal effusion samples were reclassified: 5(0.7%) ND|457(59.9%) NFM|12(1.6%) AUS|37(4.8%) SFM|252(33%) M. Risk of malignancy was, for the aforesaid categories, 57.1%;23.9%;50%;76.2%;100% in pleural effusions and 100%;26.3%;62.5%;91.7%;100% in peritoneal effusions. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were, respectively, 61.6%;100%;100%;73.3%;81.3% for pleural effusions, and 61.2%;100%;100%;70%;79.7% for peritoneal effusions.
Conclusion: Serous effusion cytology has a confirmatory role in the diagnosis of malignancy, corroborated by a high positive predictive value and specificity and a modest negative predictive value and sensitivity. The tiered classification system proposed (ISRSFC) will increase standardization, consistency and reproducibility in reporting, with an aim to improve communication and clinical decision-making.

OFP-11-010

Moesin (MSN) as a novel proteome-based diagnostic marker for early detection of muscle-invasive bladder urothelial carcinoma in liquid-based cytology

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Background & objectives: Treatment for Bladder urothelial carcinoma (BUC) highly depends on the invasiveness of cancer cells. A predictive biomarker needs to be identified for invasive BUC. Here, we employed proteomics on urine liquid-based cytology samples to demonstrate a biomarker for invasive BUC.
Methods: Proteomics methods were employed on 16 urine liquid-based cytology (LBC) samples and a set of BUC cell line library to verify candidate biomarker for invasive BUC. Furthermore, in vitro 2-dimensional (2D) and 3-dimensional (3D) invasion study and validation of immunocytochemistry were performed on an independent liquid-based cytology cohort.
Results: The proteomic analysis suggested moesin (MSN) as a potential biomarker to predict the invasiveness of BUC. Moreover, an in vitro 3D invasion study showed that inhibition of MSN significantly decreased invasiveness in BUC cell lines. Further validation of the slide-based moesin immunocytochemical test ultimately confirmed moesin (MSN) as a potential biomarker to predict the invasiveness of BUC ($p = 0.042$). The predictive ability was more powerful in the dichotomous comparison between BUC groups without invasion and the other group with invasion (p-value = 0.023, moesin immunoreactive rates, 38.5% vs. 82.4%, respectively).
Conclusion: In conclusion, we suggest moesin as a potential diagnostic marker for early detection of BUC with invasion in LBC and as a potential therapeutic target.

OFP-11-011

EUS guided FNA in diagnosing pancreatic lesions according to Papanicolaou Society of Cytopathology for pancreaticobiliary system, a single centre experience

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Background & objectives: Early diagnosis of pancreatic cancers is important for therapeutic efficacy, disease management. EUS-FNA cytology is helpful for early diagnosis, significant for cost-effectivity. Our aim is to present EUS-FNA cases diagnosed according to Papanicolaou Society of Cytopathology for pancreaticobiliary system in one centre, evaluate clinicohistopathological correlation.
Methods: This retrospective study includes 84 EUS-guided pancreatic FNA cases between 2015-2019 years in our hospital. Clinical data, laboratory tests, cytopathology, histopathology and imaging reports were included in assessment. Final diagnosis were given according to the findings of EUS-FNA cytology, cell block and/or histopathology of surgical specimens. All results were compared with the final diagnosis to calculate the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).
Results: 84 EUS-FNA procedures were performed.7 cases were excluded from study. Lesions were grouped as cystic 16(21%)and solid 61(79%).Median age was 52;%37 (n=28) of patients were female,%63 (n=49) were male. According to Papanicolaou classification,5 cases were category I(12%),19 were II(24%),15 were III(19 %),4 were IVB (5%),8 were category V(10%),26 were category 6(33%).Cytological evaluations were compared with final clinical and histopathological diagnoses. Consequently, sensitivity, specificity, PPV and NPV of EUS-FNA

cytology to predict final clinicohistopathology were 91%,60%,80%,80%, respectively.
Conclusion: The EUS-FNA guided cytology with Papanicolaou Society Classification is a very helpful diagnostic tool for accurate diagnosis and interpretation of pancreatic lessions with high sensitivity (91%) and PPV (80%).

OFP-11-012
Cytomorphologic and immunophenotypic characterisation of tumour-associated circulating atypical cells in prostate adenocarcinoma
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Background & objectives: Systematic classification of tumour-associated circulating atypical cells (tCAC) in solid-tumour patients has been hampered by the inherent challenges of rare-cell detection. We present a first classification of tCAC obtained from patients diagnosed with prostate adenocarcinoma.
Methods: The study enrolled 170 patients with suspected prostate cancer scheduled for transrectal ultrasound-guided tissue biopsy. Blood was drawn immediately before the biopsy, thereby avoiding cross-contamination with cells released into circulation by the procedure. Atypical cells were isolated using hMX high-gradient magnetic cell separation and characterised by highly-multiplexed Cryoimmunostaining on standard laboratory slides in a seven channel widefield fluorescence microscope.
Results: Atypical circulating cells or cell clumps were observed in 49 out of 74 patients with a positive tissue biopsy for prostate adenocarcinoma, as well as in 22 out of 72 patients with a negative biopsy. Cells from patients with positive biopsy showed classical structural changes such as nuclear enlargement, indentation, irregularity, increased chromatin, multinucleation, and high nuclear-to-cytoplasmic ratio. The immunophenotype of atypical cells was predominantly endothelial (CD31, CD34) with diffuse overexpression of vimentin.
Conclusion: Papanicolau first systematized general criteria for cellular malignancy. The Bethesda classification, among others, later refined and elaborated such criteria. The present study demonstrates that morphologies of tCAC in prostate adenocarcinoma patients correspond well to these general criteria, and, in addition, takes advantage of highly multiplexed immunophenotyping. The present classification may improve the clinical utility and reproducibility of cell-based liquid biopsies in diagnosing prostate cancer and, possibly, other cancers.
The study was jointly funded by the Thailand Research Foundation and X-Zell Biotech Pte. Ltd. (Singapore).

OFP-12 Joint Oral Free Paper Session: Molecular Pathology / Haematopathology

OFP-12-001
Genomic and histological characterisation of gallbladder cancer identifies potentially actionable therapeutic targets in the majority of patients
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Background & objectives: Gallbladder cancer (GBC) is a highly aggressive malignancy with a low incidence in Western countries and a 5-year survival rate highlighting the need for more effective therapies. We aimed to identify potentially actionable therapeutic targets for GBC.
Methods: We collected specimens and clinicopathological data of >800 GBC patients between 2000 and 2019 using the Dutch Pathology Registry (PALGA) and the The Netherlands Cancer Registry. Pathology review was performed for 500 cases. A subset (N=79) was subjected to the Illumina TruSight™ Oncology (TSO)500 assay. We assessed variants in a panel of 54 actionable genes, tumour-mutational burden (TMB) and microsatellite instability.
Results: Histopathological subtypes comprised biliary-type (66%), intestinal-type (20%), poorly cohesive-type including signet ring cell (1%) and other (neuroendocrine carcinoma and (adeno)squamous carcinoma) (14%). Most cases were of pT1/2 stage (70%), followed by pT3/4 (29%) and pTx (1%). Vascular-, lymphatic-, and perineural invasion were observed in 47%, 53% and 37% of cases, respectively. Most tumours (58%) carried at least one (likely) pathogenic variant in an actionable target gene including *KRAS*(11%), *ERBB2*(10%), *CDKN2A*(9%) and *PIK3CA*(9%) and with varying frequency in numerous other genes. One case showed microsatellite instability. The median TMB was 5.5 mutations/Mb (range: 0 – 161.1 mutations/Mb) and 12 cases (15%) had a TMB of >10 mutations/Mb.
Conclusion: The majority of GBC patients carry a potentially actionable variant, increasing the potential for targeted therapy selection and highlighting the importance of molecular testing in this population.
Funding by: Foundation ADP

OFP-12-002
Next-generation-sequencing based molecular profiling of low-cellularity cytological specimens
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Background & objectives: Cytological specimens represent up to 50% of diagnostic cancer samples, but are seldomly used for molecular profiling, as they often contain <20% tumour cells. We use a novel NGS assay to accurately profile low-cellularity cytological specimens within a single day.
Methods: The Oncomine Precision Assay (OPA) covers 50 genes and uses unique molecular identifiers to maximize sensitivity. Libraries from of 15 previously characterized cytological specimens were prepared and sequenced on the Ion Torrent Genexus Integrated Sequencer. Sensitivity and specificity of variant detection was assessed.
Results: To assess the limit of detection we used serial dilutions as well as samples with a tumour cell content ranging from 5% – 20%. Clinically relevant cancer hotspot mutations as well as copy number alterations in HRAS; EGFR; PIK3CA and TP53 were accurately detected at <1% variant allele frequency. Preliminary analysis shows 100% concordance with previously characterized matched laser-microdissected samples. Turnaround time from sample to results was as short as one day. Comprehensive analysis of the complete dataset will be presented at the conference.
Conclusion: The OPA allows for sensitive and specific detection of variants in low-cellularity cytological samples, obviating the need for laser-capture microdissection. Using the Genexus Sequencer, NGS results can be reported to clinicians as quickly as immunohistochemical analyses.
Funding by: Thermo Fisher Scientific

OFP-12-004
Pervasive lesion segregation shapes cancer genome evolution
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Background & objectives: Cancers arise through the acquisition of oncogenic mutations and grow through clonal expansion. Sequencing and

analysis of cancer genomes have identified a wealth of driver mutations and mutation signatures, illustrating how environmental mutagens cause genetic damage and elevate cancer risk.
Methods: We chemically induced liver tumours in fifteen-day-old male C3H/HeOuJ inbred mice and performed whole genome sequencing and histological analyses of of 371 independently-evolved tumours from 104 individuals.
Results: We revealed that most mutagenic DNA lesions are not resolved as mutations within a single cell-cycle. Instead, DNA lesions segregate unrepaired into daughter cells for multiple cell generations, resulting in the chromosome-scale phasing of subsequent mutations. We characterised this process in mutagen-induced mouse liver tumours and show that DNA replication across persisting lesions can produce multiple alternative alleles in successive cell divisions, thereby generating both multi-allelic and combinatorial genetic diversity.
Conclusion: The phasing of DNA lesions enables the accurate measurement of strand biased repair processes, the quantification of oncogenic selection, and the fine mapping of sister chromatid exchange events. Finally, we demonstrate that lesion segregation is a unifying property of exogenous mutagens, including UV light and chemotherapy agents in human cells and tumours, which has profound implications for the evolution and adaptation of cancer genomes.
Funding by: S.J.A. received a Wellcome Trust PhD Training Fellowship for Clinicians (WT106563/Z/14/Z) and is now funded by a National Institute for Health Research (NIHR) Clinical Lectureship.

OFP-12-005

Influence on cancer cell energy metabolism by pharmacological inhibition of the histone modifying lysine-specific-demethylase-1

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Background & objectives: The lysine-specific-demethylase-1 (LSD1) is overexpressed in different cancer types. Additionally, to its effects on cell cycle, our studies revealed LSD1 function in cancer metabolism. To investigate the metabolic effects of LSD1 inhibition in tumours we used the novel inhibitor HCI-2509.
Methods: RNA sequencing followed by pathway analysis and qPCR validation was performed on non-treated versus HCI-2509 treated cancer cell lines. The mitochondria were investigated by mitochondrial membrane potential staining, flow cytometry quantification of the mitochondrial membrane potential and analysis of the respiratory chain, using the Seahorse device. Besides, public available patient datasets were assessed regarding differential expression of metabolic genes.
Results: Expression profiling revealed altered regulation of many metabolic genes upon pharmacological LSD1 inhibition. Especially, transcription of genes related to mitochondrial metabolism and in particular, expression of genes encoding subunits of the electron transport chain (ETC) complex I were repressed. Accordingly, we proved a decrease of the mitochondrial membrane potential, lower ATP production and lower maximal respiration upon LSD1 inhibition in cancer cells. Interestingly, the expression of various mitophagy effectors was increased. Additionally, public available datasets confirmed altered expression of metabolic genes in tumours compared to non-tumour specimens.
Conclusion: Our data emphasizes the value of LSD1 inhibition in cancer therapy since LSD1 inhibition does not only disrupt cell cycle progression but also leads to energy depletion by ETC complex I dysregulation and upregulation of mitophagy inducers.

OFP-12-006

The expression levels of microRNA 21 and microRNA 210 in renal cell carcinoma subtypes and renal cell carcinoma metastases and their relationship with prognosis

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Background & objectives: MicroRNAs are non-coding RNA groups consisting of approximately 20 nucleotides with single strands. They play roles in many biological events such as cell proliferation and differentiation, apoptosis, angiogenesis and also in cancer pathogenesis and metastasis.
Methods: Cases diagnosed between 2012-2018 were re-evaluated. 35 ccRCC, 11 CRCC, 9 PRCC and 9 metastatic ccRCC were included.
Tissues were studied using real-time PCR. Fold change, which is the change in the expression level of the target microRNA in tumour and metastatic tissue compared to normal tissue, was calculated with the formula 2-ΔΔCT. Significance was determined by P value ($p<0.05$).
Results: Expression levels of microRNA-21 and microRNA-210 are statistically significant between histological types ($p<0,001$). Only the effect of microRNA-210 expression level on survival time is statistically significant. ($p=0,034$). There was no statistically significant difference between microRNA-21 and microRNA-210 expression levels between primary and metastatic tumours ($p=0,053$; $p=0,237$). microRNA-210 has a statistically significant diagnostic accuracy for metastatic tumours ($p=0.04$). Both microRNA-21 and microRNA-210 have a statistically significant diagnostic accuracy for clear cell RCC versus choromofob RCC and papillary RCC versus choromofob RCC ($p<0,001$). microRNA-210 has a statistically significant diagnostic accuracy for clear cell RCC versus papillary RCC ($p=0,001$).
Conclusion: MicroRNAs show different ELs in kidney tumours according to histological types. This feature can make the use of microRNA-21 and microRNA-210 significant in the subtype diagnosis process. With treatment to be developed against microRNA-210, which can be used in determining survival times, patients can survive longer.

OFP-12-007

Anti-arthritic effect of hesperidin loaded lecithin NPs coated with folic acid silver nanoparticles via modulating immune mediators of inflammation and bone damage

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Background & objectives: Activated macrophages by expressing Folate receptor (FR) play significant role in rheumatic inflammation. Presently, Hesperidin loaded lecithin NPs coated with folic acid silver nanoparticles (FA-L HP-AgNPs) was investigated against CFA-induced arthritis model targeting downstream inflammatory mediators of macrophages signalling.
Methods: FA-L-HP-AgNPs characterized through UV–vis, zetasizer, FT-IR and AFM. During CFA-induced arthritis rat model, oxidative stress markers (NO & PO), M1/M2 cytokines (TNF-α, IL-1β, IL-6, IL-23, IL-10 and TGF-β1), and TLRs expressions were tested in serum, peritoneal macrophages and splenocytes, respectively. Additionally, mRNA levels of TLR-2/-4, RANK, RANKL & ROR-γt and percentage of Th17 cells were performed in spleen tissues.

Results: Oral administration of FA-L-HP-AgNPs (1 & 3mg/kg) exhibited potent anti-arthritic activity with minimal arthritic score, reduced degenerative changes and lesser influx of inflammatory cells in macroscopic, radiographic, and histological examination, respectively. The treatment not only inhibited TLRs, RANKL, MMP-9/-2 and IL-17 levels in synovium but also suppressed the serum NO and HO ($p < 0.001$) production demonstrated its immunomodulatory effects. Interestingly M1 and M2-derived cytokines was also disrupted including TNF-α, IL-1β and TGF-β1 ($p < 0.005$).
Conclusion: FA-L-HP-AgNPs (1&3mg/kg) had profound therapeutic effect on arthritic rats, consistent with reductions in bone damage and Th17-associated IL-17 and ROR-γt expressions. Moreover, FA-L-HP-AgNPs suppressed RANK/RANKL and MMPs production, which supported its anti-osteoclastic effects. Conclusively, FA-L-HP-AgNPs acted as antiarthritic agent in a pleiotropic manner in CFA rats by not only reducing the clinical signs of arthritis, inflammatory cytokines and free radical production but also attenuating the M1/M2 and RANK/RANKL signalling pathway.

OFP-12-008
Glutathione-S-transferase (GSTT1, M1 and P1) genetic polymorphisms among Sudanese acute lymphoblastic leukaemia patients
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Background & objectives: Glutathione S-transferase (GST) is an enzyme involved in metabolic activation and detoxification of carcinogens. This study examined differences in the frequencies of selected single nucleotide polymorphisms in GST (P1, T1 and M1) genes in Sudanese ALL patients.
Methods: This case-control study included extracted DNA from 280 blood samples (150 patients attending Khartoum Oncology Hospital and 130 healthy matched volunteered controls). PCR-RFLP assay was used for genotyping of the GSTP1 (Ile105Val) polymorphism. A multiplex PCR was used to amplify both GSTM1 and GSTT1 in a single PCR reaction together with ß-globin gene primer as an internal control.
Results: The risk of ALL in patients with GSTT1 null genotype was not significant (OR= 1.23, 95% CI=0.74 -2.0, P-0.44). The GSTM1 null genotype was significantly higher in the ALL group (79, 60.3 %) compared to controls (52, 39.78%) and increased the risk to ALL by two folds (OR=1.72, 95% CI=1.1-2.7, p=0.03). The frequency of GSTP1 genotypes was significantly different between the two groups (P=0.000). AG, GG and AG+GG genotypes were found to increase the risk of ALL by more than three times (P<0.000) compared to the AA genotype. Allele frequencies were significantly different (P= 0.001, OR= 1.79, CI= 1.247-2.58). High frequencies were reported in Kordofan and Khartoum states.
Conclusion: GTM1 null allele and GSTP1 mutant genotype exhibits significant association with the risk of developing ALL among Sudanese patients, either alone or with environmental factors related to some Sudan states. Accompanied environmental studies are needed to highlight possible substrate carcinogens.

OFP-12-009
Brain tumour diagnostics using a DNA methylation-based classifier as a diagnostic support tool
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Background & objectives: Methylation profiling is increasingly incorporated in the diagnostic process of central nervous system tumours at our centres in The The Netherlands and Scandinavia. We aimed to identify the benefits and challenges of MP as a support tool for CNS tumour diagnostics.
Methods: 502 CNS tumour samples were analysed using (850k) methylation profiling (MP). Profiles were matched with the DKFZ/Heidelberg CNS Tumour Classifier. For each case the final pathological diagnosis was compared to the diagnosis before MP.
Results: In 54.4% (273/502) of analysed cases, the suggested methylation class (calibrated score ≥0.9) corresponded with the initial pathological diagnosis. The diagnosis of 24.5% of these cases (67/273) was more refined after incorporation of the MP result. In 9.8% of cases (49/502) the MP result led to a new diagnosis, resulting in an altered WHO grade in 71.4% of these cases (35/49). In 1% (5/502) of cases the suggested class based on MP was initially disregarded/interpreted as misleading, but in retrospect the MP result predicted the right diagnosis for 3 of these cases. 33.7% of cases (169/502) had a calibrated score <0.9, including 7.8% (39/502) without class indication (calibrated score <0.3).
Conclusion: MP is a powerful tool to confirm and fine-tune the pathological diagnosis of CNS tumours, and to avoid misdiagnoses. However, it is crucial to interpret the results in the context of clinical, radiological, histopathological and other molecular information.

OFP-12-010
Explanation of unexpected IHC and MSI results of Lynch syndrome diagnostics
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Background & objectives: During our 10 year experience in performing Lynch Syndrome (LS) diagnostics we have encountered 28 patients where MMR IHC and microsatellite instability (MSI) analyses showed unexplained contradictory results. This study is to clarify these non-corresponding molecular observations.
Methods: Tumours of 2335 patients were tested for MMR-deficiency and MSI between 2007 and 2017 in the UMC Utrecht. Diagnostic MMR IHC and MSI analyses were repeated for patients with unexplained contradictory results. Two MSI assays were used; the Bethesda markers (mono- and di-nucleotide repeats) and the Pentaplex assay (mononucleotide repeats). Germline and somatic mutation analysis and protein modelling were performed.
Results: Repeated IHC analysis resulted in a different outcome in 7 out of 17 patients. Repeated MSI analysis with only mononucleotide markers resulted in a different result in 9 out of 10 patients. Somatic MMR mutations were identified in 10 patients. Protein modelling could explain preserved protein expression in some tumours as mutations did not cause major conformational changes. In total, in 15 patients the unexplained results could be clarified (e.g. bi-allelic somatic mutations, LOH, minor conformational changes), while 5 patients were partially explained.
Conclusion: Mononucleotide markers for MSI analysis were more sensitive than dinucleotide markers and a combined analysis including germline and somatic mutations proved crucial for identifying a definitive diagnosis as somatic mutations were frequent in this study population.

OFP-12-011
Abdominal involvement of Erdheim-Chester disease: clinical, histological and molecular characteristics of 22 cases
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Background & objectives: Peritoneal infiltration rarely occurs in Erdheim-Chester disease and other histiocytoses and may be

misdiagnosed when presenting as a single-organ involvement. We aimed to analyse clinical, histological, and molecular features of peritoneal manifestations of patients diagnosed with histiocytosis.
Methods: Twenty-two patients were retrieved from the file of Ambroise-Paré Hospital. All slides were stained with H&E, and immunohistochemistry was performed for the following markers: CD163 (or CD68), CD1a, S100 protein and phosphoERK. DNA was extracted from histiocyte-rich areas and analysed using real-time PCR, Picodroplet Digital PCR and NGS. Clinical information was obtained for each case.
Results: The final diagnosis of seventeen patients was ECD. For twelve patients, the abdominal symptoms revealed the disease, and nineteen underwent surgical biopsies. Four patients had a unique abdominal mass, while the others had diffuse peritoneal infiltration. Sixteen had subserosal histiocytic infiltration, ten of whom also had deep infiltration of adipose tissue. Histiocytes were mainly mononucleated, with multinucleated cells in seven cases. Eighteen cases contained foamy histiocytes. Most cases with low or moderate density of histiocytes had ECD. Cytosteatonecrosis was present in one patient with ECD. All cases were positive for CD163 or CD68 and negative for CD1a. Twelve cases contained phosphoERK positive histiocytes. Thirteen patients had BRAF or MAP2K1 mutations.
Conclusion: Abdominal symptoms may reveal unsuspected Erdheim-Chester disease. In more than half of these referred cases the diagnosis of ECD was not initially proposed. Molecular biology is a helpful diagnostic tool.

OFP-12-012
Prognostic value of histone modifying enzyme EZH2 and histone mark H3K4me3 in R-CHOP-treated diffuse large B-cell lymphoma
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Background & objectives: DLBCLs are aggressive, heterogeneous lymphomas. Under RCHOP-treatment, 30% of patients progress or ultimately relapse. Histone modifying enzymes' alterations are frequent, but their prognostic value is still controversial.
Aim: To ascertain the prognostic value of EZH2/H3K4me3 immunoexpression in RCHOP-treated DLBCL.
Methods: Retrospective cohort study including 127 patients with RCHOP-treated DLBCL (2008-2017). EZH2/H3K4me3 immunoexpression was evaluated using a digital imaging system for H-score calculation and dichotomized in high/low expression. Clinicopathological variables (sex/age/stage/R-IPI/bone marrow status/Hans molecular group/BCL2/CD5 positivity) were re-evaluated/collected.
Primary outcome was event free survival (EFS); secondary outcomes were lymphoma specific (LSS) and overall survival (OS). Subgroup analysis by molecular group was performed.
Results: EZH2 expression levels did not differ between molecular groups (p=0.749). Exclusively in the non-Germinal Centre (nonGC) subtype, high EZH2 expression was associated with poor EFS, both in univariable (HR 2.29; 95%CI[1.08- 4.85]; p=0.031) and multivariable analysis (HR 2.78; 95%CI[1.18- 6.54]; p=0.019). EZH2 expression was not significantly associated with LSS (p=0.046*) or OS (p=0.031*). [*alpha=0.01 for secondary outcomes]
We did not find an association between H3K4me3 expression levels and survival.
Conclusion: High EZH2-expression was associated with worse EFS in nonGC-DLBCL, supporting its role as prognostic biomarker in this subgroup.
Although EZH2-mutations are almost exclusively found in GC-DLBCL, both subgroups shared similar expression levels, suggesting EZH2-antagonists might also be beneficial in nonGC-DLBCL.

Oral Free Paper Session: One-Day Computational Pathology Symposium

CP-03 One-Day Computational Pathology Symposium - Selected Abstracts

CP-03-001
Deep learning-based tumour bud detection in pan-cytokeratin stained colorectal cancer whole-slide images
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Background & objectives: Tumour budding (TB) is an established prognosticator for colorectal cancer. Deep learning-based TB assessment has the potential to improve diagnostic reproducibility and efficiency. We developed an algorithm that can detect individual tumour buds in pan-cytokeratin stained colorectal cancer slides
Methods: Tumour-bud candidates (n=1765, collected from 58 whole slide images; WSI) were labelled by seven experts as either TB, poorly differentiated cluster, or neither. The 58 slides were randomly split into a training (49) and test-set (9). A deep learning (DL) model was trained using the buds identified by the experts in the training set.
Results: The algorithm was tested on the nine remaining WSI and 270 WSI from pan-cytokeratin stained slides from Bern University hospital, in which hot spots and TB were manually scored. An F1 score of 0.82 was found for correspondence at the bud level between experts and DL. A correlation of 0.745 was found between the manually counted buds within the hot-spots and the automated method in the 270 WSIs.
Conclusion: Assessment of tumour budding as a prognostic factor for colorectal cancer can be automated using deep learning. At the level of individual tumour buds, correspondence between DL and experts is high and comparable to the inter-rater variability. However, compared to the manual procedure, the algorithm yields higher counts for cases with relatively high bud densities (>15). Follow-up studies will focus on the assessment of TB in H&E stained slides.
Funding: This project has received funding from the Dutch Cancer Society, project number 10602/2016-2.

CP-03-002
Optimised tumour infiltrating lymphocyte assessment for triple negative breast cancer prognostics
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Background & objectives: The tumour microenvironment was shown to harbour prognostic value for breast cancer. For instance, tumour infiltrating lymphocytes (TILs) are studied using a variety of methods. This study aims to establish the most optimal (marker, region) and objective TIL assessment method.
Methods: Multiplex immunohistochemistry (mIHC) was applied on 94 triple negative breast cancer cases, using CD3, CD8 and FOXP3. Multispectral images were co-registered with serial H&E sections, to combine deep learning based automated tissue delineation with lymphocyte detection. Densities of positive lymphocytes were analysed in different regions (peri- and intratumoral, within tumour stroma etc) and correlated to relapse free and overall survival.
Results: We found that for all three markers of TILs, the presence of a high density of positive cells correlated with an improved survival, with none of the markers being superior to the others. The results of TILs

assessment in the various regions did not show marked differences: TILs assessed within the tumour stroma, in the entire tumour area or at the tumour periphery all show similar prognostic value.
Conclusion: We showed that completely automatic assessment of TILs in different regions of the tumour is feasible. The correlation between TILs and survival in our cohort are in line with previous studies. Our results provide directions for optimizing TILs assessment methodology and will be validated in larger series.
Funding: This study was funded by a Junior Researcher grant from the Radboud University Medical Center Institute for Health Sciences (RIHS), Nijmegen, The Netherlands.

CP-03-003
An AI system for predicting ER/PGR/HER2 status from H&E slides in breast cancer
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Background & objectives: Existing ER/PgR/HER2 guidelines require IHC interpretation by experts. Prior research suggests histological features in H&E images correlate with biomarker status. Here, we develop deep learning systems for predicting ER/PgR/HER2 status directly from H&E slides.
Methods: Paired H&E and IHC slides were prepared using representative tissue blocks from 260 cases from two independent institutions. Board-certified pathologists annotated H&E images using the IHC images for reference. Using these annotations, we developed convolutional neural networks to predict ER/PgR/HER2 status directly from H&E slides.
Results: Each model was trained on 200 cases and evaluated on 60 held-out cases. Rates of biomarker positivity in our sample were 0.76/0.72/0.32 for ER/PgR/HER2, respectively. The deep learning system demonstrated an accuracy of 0.87, 0.93, 0.79 (95% CIs: 0.85-0.89/0.91-0.94/0.77-0.81) and an area under the receiver operating characteristic curve (AUC) of 0.87, 0.82, 0.76 (95% CIs: 0.89-0.91/0.81-0.87/0.73-0.79) on slide-level status of validation cases for ER/PgR/HER2, respectively.
Conclusion: Histopathological features present in H&E slides can be used to predict ER/PgR/HER2 status as demonstrated by our deep learning system. Recent guideline updates recommend repeated testing when biomarker results are discordant with the histopathological review, highlighting the value of understanding biomarker status' association with morphological features. Further research into the features learned by our models may provide novel insights into biomarker status in breast cancer.

CP-03-004
Grading nuclear pleomorphism in breast cancer using deep learning
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Background & objectives: Nuclear pleomorphism is defined as the variability in size and shape of tumour cells as compared to normal epithelial cells. Objective of this study is to train a deep neural network that can achieve pathologist-level pleomorphism grading performance.
Methods: We collected 29 whole slide images (WSI) of breast cancer resections in which we manually selected 90 regions of interest, ensuring grade homogeneity of tumour cells within a region. Subsequently, we cropped regions of ~0.38 mm2 at 40X magnification (0.25 um/px) and asked six pathologists to grade each region independently.
Results: We used an epithelial cell detector network to detect the epithelial cells in each region and extracted fixed-size patches from these regions with high tumour density. For the task of pleomorphism grading, we trained a densenet model on those patches with the majority voting of the grades of the pathologists (majority grades). The variation of kappa scores of the pathologists with the majority grade was very high, ranging between 0.37 and 0.69 on the standalone test set consisting of 18 regions from 7 WSI. On the same test set, our densenet model had a kappa score of 0.47 with the majority grades.
Conclusion: We demonstrated that our network trained only on tumour cells achieved performance on the task of pleomorphism grading of breast cancer around the low mid-range of the inter-pathologist variability where the inter-observer variability of pathologists was very high. Future research will include scores of a larger panel of pathologists, and study alternative deep learning strategies to improve the performance.

CP-03-005
Artificial intelligence to aid the diagnosis of head and neck precancerous and cancerous lesions: a systematic review
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Background & objectives: This systematic review aims to evaluate the published literature on AI/machine/deep learning applications for detection, grading and classification of head and neck precancerous and cancerous lesions using digitised human tissue.
Methods: Electronic database search was conducted using MEDLINE via OVID, Scopus and Web of Science to retrieve relevant articles (2009 and 2019). A tailored search strategy using database specific search terms and text words were used, and studies screened against an eligibility criteria. Modified QUDAS-2 tool was used for risk of bias assessment.
Results: 11 articles met the inclusion criteria which used a combination of heuristics, supervised and unsupervised learning methods, including more than 10 different classification and segmentation techniques. Automated detection was based on analysis of specific histological markers for oral precancer (n=1), oral submucous fibrosis (n=5), oral cancer (n=4) and oropharyngeal cancer (n=1). Most studies used small unicentric datasets (range 40-270 images) comprising small visual fields. Detection accuracy ranged from 79%-100%.
Conclusion: Most studies have shown a high risk of bias which is likely to have contributed to high accuracy rates. Traditional supervised learning methods were most commonly used highlighting the need for modern state-of-the-art deep learning techniques in future research.

CP-03-006
Validation of computer-assisted tumour-bud and T-cell detection in pT1 colorectal cancer
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Background & objectives: Tumour budding, and T-cells are robust prognostic biomarkers in colorectal cancer. A combined analysis is complex and can be greatly expedited and automated using deep learning. The implementation of computer-based analysis in diagnostics is challenging and necessitates extensive validation.
Methods: Randomly selected (n=61) double-stained immunohistochemical slides (AE1-AE3 pancytokeratin for tumour buds and CD8 for cytotoxic T-cells) from our pT1 cohort from 3 different institutions were used to validate the deep learning algorithms for tumour budding and CD8 T-cell detection developed by the International Budding Consortium Computational Pathology Group. Staining and scanning were performed in a single laboratory.
Results: In the visually identified tumour budding hotspot (0.785 mm2), tumour buds were manually annotated, and the output of the T-cell algorithm manually corrected by a single observer. For budding, 645 out of the 1'306 buds were correctly identified by the algorithm. Recall and precision were 49.4% and 61.4%, respectively. For the T-cells, 89.3%

were correctly detected (from a total of 16'296). The recall was 90.3% and the precision was 87.3%. Reasons for misclassified T-cells included staining intensity, suboptimal tissue recognition and slide artifacts.
Conclusion: Our preliminary data demonstrates satisfactory results for T-cell detection. Automated budding detection is more difficult, as inter-observer variability of bud calling is high among experts. These issues merit consideration when developing reliable deep learning algorithms examining the tumour/host interface.
Funding: The work presented here has been supported by the Rising Tide foundation with the grant number CCR-18-130.

CP-03-007
Characterisation of the tumour-host interface as a prognostic factor through deep learning systems
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Background & objectives: Interpretation of the tumour-host interface can provide relevant prognostic information. Through H&E and IHC double staining in combination with deep learning, we set out to find a novel way of characterizing features of the invasive margin in colorectal carcinoma (CRC).
Methods: Formalin-fixed-paraffin-embedded human CRC tissue obtained from the Radboudumc (Nijmegen, Netherlands) was automatically H&E stained and digitized. A double staining procedure using anti-CD3 and pan-cytokeratin was conducted on the same slides and scanned, generating a 2nd whole slide image (WSI) per sample. WSIs were processed using a series of deep learning neural networks (automated lymphocyte detection, tissue classification, tumour budding detection).
Results: Our method was successfully implemented as the tumour budding and lymphocyte detection algorithms were able to automatically detect peritumoral budding in pan-cytokeratin and CD3+ lymphocytes respectively in the immuno-stained WSIs. The tissue classifier segmented the H&E-stained WSIs into 13 classifications. This technique allows us to combine the relevant data and link the density of peritumoral budding with immune infiltration, tumour cell ratio, mismatch repair (MMR) status and clinical outcome. Data correlations on a cohort of 150 colorectal cancer patients with varied MMR status will be presented at the meeting.
Conclusion: Automated classification of the invasive margin in combination with clinical outcome can lead to an improved understanding of patient prognosis. This unbiased and transferable method could improve diagnostic accuracy as well as broaden our understandings of tumour budding and other poor prognostic factors.
Funded by the Dutch Cancer Society.

Oral Free Paper Sessions: One-Day Molecular Pathology Diagnostics and Translational Research Symposium

MD-02 Joint Session One-Day Molecular Pathology Diagnostics and Translational Research Symposium, Molecular Pathology & Trainees: Case Presentations

MD-02-001
First ESWR1-SMAD3 rearranged tumour arising in bone: expanding the clinical and histological spectrum of this emerging tumour type (case presentation)
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Background & objectives: EWSR1-SMAD3 fibroblastic tumours are an emerging group of rare soft-tissue neoplasms, defined by characteristic genetic alteration, similar fibroblastic morphology and predilection for hands and feet. We describe the first case of an EWSR1-SMAD3 rearranged tumour arising in bone.
Methods: We reviewed the imaging, clinical records, histopathology and genomic findings of a patient diagnosed at our institution with an unusual bone tumour. Whole genome sequencing (WGS) was performed on fresh frozen tissue as part of the 100,000 genomes project, and data was analysed using standard bioinformatics pipelines in the Genomics England research environment.
Results: A 44-year old male presented with a 9-month history of a painful right knee swelling, with no significant functional defects. MRI revealed a partly ossified mass involving the proximal tibia with a large extraosseous component. The pathology showed a biphasic tumour comprising cellular regions of atypical spindled to oval cells and interspersed hyalinised nodular areas, in places resembling cartilaginous differentiation. The differential diagnosis at the time included a mesenchymal chondrosarcoma and a dedifferentiated chondrosarcoma. Subsequently in the analysis of WGS data, an EWSR1-SMAD3 fusion was discovered.
Conclusion: We present, to our knowledge, the first case of an EWSR1-SMAD3 fibroblastic tumour occurring in bone. This case highlights the role of next generation sequencing in the accurate classification of mesenchymal tumours, particularly in difficult cases showing atypical histological features.

MD-02-002
A case report of ROS1 fusion detection by FISH - a possibility of false positive results
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Background & objectives: While fluorescence in situ hybridization (FISH) is commonly used for the detection of drug-targetable fusion events, false positive results can hamper profitable treatment decisions. This case report visualizes the possibility of false positive ROS1 FISH results.
Methods: ROS1 FISH and ROS1 immunohistochemistry (IHC) were performed using a SPEC ROS1-Dual Colour Probe (ZytoVision) and a ROS1 antibody Clone D4D6 (Cell Signalling Technology). RNA was extracted from formalin-fixed, paraffin-embedded (FFPE) material. Gene fusion detection by parallel sequencing was done using the FusionPlex CTL panel (Archerdx) on a MiSeq (Illumina).
Results: A 44 –year-old male, diagnosed with an NSCLC adenocarcinoma showed a ROS1 translocation with aberrant signals in 79% of nuclei in FISH analysis. Further evaluation revealed a pattern of 78 nuclei with isolated 3' extra green signals and 1 nucleic signal with break apart signal. Follow up IHC showed no ROS1 protein expression. Parallel sequencing was also negative for ROS1, indicating a false positive FISH result. Analysing a larger cohort of FISH positive cases by isolated 3' green signals demonstrated that 48% were not confirmed by alternative methods.
Conclusion: This case report showed that isolated 3' green signals in ROS1 break-apart FISH should be confirmed by alternate methods. It seems that isolated 3' green signals could indicate a chromosomal break albeit not generating a functional fusion product.

MD-02-003
Molecular characterisation of high grade papillary urothelial carcinoma with divergent glandular differentiation reveals the clonal origin of both components
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Background & objectives: Urothelial carcinoma with divergent glandular differentiation is a recognised variant of urothelial

carcinoma. There is no clear evidence about the clinical significance of this neoplasm, although some studies associate it with worse prognosis. There are studies about the immunophenotype of tumours with divergent differentiation, but there are no publications to date about the possible different genomic profiles of the urothelial and the glandular components.
Methods: We present the case of a high grade papillary urothelial carcinoma with divergent glandular differentiation, on which we performed immunohistochemical and molecular analyses of the two areas. For the molecular analysis, both components were sequenced with next generation sequencing (NGS) techniques, using a 59 gene custom panel.
Results: The high grade papillary urothelial component was only positive for GATA3, p63 and CK7. The glandular area was only positive for CDX2 and CK20.
Both components shared the same mutations on FGFR2, CDH19, KMT2C, MKI67 and PMS2. The glandular component had additional mutations on TP53, ARID1B, ARID5B, CDH19, CTNNB1 and PMS2. Immunohistochemical analysis showed p53 loss of expression (mutated "null" pattern) only in the glandular area, confirming the NGS result.
Conclusion: The molecular analysis, showing the same mutations on both components and the acquisition of new mutations on the glandular component, suggest a common clonal origin. To our knowledge, this is the first study reporting this finding.

MD-02-004
A case of Burkitt-like lymphoma with 11q aberration arising in Waldeyer's ring
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Background & objectives: A 35-year-old female with Crohn's disease under azathioprine and mesalazine presented with a right rhinopharyngeal tumour causing local symptoms over the last 4 months, without B-symptoms, lymphocytosis, lymphadenopathy or organomegaly. LDH levels were normal. A tumour biopsy was performed.
Methods: H&E: Mucosal involvement by a diffuse population of large cells with vesicular nuclei and conspicuous nucleoli and medium-sized, relatively monomorphic cells with a "starry sky" pattern. Immunohistochemistry: Strong, uniform co-expression of CD20, PAX5, CD10, BCL6; c-MYC>80%, MUM1/IRF4-, BCL2-, CD5-, CD23-, cyclin-D1-, CD30-, Ki67>99%. EBER-ISH: negative. Break-apart FISH for MYC, BCL2, BCL6: negative. Triple-colour FISH revealed 11q23.3 gains and 11q24.1-q25 losses.
Results: A Burkitt-like lymphoma with 11q aberration [BLL-11q] diagnosis was rendered. The demonstration of 11q aberrations without detectable MYC, BCL2 or BCL6 rearrangements helped exclude high grade B-cell lymphoma, NOS (see mixed Burkitt-like and DLBCL cytology) and a morphologically "atypical" Burkitt lymphoma (BL) with a cryptic MYC translocation (see c-MYC>80% and "BL immunophenotype").
The patient received R-DA-EPOCH including CNS prophylaxis, switched to R-CHOP, and is disease-free 5 months after the diagnosis.
Conclusion: BLL-11q explains some "MYC-negative BLs" or BLs with presumed cryptic translocations. Copy number arrays are the gold standard, but no false positive cases have been reported with FISH. The azathioprine-induced immunosuppression is noteworthy, as cytogenetically similar lymphomas arise in post-transplant patients. Transformed follicular lymphoma may have similar 11q aberrations, but this case lacked such evidence. 11q22-q24 and 11q12.3-q25 gains without telomeric losses, seen in DLBCL and LBCL-IRF4 respectively, are nonspecific.

MD-02-005
Spindle cell tumour of the liver with an ETV6-NTRK3 fusion
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Background & objectives: A 31-month-old girl suffered from abdominal pain, sickness, and fever. Radiologically, she showed a 7.9 cm large tumour of the liver.
Methods: Hematoxylin and eosin, and immunohistochemical staining was done on a formalin-fixed, paraffin-embedded biopsy. For mutation and fusion analysis, the Oncomine Focus Assay (ThermoFisher Scientific, Waltham, MA, USA) was performed and for confirmation of fusions the Archer FusionPlex solid tumour panel (ArcherDX, Boulder, CO, USA) was used.
Results: The tumour composed of a spindle proliferation with ovoid or elongated nuclei and medium sized cytoplasm undermixed with inflammatory cells. Immunohistochemically, the cells showed a weak and heterogenous positivity for SMA, but were negative for desmin, myogenin, CD23, S100, ALK, pancytokeratin, CD21, lysozyme, CD1a, glypican 3, HepPar1, and didn't show loss of INI1. MIB1 staining indicated 10% proliferation activity. Molecular analysis detected an ETV6-NTRK3 inframe fusion gene.
Conclusion: The tumour was diagnosed as a spindle cell tumour with ETV6-NTRK3 fusion with differential diagnoses infantile fibrosarcoma and ALK negative inflammatory myofibroblastic tumour (IMT). The morphology, the interspersed inflammatory cells and the localization are more in line with IMT.

MD-02-006
Fusion and mutation-negative inflammatory myofibroblastic tumour in bladder: a case report
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Background & objectives: A 71-year old patient underwent a radical cystoprostatectomy due to a rapidly growing bladder tumour with bilateral hydronephrosis and infiltrative growth on imaging. The bladder contained a 7.4 cm polypoid lesion, invading the detrusor muscle and the perivesical tissue.
Methods: The lesion was examined with hematoxylin-eosin (H&E) and immunohistochemical stainings, including ALK-1. The morphology showed a spindle cell lesion, organised in fascicles, with an intervening mixed inflammatory infiltrate. The *ALK* and *ROS1* fluorescent in situ hybridisation (FISH) assay was performed, followed by a DNA analysis and an RNA gene fusion panel assay (Archer) using next-generation sequencing.
Results: Using the H&E and immunohistochemical stainings, the morphology of the tumour was consistent with an inflammatory myofibroblastic tumour (IMT), although ALK-1 was negative. No *ALK* and *ROS1* gene alterations were detected in the FISH assays. The Archer gene fusion panel assay (*ALK*, *CAMTA1*, *CCNB3*, *CIC*, *EPC1*, *EWSR1*, *FOXO1*, *FUS*, *GL1*, *HMGA2*, *JAZF1*, *MEAF6*, *MKL2*, *NCOA2*, *NTRK3*, *PDGFB*, *PLAG1*, *ROS1*, *SS18*, *STAT6*, *TAF15*, *TCF12*, *TFE3*, *TFG*, *USP6* and *YWHAE*) did not reveal any gene fusion either and the DNA mutation analysis detected no mutations. Despite extensive molecular testing, no gene alterations or mutations were encountered. External consultation by Prof. Dr. J.I. Epstein (JHH, Baltimore, USA) was confirmative.
Conclusion: Inflammatory myofibroblastic tumour is a rare tumour with potentially aggressive biologic behaviour. Subset of IMT can be ALK-negative and shows no molecular alteration. Additional molecular research remains necessary for potential future targeted therapy.

MD-02-007

Vulvar pilomatrix carcinoma: morphological and molecular features

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Background & objectives: Pilomatrix carcinoma (PC) is the rare malignant counterpart of pilomatrixoma, a skin adnexal tumour originating from hair matrix cells. Mutations in CTNNB1, the encoding gene of beta-catenin, have been found in both entities, but other molecular alterations are still unknown.
Methods: We present the morphological, immunohistochemical and molecular features of a PC of the clitoris, the third known reported case located on the external genitalia, which developed multiple metastases in a 53-year-old woman. Next generation sequencing (NGS) was performed with a custom-panel including 59 genes. Sanger sequencing was also carried out.
Results: The tumour showed an atypical neoplastic proliferation with scattered abrupt keratinization and shadow cells upon tumour areas. Negative immunohistochemical stain for p16 and p53 excluded the diagnosis of squamous cell carcinoma. Neoplastic cells showed nuclear and cytoplasmic beta-catenin overexpression, characteristic of pilomatrix carcinoma. Sanger sequencing identified S37F mutation in CTNNB1 and NGS also evidenced mutations in ARID1A, PTEN and PIK3CA. Posterior negative immunostaining for ARID1A confirmed NGS result.
Conclusion: PC is a rare neoplasm usually located in head and neck region. Metastasis only occur in 10% of cases. In contrast, this study presents a vulvar PC with multiple metastasis. To the best of our knowledge, this is the first case analysed by NGS, which demonstrated not only the common initiating mutation in CTNNB1, but also other mutations that could have contributed to the dismal evolution in this patient.

MD-02-008

Sino-nasal Ewing family tumour – a morphomolecular case report of a "small round blue cell tumour"

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Background & objectives: An elderly female presented with right eye pain, epiphora and proptosis. CT and MRI showed a 7.7cm mass involving the right nasal cavity, ethmoid sinus and orbit with bilateral frontal sinus involvement and early intracranial extension.
Methods: Biopsy showed a small round blue cell tumour. Focally, the lesional cells formed whorls around small blood vessels. There was no keratinization or gland formation. An extensive immunohistochemistry (IHC) panel was performed and supplemented by FISH for EWSR1 translocation, RT-PCR for EWSR1-FLI1 and SS18 fusion products and multiplex PCR for HPV-16 and HPV-18 genotypes.
Results: IHC demonstrated staining with antibodies to broad spectrum cytokeratins and focal staining with squamous markers p63 and p40. Antibodies to p16 were positive. Of note, CD99 was negative. Neuroendocrine, neural, melanocytic, skeletal and smooth muscle, lymphoid and vascular markers were negative. EBV-ISH was negative. There was no loss of INI-1 expression. There was focal cytoplasmic PAS-positive material. Molecular testing revealed EWSR1-FLI1 fusion.
A diagnosis of Ewing family tumour (EFT) was made. Sinonasal EFTs are very rare and have a wide differential diagnosis. EWSR1 translocation can also be seen in anaplastic myoepithelial carcinoma but EWSR1-FLI1 fusion is specific to EFT and is present in 85% of cases.
Conclusion: This report raises awareness of sinonasal EFT, a rare entity which has a wide differential diagnosis, and demonstrates the use of molecular analysis as an adjunct to traditional histology, histochemistry and IHC to reach a definitive diagnosis.
Hayley Morris is a NHS Education for Scotland funded Clinical Lecturer in Pathology.

MD-04 One Day Molecular Pathology Diagnostics and Translational Research Symposium - Selected Abstracts

MD-04-001

Evaluation of 1429 lung tumour samples analysed by targeted RNA-Seq

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Background & objectives: Molecular assays for fusion detection in lung tumours are widely used in routine diagnostics. However, conventional methods like fluorescence in situ hybridization (FISH) can come with several drawbacks. In this study, 1429 lung tumour samples were evaluated with targeted RNA-Seq.
Methods: For the detection of known and novel gene fusions, the Archer FusionPlex Lung panel (Archerdx, Boulder, CO) was used. In brief, 35 to 200 ng of tNA was target enriched by single primer extension. Prepared cDNA libraries were sequenced on a MiSeq (Illumina). Data analysis and fusion detection were done using Archer Analysis software versions 5.0.4, 5.1.3 and 6.2.1 (Archerdx).
Results: 1429 lung tumours were evaluated in routine diagnostics. 98% of these samples were analysable. Novel fusion partners, for example EGFR – VSTM2A or NIPBL-NRG1 were found as well as rare but clinically relevant lung fusions like ST7-MET and the EGFR VIII variant were identified. Furthermore, the assay was found to be a useful tool to verify, whether mutations and deletions in close proximity to characterized MET exon 14 skipping mutations will lead to a real exon skipping event. This assay is only hampered by the fact that fusions involving genes both outside the selectively captured region cannot be detected and false-negative results due to poor quality samples can be encountered.
Conclusion: This method has demonstrated excellent diagnostic utility for fusion detection in lung tumours. Novel and rare fusions partner can be identified by targeting one gene fusion partner only. Mutations/Deletions leading to exon skipping events can be verified.

MD-04-002

Participation in external quality assessment (EQA) for BRCA testing in ovarian cancer: lessons learned and the need for continued quality improvement

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Background & objectives: Ovarian cancer is the eighth most common cancer in women for which PARP inhibitors have proved effective therapeutic agents in eligible patients. We present data from BRCA-based EQA schemes over a 3-year period (2016-2018) involving over 300 laboratories globally.
Methods: EMQN and GenQA sent identical clinically relevant samples to each EQA participant to be tested for BRCA1 and BRCA2 gene variants using their routine methodologies. The anonymised results were assessed, peer reviewed and individual laboratory and overall summary scheme reports were produced to help laboratories improve their performance and to enable comparison (benchmarking) of results and reporting.
Results: Over the three years, there has been significant improvement in the quality of testing, clinical reporting of results and standardisation with respect to the nomenclature used for the reporting of sequence variants. Improvement in the clinical interpretation is also evident but there are areas where further work is required.
Conclusion: Although errors persist, we conclude that annual participation in these EQA schemes can improve the quality of diagnostic testing

for ovarian cancer and considerably contribute to the achievement of the promise of accurate personalised medicine.
The EQA schemes in question were sponsored by an educational grant from AstraZeneca.

MD-04-003
Diagnosis of microsatellite instability in routine practice in colorectal adenocarcinoma: what we learn from the rereading of discordant cases
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Background & objectives: In the era of immunotherapies in Microsatellites Instability, efficiency of diagnostic is challenged as routine screening is not standardized. The two methods used, immunohistochemistry and molecular testing, give discordances.
These discordances are studied in a retrospective series of colorectal adenocarcinomas.
Methods: In 2128 colorectal patients, MMR and MSI status were established between 2013 and 2018. MSI testing was carried out using the pentaplex panel and MMR immunohistochemistry testing two MMR proteins (MLH1, MSH2). The primary endpoint was the rate of real discordance between MSI and MMR IHC tests. Each discordance case was thoughtfully examined to be confirmed and explored.
Results: This cohort initially presented 28 (1.3%) discordant cases. After rereading of 2 tests (immunohistochemistry and molecular testing) and/or new tests, 75.0% of discordant cases (n=21/28) were reclassified as non-discordant. After rereading and addition of MSH6/PMS2 IHC, 32,1% of discordant cases, initially pMMR (n=9/28) were reclassified as non-discordant. Among the 19 remaining discordant cases (0,68%), 4 were MSI/pMMR and 16 MSS/dMMR. For 9 of them, the discordance was the result of sampling error (47% of the remaining cases). The genetic profile of the three cases pMMR that are MSI, has to be explored. The 7 MSS/dMMR tumours demonstrated loss of any of the four MMR protein.
Conclusion: Our study emphasises the importance of accurate and careful material sampling and the advantage of combination of two complementary techniques. Discordant cases must be reviewed, since it is a major issue to select patient for appropriate treatment.

MD-04-004
Real-world challenges of EGFR mutation testing in advanced non-small cell lung cancer: complementary roles of next generation sequencing and Idylla
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Background & objectives: This real-world study aims to weigh up benefits/challenges of next generation sequencing (NGS) versus the Idylla™ Epidermal growth factor receptor mutation (EGFRm) Test in non-small cell lung cancer (NSCLC), regarding pathology lab applicability, turnaround-time (TAT) and EGFRm test performance.
Methods: A central lab analysed 193 routine diagnostic NSCLC samples in parallel with in-house validated NGS and Idylla™ EGFR Mutation Test (CE-IVD, Idylla™).
Results: Ease-of-use and short TAT were confirmed for Idylla, with shortest TAT of 1 versus 13 calendar days with NGS. 19 samples (10%) contained <5% tumour cells and were excluded from EGFRm analysis. Extracted DNA quantity was insufficient for NGS in 17 samples (10%), but 65% of those had a valid Idylla result. 27 contributive samples (16%) gave an Idylla result with reservation because Cq>26.0: 15 of those had a NGS result with reservation suggesting inferior DNA quality; 6 had insufficient DNA for NGS; another 6 had a conclusive NGS result. If sample/test quality criteria were met, 7 concordant EGFRm (5%) were detected with NGS and Idylla for known actionable variants.
Conclusion: This regional study reveals pre-analytical challenges of NSCLC biopsies. NGS and Idylla demonstrate a complementary role to improve clinically relevant molecular results. Both have distinct advantages and labs will have to determine locally the appropriate EGFRm test algorithm.
Funding: Unconditional grant provided by AstraZeneca for the purchase of Idylla cartridges, Idylla demo instrument provided by Biocartis.

Poster Sessions

PS-01 Breast Pathology

PS-01-001
Comparing histological grading of breast cancer on core biopsy and excision specimen
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Background & objectives: Histological grade of breast cancer is one of the key variables in treatment decisions following a breast cancer diagnosis. Concordance in breast cancer grade between core biopsy and excision specimens is reported as around 75%.
This study aims to look at the concordance rate of primary breast cancer grading on core biopsy and excision specimens from three centres over a period of two years reported at Addenbrooke's Hospital.
Methods: A retrospective computer search for all breast core biopsies with a B5b classification diagnosed between April 2017 and March 2019, and subsequent surgical excision specimens identified. Overall grade and the three individual grade components were extracted from the paired reports. Concordance for overall grade and each of the grade components was determined, along with percentage of cases upgraded or downgraded.
Results: A total of 980 primary surgery and 89 post-neoadjuvant cases were included.
The grade concordance following primary surgery was 82.8%, with 12.8 % upgraded and 4.4% downgraded. The concordance rates for tubule formation, pleomorphism and mitoses were 84.4%, 80.5% and 76.7% respectively.
Amongst the neoadjuvant cases overall concordance was only 45%, with upgrading and downgrading in 1.1% and 53.9% of cases respectively. Mitotic count reduction accounted for most downgrading (56.2%).
Conclusion: The concordance rate of primary breast cancer grading on core biopsy and excision specimens is in line with published literature. Reduced mitotic count following neoadjuvant chemotherapy is well described, and has been associated with improved survival, reflecting response to therapy.

PS-01-002
Adenomyoepitheliomas of the breast: a 15-year case series
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Background & objectives: Adenomyoepitheliomas (AME) of the breast are uncommon biphasic tumours composed of prominent myoepithelial cells around glandular spaces. Rarely, the epithelial or myoepithelial component, or both, becomes malignant (malignant

AME). AME should be considered in the differential diagnosis of several lesions.
Methods: We present a retrospective study reviewing the main clinical-pathological findings diagnosed in our institution in the last 15 years. All AME from 2004 to 2019 were collected, recording the relevant information from the pathology reports and medical histories. 13 cases of AME were identified, which corresponded to 24 biopsies.
Results: Patients' age ranged from 20 to 88 years (mean of 59 years). Most presented with a single tumour on imaging, but in three cases (23.1%) synchronous lesions were found.
In all the cases a core biopsy and a lumpectomy were performed. In 9 cases (69.2%) the first diagnosis was confirmed. 2 cases (15.4%) were initially misdiagnosed as juvenile secretory carcinoma and complex sclerosing lesion. 2 cases first diagnosed as AME finally appeared to be solid papillary carcinoma and complex fibroadenoma.
In one single case (7.7%) malignant criteria were detected, as both the myoepithelial and the epithelial component presented cytologic atypia and increased mitotic activity.
Conclusion: Due to its highly morphological variation, AME should be considered in the differential diagnosis of both benign and malignant breast lesions when a biphasic pattern with extensive adenosis and a prominent myoepithelial component is observed, especially in small biopsies.

PS-01-004
Molecular profiling of breast carcinoma in patients of African origin
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Background & objectives: Breast carcinoma represents a major health problem in Africa. Natural history and molecular profile of the disease remain poorly understood. We aim to study the molecular profile of African breast cancer at protein level as compared to published European data.
Methods: One North African (Egyptian, n=84) and two West African (Nigerian, n=176) breast cancer cohorts were assembled into tissue microarrays. Sections were immunohistochemically stained for ER, PR, Androgen receptor (AR), CK14, ki67, GATA3 and scored by two pathologists.
Results: 37.2% of Egyptian and 47.7% of Nigerian patients were younger than 50 years. Grade 3 carcinomas were diagnosed in 22.8% and 31.7% of Egyptian and Nigerian cases respectively. 61% of the Egyptian cases showed luminal and 23.4% triple negative phenotype. 68.3% of Nigerian patients were triple negative and only 24.2% of them were of luminal phenotype. AR was positive in 53.3% and 45.5% of Egyptian and Nigerian cancers respectively. GATA3 was positive in 79.2% of Egyptian and only 8.6% of Nigerian cases. 21.5% of Egyptian and 25.6% of Nigerian patients were of the basal phenotype. High Ki67 expression (>10%) was seen in 46.1% of Egyptian and 12.8% Nigerian patients.
Conclusion: Breast cancer in Nigerian was predominantly of triple-negative phenotype compared to Caucasians. GATA3 expression was remarkably low in the Nigerian cohort. The proportions of luminal and AR positive cancers were low in both cohorts. Basal subtype was more common in African in comparison to Caucasian patients. Unexpectedly, Ki67 showed very low expression in Nigerian patients. Our data highlight differences in the immunohistochemical profile between the African and European breast cancer.

PS-01-005
Immunohistochemical expression of tetraspanin 6 (TSPAN6) in inflammatory breast carcinoma and correlation with tumour microenvironment
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Background & objectives: Inflammatory breast cancer (IBC) is an aggressive form of breast cancer. Tumour immune microenvironment and tetraspanins are thought to play role in tumorigenesis of various malignancies. We aim to correlate Tspan6 expression with clinical parameters and characteristics of IBC microenvironment.
Methods: 124 IBC core biopsies were immunohistochemically stained for Tspan6. Multiplex immunofluorescent staining of CD4, CD8, CD68, CD20, and FOXP3 was performed on 75 cases. Machine learning with Inform 2.2.1 software was used to analyse images. Clinicopathological parameters including tumour characteristics, neoadjuvant pathological response, oestrogen receptor, HER2 status, and overall survival were collected.
Results: Half of the cases were ER positive and 29.5% were HER2 positive. 53.3% showed high grade tumour morphology. Pathological complete response was achieved in 20.9% of cases. Survival ranged from one to 138 months with a median of 32.5 months. 58.9% of cases were Tspan6 positive. Positive Tspan6 expression correlated with pathological response (p=0.04) and increased intratumoral CD20+ cell infiltration (p=0.02). Stromal CD20+ cell infiltration correlated with grade I and II (p=0.04) while high stromal CD68+ cells correlated with grade III tumour (p=0.03). High intratumoral CD68+ density correlated with no pathological response (p=0.02). Intratumoral co-localization of CD20+ and CD68+ cells correlated with positive Tspan6 expression (p=0.04).
Conclusion: The expression of Tspan6 was significantly associated with increased B-lymphocyte (CD20+) cell counts and increased response rates. B-lymphocytes were shown to be closer to other immune subsets in those patients with higher Tspan6 expression. We show for the first time Tspan6 role in tumour response to neoadjuvant chemotherapy and the ability of tumour cells to interact with the immune cells in different locations of the IBC microenvironment.

PS-01-006
Neoadjuvant chemotherapy for breast cancer – analysis of changes in breast cancer phenotype, hormonal and HER2 expression
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Background & objectives: Neoadjuvant chemotherapy (NACT) is being used for primary breast carcinoma with the aim of down-staging and facilitating conservative surgery. We assessed the effect of NACT on pathological characteristics, hormone receptors and HER2 expression and whether post-treatment re-testing is warranted.
Methods: Patients who received neoadjuvant chemotherapy for primary and operable invasive breast cancer were selected from the database of a large UK tertiary referral centre in the period between 2006 and 2019. Comprehensive clinical, histopathological and follow up data were collected. Statistical analysis of the data was performed using SPSS V.26.
Results: A total of 351 cases were identified. 68.7% patients were Caucasians and 50.4% were younger than 50 years. No special type carcinoma was diagnosed in 80.3% and 51.3% were grade 3 tumours. Pathological complete response was achieved in 23.1% of cases

particularly in HER2 positive group (35.8%) (p=0.043). 39.9% of cases with pre-treatment positive lymph nodes showed complete response. There was a change in the histological type in 20.1% (p<0.001). Significant down-grading was seen in 59% (p<0.001). ER status changed in 3% of cases. PR and HER2 status showed significant changes post-treatment in 11.2% and 5.9% of the cases respectively, (p<0.001). Patients with luminal cancer showed better overall survival (p<0.001).
Conclusion: Significant changes in tumour morphology, grade and marker expression occur following NACT. Pathological complete response was achieved in more than fifth of cases especially with HER2 positive status. We recommend o repeat testing of hormone receptors and HER2 on residual tumours. This can provide alternative treatment options for those patients.

PS-01-007
Correlation between PD-L1 expression and clinicopathological characteristics in triple-negative breast cancer patients
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Background & objectives: While immunotherapy is emerging as an effective treatment option for advanced triple-negative breast carcinoma (TNBC) patients, the clinicopathological significance of PD-L1 expression in TNBC remains unclear. Our objective was to investigate the association between PD-L1 expression and clinicopathological characteristics in TNBC.
Methods: The study group comprised 47 TNBC patients in which PD-L1 status was evaluated by immunohistochemistry with SP142 assay on the Ventana BenchMark. All PDL1(+) tumour-associated immune cells (IC) were quantified as % of the tumour area. Tumours were classified as PD-L1(+)(≥1%) or PD-L1(-)(<1%). The statistical significance of the correlation between PD-L1 status and clinicopathological characteristics was determined by chi-square test.
Results: PD-L1(+) were 24(51.1%) of the 47 TNBC patients whose median age at diagnosis was 59 (range, 39-79). 53.5%(23/43) of the primary and 25%(1/4) of the metastatic TNBC cases were PD-L1(+). 21(87.5%) of the PD-L1(+) TNBC had IC1(≥1 and <5%), 2(8.3%) had IC2(≥5 and <10%), and 1(4.2%) had IC3(≥10) score. The PD-L1(+) status significantly associated with high histological grade (G3, P=0.022), and higher proliferative index (Ki-67>35%, P=0.004), while the correlation with larger tumour size (>2 cm, P=0.055) did not reach statistical significance. No significant relationship was found between PD-L1 status and other variables such as patients` age, postoperative stage, tumour status, lymph nodal status, tumour type, vascular invasion, and p53 expression.
Conclusion: Our preliminary results suggest that PD-L1 expression is associated with several high-risk clinicopathological parameters in TNBC patients. Further larger studies are warranted to clarify the clinical relevance of PD-L1 expression in TNBC patients.

PS-01-008
The significance of tumour budding in breast carcinomas and its relationship with E-cadherin, CD44 and CTLA-4 expressions
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Background & objectives: Tumour budding(TB) (isolated <5 tumour cells at invasive edge)are thought to be effective in prognosis in breast carcinomas(BC).We aimed to investigate TB in BC using E-cadherin that provides cell-cell interaction,CD44 as stem cell marker and CTLA-4 receptor as self-tolerance marker.
Methods: 179 BC patients (172 invasive ductal, 7 metaplastic) included. For each case, buds were counted at x200 magnification. 90% for E-Cadherin and 10% for CD44 were regarded as positive staining cut-offs. Staining intensity and percentage of CTLA-4 in bud and bud microenvironment lymphocytes were evaluated. Tumours were separated into low (<5) and high bud groups (≥5) according to median bud number.
Results: High bud tumours were likely to have lymphovascular (p= 0.001), perineural invasion (p<0.001), higher pT stage(p=0.025). Tumour bud number is correlated with higher metastatic lymph node number (p<0.001) and tumour size (p<0.01). No significant relation was found between number of buds and peritumoral lymphocytic reaction, immunohistochemistry based molecular subtyping, E-cadherin, and CD44 staining (p>0.05 for all). E-cadherin was significantly lost in buds in regard to corresponding tumour (p<0.001), while CD44 staining pattern is preserved (p = 0.76). In high bud tumours, CTLA-4 staining percentage of lymphocytes in bud microenvironment was found to be significantly higher (p =0.026). Every increase in tumour bud number, decreases overall survival risk 1.07 times (1.01-1.12 95%CI, p=0.013).
Conclusion: Tumour bud is a poor prognostic factor in breast carcinomas. Increased CTLA-4 can block antitumour response, causing an increase in the number of buds. Anti-CTLA-4 immunotherapies may be beneficial in patients with high bud detected breast carcinoma.

PS-01-009
A dynamic macrophagic environment in xanthogranulomatous mastitis: a broader clue to xanthomatous diseases pathophysiology and clinical evolution?
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Background & objectives: Xanthogranulomatous mastitis is an inflammatory condition. Usually no immunohistochemistry (IHC) characterization is performed in routine surgical pathology. In this study, we explored by IHC the macrophagic polarization status of M1 and M2 subtypes.
Methods: A retrospective single-institution case retrieve was performed from the archives. IHC was performed for CD68, Arginase I, Arginase II, NOS-2, and TGF-Beta. Sequential 400x images were acquired through a microscope coupled camera and quantified through an optical threshold method in ImageJ for each marker. Statistics were executed on SPSS 25 (ANOVA and Spearman's test), p-value less than 0.05 was significant.
Results: We reviewed 11 cases. All patients were female, median age of 56,5 years (29-72). Seven (63%) cases were radiologically described as an irregular nodule/asymmetry, while 4 (36%) as circumscribed nodule. The mean ratio of IHC stain was: Arginase I (0.80), Arginase II (0.70), NOS-2 (0.85), and TGF-B (0.60). M1 polarization elements (ArgI, II and TGF-B) were correlated (p=0.005 for ArgI-ArgII and p=0.001 for TGF-B-ArgI/II). Both M1 and M2 surrogate markers were expressed in all cases, characterizing a bipolar macrophagic activation status. No significant expressed in all cases, characterizing a bipolar macrophagic activation status. No significant correlation was evidenced between macrophage status and radiological presentation, necrosis or epithelioid giant cells.
Conclusion: XM is an uncommon diagnosis and this is the first attempt at classifying MC in indexed English-language literature. The bipolar status may translate as the destructive and reparative dynamic of lesions, evoking a slow-progressing evolution until reparative pole is reached.

PS-01-010

Synchronous phyllodes tumour and ductal carcinoma in situ of breast

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Background & objectives: We present a case of a phyllodes tumour coexisting with ductal carcinoma in situ (DCIS). Rarely, those two lesions are part of the same tumour, but in this case they represent two different neoplasms.
Methods: A 70-year-old female patient presented in our hospital complaining of a lump within the left breast. The lesion appeared 5 months before and it didn't increased in size until lumpectomy was performed. For the histological examination we used hematoxylin&eosin stained slides and immunohistochemical markers: CK5, ER, Ki67 and p-53.
Results: Histology analysis of the lumpectomy specimen showed phyllodes tumour with a 20% proliferative index and approximately 10 mitoses/10 HP, p-53 positive stromal cells. Following the histopathological result, modified radical mastectomy with lymph node dissection (Madden technique) was effectuated. The mastectomy specimen revealed multifocal high grade DCIS with comedo and non-comedo pattern; CK5 was expressed focally or in a continuous layer in the myoepithelial cells, excluding an invasive component, the tumour cells being diffusely and intensely positive for ER.
Conclusion: The coexistence of phyllodes tumour and ductal carcinoma in situ as different lesions is a rare occurrence which complicates the evolution and treatment. As far as we know, this is the first case of synchronous malignant phyllodes tumour and ductal carcinoma in situ diagnosed in our department.

PS-01-011

PD-L1 status by SP142 and sp263 immunohistochemistry in triple-negative breast cancer

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Background & objectives: Triple-negative breast cancer (TNBC) is the most immunogenic subtype with a higher proportion of tumour-infiltrating lymphocytes (TILs). TNBC is very aggressive but the choice of Immunotherapy based on PD-L1 expression seems to be a promising therapeutic option for this subtype.
Methods: PD-L1 expression was evaluated with SP142 and SP263 antibody clones in 100 TNBCs included in tissue microarrays. We assessed the presence of evaluable PD-L1 staining in inflammatory cells (ICs) in the intratumoral stroma, considering positive if present in ≥1% of the area occupied by ICs. The presence of TILs were also evaluated.
Results: The percentage of patients with PD-L1 positive ICs was 46% and 82% by using SP142 and SP263 antibody, respectively. SP142 is the approved diagnostic test to identify patients who most likely would benefit for the treatment with PD-L1 inhibitor (atezolizumab).The overall percentage agreement between both systems was 55%.The SP263 PD-L1 assay (IC ≥1%) identified a larger number of TNBC than SP142 PD-L1 assay (IC ≥1%).
Conclusion: All SP142-positive cases were also SP263-positive.SP142 and SP263-positive cases displayed higher number of TILs.Additional studies about PD-L1 expression with different clones and the identification of improved biomarkers to predict clinical benefit are needed.

PS-01-012

Adenoid cystic carcinoma of the breast, 20-year experience

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Background & objectives: Adenoid cystic carcinoma (ACC) is an uncommon breast cancer (< 0.1%). ACC is typically triple negative with good prognosis. Due to its low frequency there's no therapeutic consensus. We report a series of ACC collected during the last 20 years.
Methods: A retrospective study of all breast ACC cases diagnosed in Complejo Hospitalario de Navarra, between 1998-2018 was performed. Clinical and pathological characteristics were assessed and compared with current literature. We identified twelve cases of ACC, from a total of 18,241 patients. Mean age patients years was 63.5. All of them were clinical stage I-II at diagnosis.
Results: Average tumour size of 23.84 mm. According to Nottingham grading system, eight cases were grade 1, two grade 2 and two grade 3. When compared with Ro classification three were grade 1, four grade 2 and five grade 3. One out of 12 cases was ER positive, the rest of them were triple negative. One case presented a lymph node micrometastases. None of them presented local recurrences (77.5 months mean follow-up), and one developed metastases 5 months after diagnosis. None of them were BRAF-V600E immunoreactive.
Conclusion: Prognosis of breast ACC remains uncertain.Seldom usually ACC shows an indolent course, we report one case with an aggressive behaviour.Sentinel node biopsy can't be avoided according to our study (one micrometastases).Despite of previous reports of BRAF-V600E expression in ACC, all our cases were negative.

PS-01-013

Predictive factors of pathological complete response to neoadjuvant therapy in triple-negative breast carcinoma

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Background & objectives: Triple-negative breast carcinoma (TNBC) is a heterogeneous disease, both clinically, pathologically and molecularly. There is increasing evidence that response to neoadjuvant therapy (NAT) may be affected by certain molecular and morphological features.
Methods: Core-needle biopsies of TNBC patients submitted to NAT in our institution (2016-2018) were reviewed. Clinicopathological features and expression of biomarkers (Ki67|vimentin|androgen receptor (AR)|SOX-10|p63|PD-L1) were recorded and correlated with pathological response to NAT (complete response/near complete response with ≤10% residual tumour (pCR/pNCR) group versus partial response with ≥10% residual tumour/no evidence of response (pPR/pAOR) group). Statistical significance was considered as $p<0.05$.
Results: Biopsies of 45 patients with a median age of 51 years were reviewed. 27(60%) presented as stage I-II and 18(40%) as stage III-IV. 20(44.4%) presented pCR and 6(13.3%) pNCR, after NAT. 35(77.8%) were diagnosed with invasive carcinoma NST, 40(88.9%) had histological grade 3. When comparing the pCR/pNCR group versus the pPR/pAOR group, p63 was positive in 12(46.2%)vs.4(21.1%), vimentin in 19(73.1%)vs.11(57.9%), SOX-10 in 20(76.9%)vs.10(52.6%), AR in 13(50%)vs.11(57.9%) and PD-L1 in 17(65.4%)vs.11(57.9%). The pCR/pNCR group had a significantly higher proportion of cases with Ki67>50% when comparing to the pPR/pAOR group (23(88.5%)vs.6(31.6%),$p<0.001$), corresponding to almost 17 times more odds of having pCR/pNCR in patients with Ki67>50% (OR=16.61(95%CI=[3.55;77.78])).
Conclusion: TNBC express a wide range of myoepithelial markers, as well as variable expression of AR and PD-L1, with potential therapeutic applications. High values of Ki67 are significantly associated with pCR/pNCR. The size of the cohort may have impacted our results.

PS-01-014

Breast myofibroblastoma – a benign rarity on biopsy

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Background & objectives: Breast myofibroblastoma is a rare benign mesenchymal tumour, with <90 cases described in the literature. We report a case of myofibroblastoma of the breast. The purpose of this case report was to review the characteristics of this rare neoplasm.
Methods: A 72-year old woman with a clinical history of HIV infection under antiretroviral therapy and depressive syndrome, which during her routine breast ultrasonographic screening exam was revealed a well-circumscribed hypoechogenic breast nodule with 8 mm, biopsied under the clinical and radiographic suspicion of being a fibroadenoma.
Results: Histologically, the nodule was composed by a proliferation of spindle cells arranged in haphazardly intersecting fascicles, interspersed by bands of collagen. The cells had abundant eosinophilic cytoplasm with oval nuclei, occasionally with small nucleoli; necrosis was absent, mitoses were rare (1/10 HPF), without atypia. With this morphological aspects, the differential diagnosis should include nodular fasciitis, fibromatosis, leiomyoma, spindle cell metaplastic carcinoma and spindle cell lipoma. The neoplastic cells showed diffuse and strong staining for CD34, BCL2 and oestrogen receptors, focal staining for desmin, smooth muscle actin and h-caldesmon, and were negative for cytokeratins, β-catenin, S100 and p63. The morphological and immunohistochemical features were compatible with myofibroblastoma.
Conclusion: Myofibroblastoma of the breast is a benign mesenchymal tumour composed of fibroblasts and myofibroblasts, which could have a wide variety of morphological features, frequently similar to spindle cell lipoma. The molecular study of this entities has revealed the same genotype.

PS-01-015

Comparison of the hormone receptor status, HER2 status and Ki67 index between preoperative core needle biopsy and surgical specimens in invasive breast cancer

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Background & objectives: Accurate analysis of hormone receptor status, HER2 status and Ki67 of breast core needle biopsy (CNB) tissue is important for determining neoadjuvant systemic therapies for invasive breast cancer.
Methods: We aimed to evaluate the concordance rate (CR) of oestrogen receptor (ER), progesterone receptor (PR), HER2, and Ki67 between CNBs and surgical specimens. The study was conducted with invasive breast cancer patients who underwent surgery after CNB without preoperative systemic therapy at Moscow Bakhrushin brothers Hospital between December 2013 and December 2019.
Results: ER, PR, HER2, and Ki67 were analysed using immunohistochemistry. ER and PR were evaluated by Allred score (0-8). HER2 was graded from 0 to +3, and all 2+ cases were tested with in situ hybridization. The labelling index of Ki67 was counted manually. The cutoff value for Ki67 was 20%. In total, 239 patients were evaluated. The median age was 65 (range, 29 to 88 years).The CRs of ER, PR, HER2, and Ki67 were 97.1% (kappa, 0.805; p<.001), 89.5% (kappa, 0.589; p<.001), 97.4% (kappa, 0.81; p<.001), and 79.1% (kappa, 0.555; p<.001), respectively.
Conclusion: CNB was reasonably accurate for determining ER, PR, HER2 and Ki67.

PS-01-016

Clinical features and pathological findings in a series of MRI-guided breast biopsies

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Background & objectives: Breast magnetic resonance imaging is used for high-risk screening and in evaluation of extent of disease in newly diagnosed breast cancer patients. We wanted to correlate the pathology results of MRI-guided biopsies to MRI findings and patient clinical history characteristics.
Methods: We retrospectively reviewed clinical history, MRI features and pathology outcomes of MRI-guided vacuum needle biopsies performed at our institution between September 2015 and July 2019.
Results: 45 patients were biopsied. 48% had newly diagnosed breast cancer, the strongest predictor of malignancy (malignancy rate 56%). 46% of biopsies were from women on surveillance (malignancy rate 16.7%) and 6% in women with conventional imaging and suspicious symptoms (malignancy rate 33%). 18 (40%) lesions were malignant: 12 invasive carcinomas; 6 DCIS. Non-mass like enhancement was the most frequent descriptor of both malignant (8/19, 42.1%) and benign lesions (11/26, 42.3%).
Conclusion: MRI detects malignancies undetected by other imaging modalities but also detects a wide variety of benign lesions and MRI features of both can be similar necessitating biopsy for histological evaluation. There should be a low threshold for proceeding to MRI-guided biopsy particularly in women with newly diagnosed breast cancer.

PS-01-017

Two cases of intramammary metastases from cutaneous melanoma

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Background & objectives: We present here two cases of histologically diagnosed metastatic small cell achromatic malignant melanoma. Each of these cases presented a challenge for the pathologist in a different way.
Methods: The first case is of a 49-year-old woman with subsequent sectoral resections of both breasts (2017 and 2019), histologic findings interpreted as triple negative mammary carcinoma. Later on, pulmonary lesions appeared and transthoracic thick-needle biopsy was performed. Histology and immunohistochemistry revealed small cell achromatic malignant melanoma. Meanwhile, regressive melanoma of the skin over the sternum was suspected.
Results: So, previous biopsies were revised and the diagnosis of achromatic malignant melanoma, producing bilateral mammary and pulmonary metastases was confirmed. Finally, BRAF V600 mutation was proven in the breast metastasis. The second case is a 45-year-old woman, with a malignant melanoma of the breast skin 13 years ago. Because of the staging (pT1, Clark 1) treatment with Calgevax was performed only. In 2020 intramammary lesion was detected, clinically suspected for mammary fibroadenoma. The lesion was surgically removed and the histology and immunophenotyping were consistent of a small cell malignant melanoma - a metastasis of the primary skin tumour.
Conclusion: Achromatic melanoma, "the great imitator" has always been a challenge for pathologists. In the first case metastases were interpreted as a primary tumour, and in the second – late metastases appeared. Careful interpretation of histological findings with correlation of clinical data is of pivotal importance.

PS-01-018

High HER2 signals and HER2/CEP17 ratio tumours achieve better responses in breast cancer

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Background & objectives: HER2 molecular subtype is one of those which achieves most pCR rates in breast cancer. The objective of this study is to evaluate the relationship between HER2 signals and pCR and HER2/CEP17 ratio and response to neoadjuvant chemotherapy.
Methods: 37 HER2-overexpressing early breast cancer patients who had received neoadjuvant trastuzumab were included in this study. We performed in situ hybridization and measured HER2 and chromosome 17 centromere (CEP17) copy numbers. HER2/CEP17 ratio was calculated. Analysis between that and response to neoadjuvant chemotherapy assessed by RCB were examined.
Results: In trastuzumab treated patients, 83,8% were HER2-Luminal and 16,2% HER2 hormone receptor (HR) negative. 46% of patients were Nottingham grade 2 and 54% were grade 3. From 37 patients, 29,7% achieved pCR. 43,5% of patients with high-level amplification (HER2/CEP17 ratio ≥ 6) obtained pCR compared to 2,7% of patients with low-level amplification (HER2/CEP17 <6 ratio) (p=0.030). Regarding to HER2 number of signals, 27% of patients with HER2>6 signals per nuclei obtained pCR compared to 2,7% of patients with HER2<6 signals per nuclei (p = 0.04852).
Conclusion: An HER2 copy number>6 in the pretherapeutic tumour biopsy is associated with a significantly higher pCR rate. Also HER2/CEP17 ratio>6 is related to pCR in HER2+ tumours treated with neoadjuvant trastuzumab.

PS-01-019
Columnar cell lesion in breast tissue biopsies: an often underreported diagnosis
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Background & objectives: Columnar cell lesion (CLL) of the breast belongs to the spectrum of proliferative breast disease with premalignant potential, although it is often underreported. This study investigated the frequency of CCL in non-malignant breast biopsies in a single general pathology practice.
Methods: H&E stained slides of non-malignant breast biopsies received over a four-year period were reviewed for the presence of columnar cell features (columnar cell change with/without atypia, columnar cell hyperplasia with/without atypia, and flat epithelial atypia) following established protocol. Information on patient age at diagnosis was obtained from the surgical pathology records. Data generated was presented as percentages.
Results: Columnar cell lesions were present in 22 (7.7%) of 286 cases reviewed. Of these, 18 (81.8%) were columnar cell change, whilst 2 (9.1%) each were columnar cell hyperplasia and flat epithelial atypia. The median age was 39 years (18-64years) with modal age at 5th decade of life. Eleven (50%) cases occurred in individuals who were aged 40 years and below. Flat epithelial atypia was seen at 4th and 5th decades.
Conclusion: This study suggests that CCL occur in about 7% of benign proliferative breast lesions in our practice and are predominantly non-atypical. The observed median age of occurrence suggests a frequent occurrence in the young. This might influence the earlier occurrence of breast cancers in our population.

PS-01-020
Interaction between the expression of mTOR and PD-L1 signalling pathway in triple-negative breast cancer
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Background & objectives: Programmed death ligand 1 (PD-L1) and mammalian target of rapamycin (mTOR) are pathways expressed on tumour cells that interact with the immune system function. We investigated the relationship between their expression in Triple-Negative Breast Cancer (TNBC) based on clinicopathological variables.
Methods: 50 consecutive TNBC cases were collected, the histopathological report and paraffin block were obtained from each case. The expression of mTOR and PD-L1 on tumour cells was evaluated by immunohistochemistry using their respective antibodies. The results were correlated with the age, clinical stage, metastatic lymph nodes and tumour size.
Results: The results from the immunohistochemistry show a positivity for mTOR in 38 cases (76%) and for PD-L1 in 11 cases (22%), a joint expression of 21.05% was demonstrated. PD-L1 and mTOR expression did not correlate with clinical stage, age, metastatic lymph nodes or tumour size, however the analysis of the number of metastatic lymph nodes shows a slight significant tendency in tumour cells when both markers were shown positive (p=.068). The results of PD-L1 and mTOR appears to have a correlation with the lymph nodes status based on the TNM staging system.
Conclusion: mTOR pathway has been poorly studied in TNBC and seems to favour PD-L1 expression, the results suggest new scenarios with drugs that inhibit both pathways. More clinical response-related TNBC cases are needed to assess the correlation between mTOR and PD-L1.

PS-01-021
A case of tall cell carcinoma with reversed polarity of the breast with a recent history of gastric carcinoma
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Background & objectives: Tall cell carcinoma with reversed polarity (TCCwRP) is a rare breast tumour. Despite the triple negative profile, it has an indolent behaviour. However, cases with lymph node and bone metastasis were published in literature.
Methods: The patient was a 62-year-old female who complained of multiple lumps in both breasts and had a history of surgery and chemotherapy for gastric carcinoma, 12 months before mastectomy. Grossly, there were two tumours, measured 14 and 13-milimeters, which were partly and totally well-demarcated respectively. Both had brown and white cut surfaces.
Results: Microscopically, both tumours were composed of nests surrounded by artefactual empty space and separated by dense fibrous stroma. Both exhibited no sign of chemotherapy-induced regression. The tumour cells were columnar to cuboidal with abundant eosinophilic cytoplasm and oval, bland-looking nuclei which were located at the apical rather than basal pole of the cells. Foci of ductal carcinoma in situ were also found. Lymphovascular invasion and necrosis were absent. One of 22 axillary lymph nodes showed metastasis. The neoplastic cells were positive for GATA-3 and mammaglobin and negative for PAX-8 and TTF-1, excluding metastasis of thyroid carcinoma. They displayed diffuse expression of cytokeratin 7, cytokeratin 5/6 and 14, and were negative
Conclusion: for oestrogen receptor, progesterone receptor and HER2. Ki67 proliferation rates were 18% and 15%, respectively. EMA highlighted the apical membranes of neoplastic cells and pointed out the apical positioning of nuclei, therefore was helpful to designate the term reversed polarity. TCCwRP is a rare breast neoplasm, may mimic thyroid carcinoma metastasis. Hence, pathologists should keep it in mind and be aware of its morphological and immunohistochemical features.

PS-01-022
High molecular weight cytokeratin expression in ductal carcinoma in situ of the breast: a diagnostic pitfall
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Background & objectives: In breast pathology, the distinction between intraductal epithelial hyperplasia of usual type (HUT) and

neoplastic lesions is challenging and often requires immunohistochemistry for confirmation. However, deviations from well-known patterns of expression exist in routine practice making such diagnoses challenging.
Methods: We present two cases of mammary Paget's disease (PD) that underwent central excision of the nipple-areolar complex.
Histology confirmed PD with underlying intraductal epithelial proliferations difficult to differentiate between HUT and intermediate grade DCIS. Basal cytokeratins (CK5/6 and CK14) and oestrogen receptor (ER) immunohistochemical staining were performed to differentiate between the two entities, as well as HER2.
Results: Immunohistochemistry showed mosaic positivity of both basal cytokeratins akin to HUT. ER immunohistochemistry was heterogeneous in one case and negative in the other. However, the diagnosis of DCIS was confirmed in both cases by strong HER2 positivity and by extension of the proliferating cells into the epidermis as PD. Further morphological evaluation revealed nuclear hyperchromasia and occasional prominent nucleoli, features not seen in HUT.
Conclusion: These cases demonstrate the importance of cellular morphology in diagnosing intermediate and high-grade DCIS and the potential diagnostic pitfall of relying on immunohistochemistry alone. The mosaic pattern of expression for basal CKs may represent basal-like differentiation of the neoplastic cells and this pattern of immunostaining should be interpreted in the appropriate context.

PS-01-023

Comparison of the pam50 intrinsic subtypes with immunohistochemistry in breast cancer patients

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Background & objectives: PAM50 classifies breast tumours, predicts risk of recurrence and evaluate the need of adjuvant chemotherapy. Clinical subtyping, however, is based on immunohistochemistry (IHC) biomarkers. We aimed to analyse the discordance between immunohistochemistry based surrogate subtyping and PAM50 intrinsic subtypes.
Methods: PAM50 intrinsic subtypes were determined according to 50 cancer genes expression in a total of 74 breast tumours, oestrogen receptor positive, HER-2 negative, T<=30 mm, pN0, pN1mi or pN1. Subtype Luminal A was defined by IHQ as Ki67 < 14% and Luminal B as Ki67 >=14%. Clinicopathological parameters were collected, including grade and stage in all tumours.
Results: A 33% of tumours, showed discrepancy between IHC subtype and PAM50 intrinsic subtype in our study. Out of 41 Luminal B tumours subtype performed by IHC, PAM50 reclassified 7 (17%) as Luminal A and low risk of recurrence, indicating that no adjuvant chemotherapy was needed. On the other hand, 7 (20.5%) Luminal A tumours classified by IHQ, changed to high risk by PAM50, being able to benefit from chemotherapy. The tumours reclassified by PAM 50 as low risk of recurrence were grade 1 and stage IA (71.4% Vs 17.7%, p=0.036) while the tumours reclassified as high risk, were grade 2 and stage IIA (60.0% Vs.47.8% p=0.048).
Conclusion: A substantial portion of tumours showed discrepancy between IHC subtype and PAM50 subtype in our study. Gene expression-based classification shifted some tumours categorized as low risk by IHQ criteria to higher-risk subtypes and vice versa. Current IHC-based classification could mislead the treatment and result in poor outcome in 20% of breast cancers. Subtypes from PAM50 seem better able to predict tumours with poorer outcomes compared with using IHC markers.

PS-01-024

A rare case of tumour-to-tumour metastasis from invasive lobular breast carcinoma to ovarian cystadenoma

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Background & objectives: Tumour-to-tumour metastasis is an unusual phenomenon. The most frequently reported donor tumours are lung and breast carcinomas, whereas meningiomas represent the most common recipients. We hereby describe a rare case of metastasis from invasive lobular breast carcinoma to ovarian cystadenoma.
Methods: A 60-year-old female presenting with a 9 cm ovarian mass and a right breast lesion. Ultrasonography report of the breast lesion revealed features suggestive of malignant mass (BIRADS 4b). Fine needle aspiration of the breast tumour yielded malignant smear. Patient underwent right modified radical mastectomy, right oophorectomy and infracolic omentectomy.
Results: Histopathologic evaluation of the breast mass revealed invasive lobular carcinoma, positive for oestrogen, progesterone receptors and Her2-neu negative. The ovarian mass exhibited features of benign ovarian cystadenoma harbouring a distinct malignant component, histologically similar to invasive lobular carcinoma of the breast. Immunohistochemical assessment of the aforementioned invasive component using GCDFP15 and E-cadhrin confirmed the breast origin of the tumour and the lobular carcinoma diagnosis. Other markers were used to exclude metastasis from different sites such as Napsin-A and CDX-2
Conclusion: This is the first reported case of invasive lobular breast carcinoma metastasis to ovarian cystadenoma. The possibility of tumour-to-tumour metastasis rises if any tumour exhibits dimorphic histology, which is diagnostically challenging. This indicates poor outcome, disease dissemination and aggressiveness.

PS-01-025

Audit of histopathology reports for mastectomy specimens in a tertiary hospital, south west Nigeria

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Background & objectives: Mastectomy remains the mainstay of the treatment of breast cancer in Nigeria. Pathologic diagnosis and reporting is one of the basic available resources. It is therefore critical that reports contain key diagnostic and prognostic indicators guide the management of patients.
Methods: Copies of histopathology reports were retrieved from the histopathology department for all mastectomies reported between January 2016 and December 2019. Completeness for reporting of the mastectomies was examined for 7 key items: tumour size, tumour type, histological grade, margins of excision, vessel invasion, nodal status and TNM stage. The items were indicated as present or absent from the report.
Results: The histological type had the highest frequency of 100%, while the lymph node status and tumour size were reported in 92.3% and 82.1% respectively. The least frequently reported items were the TNM staging and the vessel invasion at 23.1% and 25.6% respectively. Only 2.6% of reports had all the variables reported. In addition, histological grade was reported in 76.9% while statements about margins of excision were contained in 71.8% of the report.
Conclusion: There is currently no local guidelines to adhere to in the reporting of mastectomy specimens, therefore having discussed the results with the local team, the royal college of pathology datasets have been adopted for use. Synoptic reporting will allow for more consistent and complete reports. A similar study will need to be repeated after the synoptic reporting is introduced to evaluate its effectiveness in improving the quality of pathology reports.

PS-01-026

Neuroendocrine neoplasms of the breast showing peculiar forms of recurrence and/or metastasis

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Background & objectives: This is the first report of a mammary neuroendocrine tumour (NET) showing a relapse related to needle implantation (Case 1). Furthermore, we describe the first case of a NET resulting in a huge tumour embolization in the breast (Case 2).
Methods: [Case 1] A 60-year-old Japanese woman presented with skin retraction in the right breast. Ultrasound-guided core needle biopsy (CNB) of the irregular, hypoechoic breast mass yielded a pathological carcinoma diagnosis. [Case 2] A 42-year-old Thai woman presented with a palpable mass in the left breast. Ultrasonography revealed a sharply-marginated, hypoechoic tumour, with a cranially-extending lumen-like structure filled with solid tumour.
Results: [Case 1] A poorly-delimited tumour (12x10mm) was composed of a trabecular growth of polygonal cells with a highly-vascular stroma. We noted small subcutaneous scars with disseminated neoplastic cell clusters, causally-related to the preoperative CNB. Neoplastic cells were immuno-positive for chromogranin A and NCAM. She had become aware of a mass at the skin puncture site for the previous CNB 47 months after surgery. We pathologically confirmed the recurrent NET. [Case 2] The lesion was histopathologically diagnosed as a mammary NET, measuring 17x15mm, with extensive intravenous spread. She postoperatively received adjuvant chemotherapy. However, bone metastases were identified 36 months after surgery and liver metastases were detected 47 months after surgery.
Conclusion: [Case 1] To minimize the clinical impact of tumour displacement, we need to consider preventive radiation therapy for needle pathways, their excision and/or use of vacuum-assisted biopsy devices (Virchow Archiv, 2015). [Case 2] Our patient, who had a relatively-small, well-differentiated NET with no nodal involvement and a low MIB-1 index (6.7%), followed a rather aggressive clinical course with distant metastases, probably associated with the extraordinary intra-mammary tumour emboli (Histopathology, 2014).
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PS-01-027

Immune microenviroment in triple negative breast carcinoma

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Background & objectives: Immune microenviroment has been researched in many cancer types including breast carcinoma, especially the triple negative subtype. Our aim is to evalaute immune microenviroment in triple negative breast carcinoma and to understand its relationship with prognosis.
Methods: Fifty-one cases of triple negative breast carcinoma with no history of neoadjuvant therapy, whose resection specimens were examined in our department between 2012 and 2017, were retrospectively evaluated using CD8 (C8/144B, monoclonal, mouse, Dako), FOXP3 (EP340, monoclonal, rabbit, Epitomics), PDL1 (SP142, monoclonal, rabbit, Ventana) antibodies.
Results: Median age was 49. Majority of the cases (54.9%) were diagnosed as invasive breast carcinoma, no special type; while 35.3% were lymphocyte-predominant breast carcinoma and 9.8% were metaplastic carcinoma. All cases were histological grade 3. Nine (17.6%) cases ended with exitus. Five-year overall survival rate was 75.6%. Immunexpressions of all three antibodies were found to be correlated with each other ($p<0.01$). Lymphovasculary invasion and axillary lymph node metastasis were associated with lower FOXP3 expression ($p<0.05$). Higher expression of PDL1 was found in lymphocyte-predominant breast carcinoma cases ($p<0.01$). PDL1 expression was related to prolonged overall survival ($p<0.01$), whereas neither CD8 nor FOXP3 was associated with survival.
Conclusion: Tumour immune microenviroment is an important prognostic parameter in triple negative breast carcinoma. Further investigation is needed to better understand the prognostic role of immune microenviroment and to manage medical therapy.

PS-01-028

Expression of WNT, Hedgehog, NOTCH, PI3K, NF-kB, PTEN signalling molecules in HER-2 overexpressed and triple negative breast cancer with positive and negative ALDH1A1 expression in cancer cells

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Background & objectives: We investigated the expression of NF-kB, PI3K, PTEN molecules, as well as WNT, Hedgehog, NOTCH in cells of triple negative and HER-2 overexpressed breast cancer with high and low content of cancer stem cells (positive and negative ALDH1A1 expression).
Methods: We studied 110 cases of invasive breast cancer. To determine stem cells in tumour population, the presence of ALDH1A1 protein in cancer cells was investigated. In all cases, expression of oestrogen, progesterone receptors, HER-2 and Ki-67 was studied by immunohistochemistry to determine a subtype of breast cancer. The expression of molecules PI3K, NF-kB, PTEN, WNT, Notch, Hedgehog was also explored.
Results: All cases, that were investigated for the expression of ALDH1A1, were divided into two groups - with a low content of cancer stem cells (cases with expression of ALDH1A1 0 and 1+), and with a high content of cancer stem cells (cases with expression ALDH1A1 2+ and 3+). The results are shown in the Table.

		NF-kB	PI3K	PTEN	NOTCH	WNT	Hedgehog
Low level ALDH1A1	Triple negative	100%	98%	20%	27%	33%	14%
	HER-2 overexpressed	100%	100%	11%	30%	29%	7%
High level ALDH1A1	Triple negative	100%	100%	33%	11%	11%	0%
	HER-2 overexpressed	100%	100%	9%	36%	36%	0%

Conclusion: Activation of Notch and WNT signalling pathways was more common for cells of HER-2 overexpressed than Triple-negative subtype ($p<0.05$) in the group with high level of ALDH1A1. Expression of Hedgehog signalling molecule was only positive in the group of low level of ALDH1A1 expression, it was higher in cancer cells of Triple negative subtype than HER-2 overexpressed subtype ($p<0,05$). PTEN signalling was found more often for Triple negative cases ($p<0.05$).

PS-01-029

The value of templates to histopathology trainees in cut-up of breast specimens

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Background & objectives: Junior histopathology trainees often find cut-up daunting. Cut-up is often protocol driven, and especially for similar specimens like breast, it suits template usage. Wycombe ST1 to ST4 histopathology trainees were not using cut-up templates. They reported a lack of confidence in cut-up of mastectomies and wide local excisions

(WLEs) and problems with dictation due to lost recordings. 88% of the trainees felt templates would be helpful.
This project aimed to assess whether cut-up templates help trainee confidence and dictation problems.
Methods: The authors wrote templates for breast WLE and mastectomy cut-up using Standard Operating Procedures and Royal College of Pathologists datasets. They were reviewed by departmental consultants, trainees and the lead biomedical scientist (BMS) and trialled in cut-up for 6 weeks. The BMS completed the printed template as requested by the trainee performing cut-up. Trainees answered pre and post-trial questionnaires.
Results: All trainees used both templates during the trial. 75% found them very helpful. For 39% it helped as a memory aide, 33% it made dictation easier and 11% it helped with a lost dictation. Trainee confidence improved from 37% to 75% post-trial. For 75% it was quicker or time equivalent to complete the case. 100% would continue using the templates. 75% would like templates for other specimens, especially renal.
Conclusion: Wycombe Hospital histopathology trainees found templates for breast WLE and mastectomy specimens valuable and helped with dictation problems. Trainee confidence improved. Most wanted further templates for other specimens and a template for renal specimens is currently being trialled with trainees.

PS-01-030
Fibulin-2 expression associates with stromal elastosis and is inversely related to vascular invasion in breast cancer
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Background & objectives: Stromal elastosis relates to good prognosis in breast cancer, and fibulin-2 helps to stabilize elastic fibres in basement membranes. We explored perivascular fibulin-2 expression in relation to elastosis content, vascular invasion, molecular subtypes, tumour detection mode, and breast cancer survival.
Methods: We performed a population based retrospective study of invasive breast cancers from the Norwegian Breast Screening Program, Vestfold County (2004-2009) including 200 screen-detected and 82 interval cancers. Perivascular fibulin-2 staining was semi-quantitatively graded and dichotomized using immunohistochemistry. Elastosis content was graded and dichotomized as high and low expression, whereas lymphatic (LVI) and blood vessel invasion (BVI) were recorded with immunohistochemistry.
Results: High perivascular fibulin-2 expression was strongly related to stromal elastosis ($p<0.001$), and inversely associated with BVI and LVI ($p<0.001$ for both). High perivascular fibulin-2 was associated with luminal breast cancer subgroups ($p<0.001$) and inversely with interval cancers compared with screen-detected tumours ($p<0.001$). By univariate analysis, low perivascular fibulin-2 was associated with reduced recurrence-free survival ($p=0.002$) and disease specific survival ($p=0.019$) compared to high perivascular fibulin-2 expression.
Conclusion: Presence of low perivascular fibulin-2 expression was strongly related to vascular invasion, low stromal elastosis, non-luminal breast cancer subtypes, interval presentation, and adverse prognosis.

PS-01-032
A new method based on internal extractive electrospray ionization analysis of breast cancer samples for detection metastases in sentional lymph nodes
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Background & objectives: Breast cancer is accompanied by metastases in lymph nodes in about 30% of cases. Pathological methods is used to verify metastatic lymph nodes. Faster and specific methods are required for the identification of metastatic lymph nodes directly during the surgery.
Methods: New method based on internal extractive electrospray ionization (iEESI) combined with high-resolution mass spectrometry analysis was developed. It allows to perform rapid (less than in 5 minutes) molecular profiling of the breast cancer tissue and the sentional lymph nodes tissue with regard to presence of metastatic lesion. Distinctive feature of proposed method allows direct extraction of whole-volume tissue samples rather than their surface.
Results: Rapid diagnosis of the metastatic lesion of the signal lymph nodes upon invasive breast cancer on the biopsy tissue samples was performed in 50 patients. The signals of differential metabolites associated with the occurrence of lymphatic lesion were identified using high resolution tandem MS analysis and reference LC-MS analysis. Bioinformatics approaches were developed in order to study the complex relationships between the identified metabolites. It makes it possible to substantially increase the sensitivity, accuracy and reproducibility of analysis compared with existing analogues. New analytical advancements were implemented which allow the sequential ionization of lipids, metabolites and proteins from the same single biopsy tissue sample.
Conclusion: A fast method, which allows to avoid injury of lymph nodes, has been developed for the verifying breast cancer metastases in sentional lymph nodes based on direct mass spectrometric analysis. A mechanism for metastasis to sentional lymph nodes in breast cancer was proposed.
The reported study was supported by RFBR grant, research project No.19-515-55021

PS-01-033
Methylation of genes CDO1 and MEST in primary ER-positive breast cancer with metastases to lymph nodes
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Background & objectives: Aberrant methylation of genes is associated with the development of malignant tumours; however, there is insufficient data on the relationship between methylation and metastasis to regional lymph nodes.
Methods: 116 patients with breast cancer were enrolled into the study. Of these, 61cases had Luminal A subtype and 49 cases Luminal B subtype by immunohistochemistry. To assess the level of methylation MS-HRM (Methylation Sensitive High-Resolution Melting) method was used on breast cancer samples taken immediately after surgery. The results were confirmed by pyrosequencing.
Results: The aim of this work was to access the relationship between the level of genes CDO1 and MEST methylation in the primary breast tumour and metastasis to lymph nodes. It was found that in the tumours of LumB subtype there was a statistically significant increase in the level of gene CDO1 methylation and a decrease in the level of gene MEST methylation. In the tumours of LumA subtype there was an increase in the level of both CDO1 and MEST genes methylation. The differences were close to statistical significance (for Mest gene $p=0.12$, for CDO1 gene $p=0.09$).
Conclusion: The results obtained expand our knowledge about pathogenesis of breast cancer development. Along with other molecular events associated with the primary tumour they can predict metastasis to lymph nodes.
The reported study was supported by governmental grant № НИОКТР AAAA-A18-118053190016-7

PS-01-034

Antibody clone-dependent thyroid transcription factor-1 expression in a primary breast carcinoma

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Background & objectives: Thyroid Transcription Factor-1 (TTF-1) can be a useful marker for lung and thyroid primaries. However, TTF-1 expression has been reported in up to 2.5% of breast carcinomas. There are two main commercially available TTF-1 antibody clones: 8G7G3/1 and SPT24.
Methods: A 60-year-old woman presented with a large tumour involving the entire right breast together with multiple pulmonary and mediastinal tumour masses. Due to the aggressive course, the working diagnosis was a lung primary producing breast metastasis. Breast and lung core needle biopsies both revealed a TTF-1, ER and GATA3 positive adenocarcinoma, while napsin A, PR and HER2 were negative.
Results: Endocrine therapy was administered, leading to significant reduction in the size and number of pulmonary and mediastinal metastases. Two years later, a sanitary mastectomy was performed. The breast tumour was positive for ER and GATA3, and negative for napsin A and PR. This time, TTF-1 was performed with both commercially available clones, showing a positive reaction with SPT24 and a negative reaction using the 8G7G3/1 clone.
Conclusion: Breast metastases from extramammary malignancies are rare (0.2-2% of all tumours), with lung being one of the most frequent primary sites. TTF-1 clone selection can have clinical significance in the workup of a potential metastatic lung adenocarcinoma, especially in settings with limited amount of tumour tissue. In the setting of breast vs lung primary, an antibody panel including napsin A and GATA3 should be used, as occasional ER-positive lung carcinomas as well as TTF-1 positive breast carcinomas have been documented.

PS-01-035

The CD8 / FOXP3 ratio of tumour infiltrating lymphocytes (TILs) predicts the effect of adjuvant radiotherapy in breast carcinomas; an immunohistochemical analysis in the SweBCG91RT trial

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Background & objectives: The aim was to analyse the predictive role of the CD8/FOXP3 ratio of tumour infiltrating lymphocytes (TILs) on effect on radiotherapy (RT) in the SweBCG91RT trial with the primary endpoint of breast cancer recurrence (BCR) within 10 years.
Methods: Patients with stage I and IIA breast cancer were randomised to breast-conserving surgery and postoperative radiotherapy (n=444) or surgery only (n=483) between 1991-1997. Median follow-up was 15.2 years. Primary tumours were scored for TILs on whole slides. CD8 and FOXP3 were scored on tissue microarrays using immunohistochemistry and the absolute stromal area occupied by the respective cell type was calculated.
Results: Among unirradiated patients, a high absolute CD8:FOXP3 balance (CD8High/FOXP3Low) was associated with a decreased risk of BCR (HR 0.40, CI 95% 0.21-0.78, p=0.005) compared to the CD8Low/FOXP3Low group (HR 1.0). RT produced a significant risk reduction of BCR among CD8Low/FOXP3Low tumours (HR 0.49, CI95% 0.35-0.70, p<0.001), but not among tumours with CD8High/FOXP3Low (HR 1.60, CI 95% 0.71-3.6, p=0.26). The interaction between RT and immophenotype was significant for any recurrence (p=0.024).
Conclusion: As the values (CD8High/CD8Low and FOXP3High/FOXP3Low) were combined to create groups reflecting the absolute balance between CD8+ T cells and FOXP3+ T regulatory cells, it showed that a favourable immune response (CD8High/FOXP3Low) was protective for breast cancer recurrence, moreover it was predictive of less benefit from adjuvant radiotherapy. These results may have an impact on therapy choice regarding postoperative radiotherapy in early breast cancer.

PS-01-036

Evaluation of angiogenesis as a marker of progression of invasive carcinoma of no special type

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Background & objectives: Activation of angiogenesis is considered a key step in the invasion and metastatic spread of malignant tumours.
Methods: We studied 86 cases of invasive carcinoma of no special type (IC NST). The material was studied using light microscopy using IHC. We used antibodies CD 34, CD 31, VEGF, MMP2. Cases were divided into 3 groups depending on the degree of differentiation - G1 21 cases (24.4%), G2 22 cases (25.5%) and G3 43 (50%).
Results: The endothelium of atypical capillaries was unevenly stained with CD34, marked expression of VEGF and negative expression of CD31 were noted. The dependence of the degree of vascularization on the degree of differentiation of carcinoma was established. In low-grade carcinomas, the number of microvessels in the field of view increased. A significant difference in vascular density was detected in groups of tumours with moderate and low differentiation (p = 0.019). The largest difference in the number of vessels was determined when comparing neoplasias in groups with the degree of differentiation G1 and G3 (p = 0.011).
Conclusion: Establishing the number and density of tumour microvessels can help establish the degree of differentiation and determine the prognosis of the course of non-specific breast carcinoma, and continue to be used as an additional criterion in the classification of non-specific breast carcinomas.

PS-01-037

1% ER positive is not any positive cells

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Background & objectives: ASCO/CAP recommends that ER status should be considered positive if 1% or more of tumour cells demonstrate positive nuclear staining. We tested the validity of digital image analysis algorithms for the assessment low-positive ER staining in breast carcinoma.
Methods: Eighteen ER+/HER2- invasive carcinomas of NST with 1-10% expression by visual assessment were scanned (Pannoramic 250, 3D Histech) and assessed by digital image analysis (DIA) algorithms Qupath and QuantCenter (3D Histech) of whole slides images (WSI). The degree of inter observer variation was determined by using Kappa statistics (less than 1% and 1%≥) and intraclass correlation coefficient (ICC).
Results: In 40% DIA showed ER negative compared to visual positive assessment in same cases. Agreement between DIA and VA was weak (weighted kappa =0,46). ICC between DIA and VA was weak (ICC=0,58).
Conclusion: One percent as cutoff is based on the premise that patients derive benefit from endocrine therapy even with minimal receptor activity. False positive results lead to the fact that patients do not receive the necessary therapy as with triple negative carcinomas. Digital image analysis algorithms need to consider in group of low ER expression. It can be an instrument to decreases inter raters variability.

PS-01-038

Characterisation of PD-L1 expression in triple negative breast carcinoma (TNBC) in a comprehensive cancer centre in Mexico City

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Background & objectives: Breast cancer represents one of the main causes of cancer-related death. TNBC has few therapeutic options, recently the combination of chemotherapy plus immunotherapy (nab-paclitaxel+atezolizumab) showing advantage for PD-L1 positive patients. The use of PD-L1 immunohistochemistry as a biomarker shows numerous
Methods: difficulties making hard to extrapolate its analytical performance across populations and tumour histologies. We present the first study in Mexico to evaluate PD-L1 expression in TNBC using the SP142Ventana companion diagnostic-assay We reviewed the registries of the Pathology Department for TNBC. Inclusion criteria were tissue availability and medical information. IHC was performed and evaluated
Results: using the PD-L1 SP142 Ventana-Assay criteria for TNBC. Fifty cases were identified fulfilling inclusion criteria from 2009-2019. Average age at diagnosis was 54.9 years (+/- 15.9 yo). The tissue available for study was: primary breast tumour (84%), metastasis (14%) and 2%(NA). Fifty-two percent of our cases were PD-L1 positive, (IC1-22%, IC2-10%, IC3-20%). Different histologies were represented(NOS(30%), medullary-like(8%), apocrine(6%), metaplastic(4%), and pleomorphic lobular (2%), with a trend for PD-L1 positivity in higher grade tumours(84% of G3 PD-L1+ vs 64% G2 PDL-1+). We found no difference on age at presentation, smoking history, or association with previous treatment on PD-L1(positive/negative) groups.
Conclusion: We found a slight increase of PD-L1 positivity compared to the IMPASSION130 study(52%vs41%), although sample bias is a potential issue due to the number of cases studied. TNBC is a group with different immunogenicity profiles and histologic characteristics

PS-01-039

Expression of melanoma antigen - as in peripheral blood circulating tumour cells (CTCs) of breast cancer patients

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Background & objectives: The purpose of our study is to detect the expression of MAGE-A genes, including MAGE-A1,-A2,-A3,-A4and-A6, in peripheral blood circulating tumour cells of breast cancer patients.
Methods: Multiplex nested RT-PCR was used to detect the level of MAGE-A mRNA in peripheral blood circulating tumour cells of 106 breast cancer patients and 30 health donors. Restriction endonuclease treatment was used to detect the expression of each member of MAGE-A family, including MAGE-A1,-A2,-A3,-A4 and -A6 genes.
Results: The expression rate of MAGE-A gene was 40% (43/106) in breast cancer peripheral blood. The frequency of MAGE-A expression in breast cancer peripheral blood was the following order: A2>A3>A4>A1>A6.
Conclusion: MAGE-A gene expression in peripheral blood of breast cancer may be as a important maker for detection of breast cancer CTCs. The expression of MAGE-A1, -A2 and -A4 may be correlated with prognosis of breast cancer, may be an important marker for monitoring the treatment and prognosis of breast cancer.

PS-01-040

Correlation between HER2/NEU protein overexpression on immunohistochemistry and flourescence in situ hybridisation in breast carcinoma: problems in a developing country

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Background & objectives: The aim of this study was to correlate the FISH results with the IHC results and also document the problems we faced in performing FISH in our particular scenario as a developing country with limited and nonuniform medical facilities.
Methods: It was a retrospective study conducted at Shifa International Hospital spanning a period of four years from 1st Jan 2015 to 31st December 2019. A total of 451 cases of breast carcinoma who underwent florescence in situ hybridization (FISH) were analysed for correlation between Her2/Neu over expression on IHC and its amplification on FISH. Reasons for unacceptable results were documented.
Results: Out of 451 cases submitted for HER2/Neu testing by FISH from 2015 to 2019, acceptable results were obtained in 391 (86.7%) cases. Among 348 HER2/Neu 2+ cases, 97 cases (27.9%) showed HER2/Neu gene amplification on FISH and 251 cases (72.1%) were negative. Out of 39 cases (10.1%) which were scored 3+ on IHC, 36 cases (92.3%) were amplified and 3 cases (7.7%) were negative. All 4 HER2/Neu 1+ cases (1.0%) were non- amplified. Overall 63 cases (13.9%) did not yield acceptable results; 20 due to fixation artifacts (31.7%), 15 due to scanty tumour (23.8%), 15 due to eosin dye application (23.8%) and 13 due to crushing artifacts (20.63%).
Conclusion: HER2/Neu gene amplification was seen in 27.9% and 92.3% cases scored as 2+ and 3+ on IHC respectively. In order to get adequate results on FISH, optimal fixation, adequate amount of tumour without crushing and dye application are important pre-requisites.

PS-01-041

Cytotoxicity potential of tetragunola laeviceps bee propolis on breast cancer cells

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Background & objectives: The resistance of breast cancer chemotherapy triggered the researcher to study herbals alternative therapy that have been known to have anti tumour potential. Propolis has been recognised to have more than 300 chemical compounds, has pro-apoptosis effect and selective to target cancer cell, thus could be a candidate for therapy of breast cancer. Tetragunola laeviceps is a stingless bee that produce propolis, it was found a lot in Southeast Asia include Indonesia.
This study was aimed to analyse the potential of Tetragunola laeviceps propolis as a pro-apoptosis agent to MCF-7 breast cancer cell lines.
Methods: Propolis Tetragunola laeviceps was extracted by ethanol extraction (EEP extract). MCF-7 breast cancer cells, treated by EEP extract, supplemented by FBS10%, penicillin-streptomycin 1%, amphotericin 1% in CO2 5% 370C. Cytotoxic effect of EEP to MCF-7 and Vero cells was examined by MTT test 48 hours after treatment. Absorbance was measured by microplate reader (450nm) to get the viability presentation of cells.
Results: There was a decrease of MCF-7 cells viability and an increase of apoptosis cells after 48 hours of propolis treatment in 200ppm concentration (IC50 79,45 ppm). One-way Anova test showed a significant difference of mean percentage of MCF- 7 viability (< 0,0001) than control cells group.
Conclusion: Propolis Tetragunola laeviceps and its bioactive compound has a selective pro-apoptosis effect to dMCF-7 breast cancer cell lines. This was an early results of alternative therapy for breast cancer, and needs more investigations in the future
Key words: Propolis, Tetragunola laeviceps, breast cancer.

PS-01-043

High tissue inhibitor of matrix-metalloproteinase 2 expression correlates with poor prognosis in breast cancer

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Background & objectives: TIMP2, tissue inhibitor of matrix-metalloproteinase 2, inhibits the matrix-metalloproteinase, MMP2, but may activate pro-MMP2. Hence its correlation with prognosis in breast cancer (BC) is contradictory. This study investigated the correlations of TIMP2 expression in BC with clinicopathological variables.
Methods: Differential expression analysis of TIMP2 was assessed in the lymphovascular invasion (LVI) positive versus negative cohorts in the METABRIC BC dataset. Immunohistochemical analysis for TIMP2 (1:50 dilution) expression was conducted on BC tissue microarrays (n=1048) and clinicopathological correlations were assessed, including VI and expression of MMPs, 2, 14 and 15.
Results: TIMP2 was associated with positive LVI in the METABRIC cohort (p= 0.002). On immunohistochemistry, significant positive correlations were found between TIMP2 protein expression and higher grade (p=0.019), including its components nuclear pleomorphism (p=0.004), mitotic count (p=0.000087), LVI (p=0.014) and Nottingham prognostic Index (p=0.024). TIMP2 expression showed a significant correlation with negative ER status (0.014) and Triple negative status (p =0.008). TIMP2 expression also showed a positive correlation with cytoplasmic MMP2, MMP14 and MMP15 (p<0.0001) expression. A significant difference in 10-year BC specific survival (BCSS) was seen between high and low TIMP2 expression (p= 0.018).
Conclusion: Overall, the study indicates that higher TIMP2 expression correlates with poor prognostic factors in BC including high grade, negative ER status, poor NPI and LVI. These effects may be explained through its activation of pro-MMPs, reflected by positive associations with MMP expression. Further studies of the ratio between MMPs and TIMP2 may help delineate its functional role in BC.
Funding: Academy of Medical Sciences and Pathological Society of Great Britain and Ireland (CDF).

PS-01-044

Low FOXA1 expression in aggressive breast cancer associates with ER negativity, BRCA1 germline mutations, and gene expression programs for cellular plasticity and immune cell responses

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Background & objectives: FOXA1 is linked to oestrogen receptor signalling, suggested as a factor upstream of the ER-complex, and proposed to play a role in immune responses. Here, we assessed FOXA1-associated phenotypes in breast cancer (BC) and explored related gene expression patterns.
Methods: We analysed three BC cohorts. Cohort-I: Hordaland County; <70 years; n=612. Immunohistochemical staining of FOXA1 on tissue microarrays of formalin-fixed paraffin-embedded BC tissue. Cohort-II-III: Global mRNA data; METABRIC (n=997) and TCGA (n=505; including BRCA1 germline mutations). Analyses of genes differentially expressed between FOXA1 high and low cases and gene set enrichment analyses (GSEA) were performed on global transcriptomic data.
Results: Low FOXA1 associated with higher histologic grade and tumour cell proliferation (Ki67), triple- negative phenotype, and reduced survival (P≤0.008). ESR1, GATA3, AGR2, AGR3, and AR were downregulated in FOXA1-low tumours. Further, FOXA1-low cases were enriched for signatures of low ER-signalling, stemness, progenitor cells, EMT, and BRCA1 mutations. Triple FOXA1/GATA3/ER-negative status strongly predicted a basal-like phenotype (OR≥198; P<0.001) and associated with higher expression of PD1, PD-L1, and CTLA4 (P<0.001).
Conclusion: Low FOXA1 is a marker of aggressive BC and associates with BRCA1 germline positive cases. Associated transcriptional programs reflect increased cellular plasticity and stemness. A triple FOXA1/GATA3/ER negative phenotype strongly predicts a basal-like phenotype and relates to immune cell responses.

PS-01-045

Development of a novel clinical trial immunohistochemistry (IHC) assay using Ki-67, clone MIB-1, monoclonal antibody for Dako Omnis

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Background & objectives: Lack of standardized Ki-67 assay performance remains an impairment to global clinical research. Therefore, a novel IHC prototype assay and scoring algorithm were developed for the Dako Omnis platform to detect Ki-67 expression in formalin-fixed paraffin-embedded human breast carcinoma.
Methods: The Ki-67 IHC prototype assay is based on EnVision FLEX technology using Ki-67, clone MIB-1, primary antibody validated for Dako Omnis. A scoring guide was developed and optimized for high inter-observer precision. The assay has been analytically validated for sensitivity, specificity, precision (inter-day, inter-instrument, inter-lot and repeatability: intra-instrument/intra-rack/intra-day) and robustness.
Results: Ki-67 IHC detected a relevant range of Ki-67 expression in 148 breast carcinoma specimens, including resection and core needle biopsy specimens. All precision and robustness studies achieved 95% confidence interval lower bounds (LBCI) of >90% for negative percent (NPA), positive percent (PPA) and overall (OA) agreement. Specifically, observer reproducibility results demonstrated high agreement with 95% LBCI values for NPA/PPA/OA of: 97.2%/91.7%/95.4% for inter-observer and 98.3%/94.4%/96.8% for intra-observer.
Conclusion: Our studies demonstrate that the standardized Dako Ki-67 IHC assay for Dako Omnis is sensitive, specific, precise, and robust for reproducible detection of Ki-67 expression in breast carcinoma. The prototype assay is the first Ki-67 IHC in vitro diagnostic developed on the Dako Omnis platform for global use in support of patients participating in the monarchE study (NCT03155997).

PS-01-046

Identification of potential markers of aggressive behaviour in young women with breast cancer through transcriptomic analysis

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Background & objectives: Breast cancer in young women (BCYW) is usually aggressive with devastating consequences. Evidence suggests that BCYW has a distinct biological behaviour from those of older women. The study aim is to identify biological markers of aggressive behaviour of BCYW.
Methods: The young (≤40 years) and age independent reduction mammoplasty samples in the GEO datasets (GSE29431, GSE42568, GSE61304) were analysed with GEO2R. Survival analyses were performed with R survival and prodlim packages on TCGA cohorts. Statistical significance was defined as $p \leq 0.05$ or False Discovery Rate (FDR) ≤ 0.05. The identified genes were validated by qPCR, Western blotting and Immunohistochemistry.

Results: High median expression of Wntless (WLS) (HR=1.927, p0.05), low median expression of Kinesin Family KIF4A (HR=0.246, p0.006), Glycosylphosphatidylinositol Specific Phospholipase D1 (GPLD1) (HR=0.294, p0.004) and Structural Maintenance of Chromosome (SMC4) (HR=0.331, p0.04) were associated with overall poor survival. Further analysis showed that SMC4 and KIF4A mRNAs were upregulated in cancer vs reduction mammoplasty, while WLS and GPLD1 mRNAs were downregulated. qPCR and western blot revealed higher expression of SMC4 and KIF4A and low expression of WLS in breast cancer cell lines vs normal breast epithelial cells. SMC4 immunostaining showed high expression in young female breast cancer, low expression within this cancer cohort correlates with Luminal B, TNBC and higher grade.
Conclusion: SMC4, KIF4A, WLS and GPLD1 could be important biological markers of the aggressive behaviour of BCYW through unknown pathways. This provides a basis to further investigate the functional significance of these pathways in a model system.
Funding: Commonwealth Scholarship Commission UK The British Division of the International Academy of Pathology (BDIAP)

PS-01-049

Micropapillary variant of mucinous breast carcinoma: a report of two cases

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Background & objectives: Breast cancer is a heterogeneous disease composed of various histological types that differ in prognosis and response to therapy. Micropapillary variant of mucinous carcinoma (MPMC) is a subtype with more aggressive behaviour than classic, pure mucinous breast carcinoma.
Methods: We present two cases of MPMC in female patients of identical age (51-year-olds). The first patient underwent neoadjuvant therapy for an extensive right breast tumour, with partial response and extensive residual disease within the lymph nodes. The second patient underwent tumourectomy for a recurrence of mucinous carcinoma, 10 years following right mastectomy with adjuvant endocrine therapy.
Results: Both cases were characterized by micropapillary clusters of tumour cells in abundant extracellular mucin, with specific 'inside out' positive staining for EMA and E-cadherin. The first case presented with extensive lymphovascular invasion. Both tumours were positive for ER and PR, with an intense basolateral membranous staining for HER2 in the first case. Micropapillary carcinoma and micropapillary mucinous carcinoma are the only breast tumours in which basolateral HER2 staining is considered positive.
Conclusion: Greater awareness and recognition of the micropapillary variant of mucinous breast carcinoma has significant prognostic and therapeutic implications by avoiding underestimation of malignant potential for individuals whose tumours may have been diagnosed as classic mucinous carcinoma.

PS-01-051

Clinical impact of microscopic margin status on invasive breast cancer treated with breast-conserving surgery plus adjuvant radiation therapy at a specialised cancer hospital in Portugal

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Background & objectives: Most early-stage breast cancers (BC) are treated conservatively with breast-conserving surgery plus adjuvant radiation therapy (BCSART). We evaluate the clinical impact of microscopic margin status in a sample of conservatively treated invasive breast cancer (IBC) patients, compared to worldwide meta-analyses.
Methods: Unicentric, retrospective, descriptive study including all female invasive breast cancer (IBC) patients who concluded BCSART treatment in 2012 at a specialized cancer hospital in Portugal. Microscopic margins, as evaluated and measured by histopathology, were considered positive with "ink on tumour", and clinical data was collected from follow-up records. Analysis was performed with IBM's SPSS software.
Results: 92 patients were included, 3 with bilateral disease. Of the 95 surgical specimens, 8 had positive margins – 6 for IBC and 2 for ductal carcinoma in situ (DCIS) – and, of these 8, all but one were submitted to further re-excision or mastectomy surgery, prior to adjuvant radiotherapy. After a mean follow-up time of 84 months, wider margins did not prove protective against relapse, nor otherwise beneficial.
Conclusion: Breast cancer is the most common type of cancer worldwide in women. For IBC, treatment outcomes with BCSART are comparable to mastectomy, and the current consensus is to consider "no ink on tumour" as a negative margin. In patients programmed to undergo adjuvant radiation therapy, wider surgical margins are not clinically justified. Our results tend to concur with this consensus, but longer follow-up time may be of value.

PS-01-054

Deployment of a multi-tissue AI-based quality control system in routine clinical workflow

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Background & objectives: Maccabi is a large healthcare provider with centralized pathology institute handling >140,000 accessions/ year, (700 PCNBs and 6850 breast biopsies). IBEX Medical Analytics develops Galen Prostate (CE-IVD) & Breast AI-based diagnostic solutions that detect cancer in prostate & breast biopsies.
Methods: The underlying algorithms utilize state-of-the-art Artificial Intelligence (AI) and Machine Learning techniques and were trained on many thousands of image samples, obtained from slides from multiple labs and geographies, and manually annotated by senior pathologists. Galen Prostate CE-IVD detects and grades prostate core needle biopsies, and Galen Breast detects invasive and in-situ carcinomas in breast biopsies.
Results: Both algorithms were assessed for performance on independent data from various labs and demonstrated high specificity and sensitivity, including identification of cancers missed by pathologists. Maccabi has deployed both Galen Prostate and Galen Breast as a QC system on all new prostate and breast biopsies entering the lab. The system raises an alert whenever it encounters a discrepancy between the automated analysis and the original diagnosis, prompting a second human review. In this talk, we will discuss the workflow in the lab and the performance of the algorithms. To the best of our knowledge, these are the first AI-based prostate and breast diagnostic systems running in a live clinical setting.
Conclusion: The importance of accurate diagnosis in prostate and breast biopsies, together with the growing shortage of pathologists, makes a QC system like this extremely useful for diagnostic accuracy and safety.

PS-01-055

Crosstalk between programmed death ligand 1 (PD-L1) expression, Ki-67 labelling index and tumour infiltrating lymphocytes (TILs) in invasive breast cancer: a tertiary care centre study

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Background & objectives: Breast cancer is leading cancer among Indian females (25.8 per 100,000 women) and accounts for approximately one fourth of cases worldwide. Present study aimed to ascertain and correlate PD-L1 expression with Ki-67 labelling index and TILs in Invasive breast carcinoma

Methods: It was a two year (2016-2018), descriptive observational study including all the diagnosed cases of Invasive breast carcinoma. All Core biopsy, wedge biopsy, lumpectomy and MRM specimens were examined. PD-L1 expression was assessed in tumour and stromal TILs and its correlation was done with hormone receptor status and with Ki-67 labelling index. Appropriate statistical analysis was done using SPSS 23.0v.
Results: Total 114 cases were included in present study, of which 33.33% (38) showed PD-L1+ expression in tumour cells and 47.37% (54) showed PD-L1+ expression in stromal TILs. Higher Ki-67 labelling index was observed in 96 cases and low in 18 cases. 49 cases were ER- and 65 were ER+. Of these 49 cases, 22 cases showed PD-L1+ expression and from 65 cases, 49 showed PD-L1+ expression.
Present study highlighted a statistically significant relationship between expression of PD-L1 in tumour cells and stromal TILs. Significant concordance between Ki-67 labelling index and PD-L1 expression was noted in tumour cells and stromal TILs. An inverse correlation was noted between PD-L1 expression and ER.
Conclusion: PD-L1 expression in tumour and TILs with high Ki-67 index may have role in targeted chemotherapy. Also, inverse relationship with ER suggests scope for targeted therapy in ER- Invasive breast cancer cases. However, further research is required in this area.

PS-01-057

Clinical value of PD-L1 (SP142) expression on immune cells (IC) in small biopsy specimens (SBS) from untreated triple-negative breast cancer (TNBC) patients - a single institution retrospective study

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Background & objectives: This study analyses the prognostic significance of PD-L1 positivity in SBS from untreated TNBC patients, as illustrated by complete pathological response(cPR) and aims at targeting patients for PD-L1 screening by correlating its expression with tumour infiltrating lymphocytes(TILs) and MIB1 rates.
Methods: We evaluated TILs by HE staining, assessed PD-L1(SP142 assay) expression on IC and MIB1 on tumour cells by immunohistochemistry in 99 FFPE SBS of untreated TNBC patients diagnosed in 2018-2019. Cases with ≥1%PD-L1 expression were considered positive. MIB1 and TILs were evaluated according to the WHO guidelines(table 1-2). The association of PD-L1 status with TILs,MIB1 and cPR was statistically tested.
Results: 29(67,4%) of 43 so far tested cases were PD-L1-positive. PD-L1 positivity was correlated with TILs>30% and MIB1index>70%. PD-L1 positivity was seen in 75% (6/8) cases with pCR.

Table1

	Pd-L1(+)	Pd-L1(-)
MIB1 <40%	4	6
MIB1 40-70%	7	7
MIB1 >70%	18	1

Table2

		Pd-L1(+)	Pd-L1(-)
TILs <5%	Negative	2	3
TILs 5-30%	Low	13	10
TILs 35-50%	High	9	1
TILs >50%	Predominant*	5	0

*IC > tumour cells

Conclusion: Our study confirmed that PD-L1–positive IC have a positive predictive impact in TNBC cases without PD-L1 therapy and reflect a trend for better pathologic response to neoadjuvant chemotherapy.
Therefore, PD-L1 could act as a promising marker to predict neoadjuvant chemotherapy response in TNBC patients. TNBC patients with MIB1index>70% and/or TILs>30% should be screened for PD-L1 expression by immunohistochemistry as they may benefit from hybrid neoadjuvant treatment with PD-L1 inhibitor.

PS-01-058

Imaging-pathology correlation: concordance analysis between sonomammographic findings BI-RADS 4 and histopathologic result in Filipino women in a single institution tertiary university hospital

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Background & objectives: Objectives: To correlate between the sonomammographic findings and pathologic results of BI-RADS 4 lesions; compare imaging-pathologic concordance between BI-RADS 4A, 4B and 4C according to age group; Assess concordance of BI-RADS 4 category in palpable and non-palpable breast lesions.
Methods: A retrospective study in Filipino women had mammogram and/or breast ultrasound with BI-RADS 4 score underwent biopsy or surgery. Patients were classified as: BI-RADS 4 subcategory, histology, age groups, and if lesions were palpable or not. Mammogram and breast ultrasound were performed using mediolateral oblique and craniocaudal projections. Comparison was done using Chi-square or Fisher's exact test.
Results: A total of 203 BI-RADS 4 patients were included with mean age of 51.18 years old, out of which more than half were ≥50 years old. Majority were categorized as BI-RADS 4A (n=77). The results indicate similar likelihood rates of malignancy at 69%, 38% and 9% for BI-RADS 4C, BI-RADS 4B, and BI-RADS 4A, respectively, compared to the computed likelihood rate by the ACR which is validated and followed worldwide.
Conclusion: Malignancy rate of BIR-ADS 4 lesions were comparable to the likelihood of malignancy worldwide. There is positive correlation between BI-RADS 4 malignancy rates supporting the current recommendation for BI-RADS 4 category regardless of subcategory to acquire histologic diagnosis through biopsy.

PS-01-061

Intratumoral heterogeneity in pure ductal carcinoma in situ of the breast does not affect the representativity of a biopsy

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Background & objectives: Ductal carcinoma in situ (DCIS) of the breast, a non-obligate precursor of invasive breast cancer, is a heterogeneous disease in terms of morphology and genetics. Active surveillance for low risk DCIS is currently explored as a valid treatment option in randomised clinical trial setting. The current study investigated the impact of morphological intra-tumoral heterogeneity in a series of 51 large DCIS lesions by comparing biopsies with their subsequent resection specimen.
Methods: Nuclear atypia, DCIS architecture, necrosis, calcifications, stromal architecture and stromal inflammation were assessed in one biopsy slide and three slides from the resection specimen. For each histopathological feature, a histoscore was determined and compared between the biopsy and the resection. Statistical analysis comprised Friedman

tests, Wilcoxon tests with Bonferroni corrections and Spearman's correlations.
Results: Despite substantial morphological heterogeneity in up to 50% of DCIS, the assessment of each histopathological feature in the biopsy correlated significantly with the assessment of the histopathological features in the resection specimen, with the exception of necrosis. Morphological heterogeneity was not associated with patient age, DCIS size or type of surgery, except for a weak association (p=0,048) between heterogeneous stromal inflammation and smaller DCIS size.
Conclusion: Histopathological features assessed at the biopsy level correlated well with the surgical specimen, except for necrosis. Overall morphological intratumoral heterogeneity has limited impact. However, caution is warranted for the assessment of comedonecrosis in biopsies, as its presence can be underestimated.
Funding: Postdoctoral clinical mandate (2019-089) of the Foundation Against Cancer (Brussels, Belgium).

PS-01-062
The diverse molecular landscape of breast cancers with heterogeneous HER2 gene amplification
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Background & objectives: Heterogeneous HER2 amplification is noted in 5-41% of breast carcinomas, depending upon its definition. Intra-tumour heterogeneity drives cancer progression and may enable circumventing HER2-targeted therapies, thereby causing primary and acquired resistance. Here, we performed an in-depth molecular analysis of admixed HER2-positive and HER2-negative breast cancer components.
Methods: We micro-dissected formalin-fixed, paraffin-embedded breast cancer tissue of ten patients. Each tumour contained at least one HER2-negative and at least one HER2-positive component. Targeted next-generation sequencing was performed using a 53-gene panel. Somatic mutations were analysed. Copy number variations were investigated, based on the available coverage data.
Results: The following (likely) pathogenic molecular anomalies were identified in 26 genes: 3 splice site alterations, 32 missense variants, 7 nonsense variants, 9 insertions and 12 deletions. Copy number gains were identified in the CCND1, EGFR, ERBB2, FGFR1, MYC and PVT1 genes. Overall, most somatic mutations and copy number variations were heterogeneously distributed within the different HER2-negative and HER2-positive tumour components. The HER2-negative cancer components did not harbour common alternative drivers.
Conclusion: Breast cancers with heterogeneous HER2 gene amplification display several molecular anomalies that might act as alternative or collaborative drivers of carcinogenesis. However, these genetic aberrations display a heterogeneous distribution as well, and likely contain a large number of 'passenger' mutations.
Funding: Dr. Mieke Van Bockstal is supported by the Belgian not-for-profit organisation 'Foundation Against Cancer' (Grant 2019-089) and by the Mathilde Horlait-Dapsens Foundation (Brussels, Belgium).

PS-01-063
HER2-positive apocrine carcinoma of the breast: a population-based analysis of incidence, treatment, and outcome
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Background & objectives: Most of the published clinical studies on apocrine carcinoma of the breast focused on the triple-negative variant. In the current study, we investigated clinical, pathological and outcome characteristics of HER2-positive apocrine carcinomas of the breast.
Methods: We searched Surveillance, Epidemiology, and End Results (SEER) program database for HER2+ apocrine carcinomas of the breast and compared HER2+ enriched (ER-/HER2+) (n=167) and Luminal B (ER+/HER2+) (n=85) molecular subtypes. The categorical variables were compared by Chi-squared test. The mortality difference was evaluated using the Kaplan-Meier, Cox regression, and competing risk regression analyses.
Results: 75% of the patients with HER2+ apocrine carcinoma presented at an early stage (stages I/II). The average survival by the end of the study period was 31 months [range, 12.2-48.8 months]. Both HER2+ enriched and luminal B subgroups showed excellent short-term survival (~90%). After performing mortality-specific risk analysis, only early-stage patients that were treated by surgery were found to have better survival. Other clinicopathological parameters did not reach statistical significance.
Conclusion: Our study indicates that the majority of the patients with HER2+ apocrine carcinoma presented at early stages (I or II). Only the tumour stage and surgery exhibited a significant impact on overall survival. HER2+ apocrine carcinoma patients had an excellent short-term (first 2-3 years) survival, which is similar to the clinical behaviour of luminal breast carcinomas (NOS). Further studies are required to explore the long-term outcome among the HER2+ apocrine carcinomas.

PS-01-064
External quality assessment for PD-L1 testing in triple negative breast cancer
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Background & objectives: PD-1/PD-L1 inhibitors are first line treatment options for patients with advanced disease in several tumour types. They are effective in a subset of patients with advanced triple negative breast cancer (TNBC). Immunocytochemistry (ICC) assays predict which patients may benefit.
Methods: Unstained composite slides consisting of tonsil, and both TNBC tissues and cell lines of known PD-L1 expression levels were distributed. Participants stained these for PD-L1 by the same method used in their clinical testing; following return, slides were centrally assessed by a panel of experts. Methodology details and participants own interpretation scores for the TNBC cases were also collected.
Results: The UK National External Quality Assessment Scheme for Immunocytochemistry and In-Situ Hybridisation (UK NEQAS ICC & ISH) assesses the technical quality of laboratory testing. Here we present results from the first round of a pilot EQA for PD-L1 staining in TNBC. The data will be examined for associations between methodological parameters and test accuracy. In particular, results produced by the recommended companion assay (SP142, Roche Tissue Diagnostics) will be compared with non-assay results. Participants own interpretive scores will be examined and compared with those of the expert panel.
Conclusion: This is the first report presenting EQA results for PD-L1 testing in TNBC.
Funding: A generous educational grant was provided by Roche Tissue Diagnostics, 1910 E. Innovation Park Dr., Tucson, Arizona 85755.

PS-01-065
Significance of S100A8-positive immune cells in relation to other immune cell subset infiltration in pre-invasive and invasive breast cancer
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Background & objectives: Myeloid-derived suppressor cells (MDSC) suppresses anti-tumour immunity. The purpose of study is to evaluate

expression of S100A8, one of well-known MDSC markers, and see its relation to other factors including immune cell (IC) subsets in pre-invasive and invasive breast cancers.
Methods: A total of 765 cases of breast ductal carcinoma in situ (DCIS) and invasive carcinoma were included in this study. S100A8 expression in tumour cells (TCs) and ICs, and infiltration of other IC subsets (CD4+, CD8+, and FOXP3+ T cells and PD-L1+ ICs) were detected by immunohistochemistry using tissue microarrays.
Results: S100A8 expression in either TCs or ICs did not differ in frequency between DCIS and invasive carcinoma. In both DCIS and invasive carcinoma, high-S100A8 in TCs and ICs were commonly associated with aggressive pathologic features, such as histologic grade. High-S100A8-IC status positively correlated with infiltration of CD8+ T cells, and presence of PD-L1+ ICs, in both DCIS and invasive carcinoma. In survival analyses, high-S100A8 in TCs and ICs was associated with decreased overall survival in patients with invasive breast cancer, and the difference in survival was most remarkable in HR-positive tumours. In subgroup analysis, tumours containing high-S100A8 and low-PD-L1 IC showed worst overall survival compared to other groups.
Conclusion: S100A8+ ICs are already found in pre-invasive stage as much as in invasive carcinoma and are correlated with CD8+ T cells and PD-L1+ ICs. S100A8+ ICs exert immunosuppressive effect in breast cancer, especially in HR-positive and low-PD-L1 IC subgroup.

PS-01-069
Histopathological characteristics and outcome of breast cancer in non-Caucasian women - a large single institution's experience
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Background & objectives: Breast cancer in non-Caucasian females is under-studied and its management is based on Caucasian data. 17 % of the West Midlands females are non-Caucasian. We aimed to elucidate the pathologic features, molecular profile and outcome of non-Caucasian breast cancer.
Methods: We identified 7553 breast cancers of different ethnic origins diagnosed at a large Birmingham tertiary referral hospital between 2000 and 2016. Histopathological and clinical data were collected and statistically analysed.
6804 cases were excluded; British/white ancestry(n=6191), unconfirmed ethnicity/diagnosis(n=511), patients with sparse histological/clinical data(n=94) and male patients(n=8). The remaining 749 cancers comprised 735 non-Caucasian patients, of whom 14 had bilateral disease.
Results: 47 in-situ and 702 invasive carcinomas of predominantly (86.2%) symptomatic presentation and median age of 51 years were identified. Only 31.2% of invasive tumours measured <15mm and 11.98% were >50mm. Cancers were predominantly of grade3(45%), followed by grade2(42.4%). Median NPI was 4.35. 65.1% of the carcinomas were of luminal subtype, 18.6% were Her2 positive and 16.2% triple-negative. Median overall survival was 62 months. Five and ten year survival was 81% & 65.5% respectively.
Ethnicity correlated with higher NPI($p<0.001$), larger tumour size($p=0.001$) and larger number of positive axillary nodes($p=0.007$). Negative correlations were found between age at diagnosis and both invasive tumour size & grade($p<0.001$) and between tumour grade and overall survival($p=0.006$).
Conclusion: Compared with Caucasian breast cancer, Non-Caucasian tumours presented predominantly symptomatically at younger age, were of larger size, higher grade with more unfavourable phenotypes and shorter survival. This is important in counselling, planning management and follows up of those patients.

PS-01-070
Multiplex immunophenotyping of breast cancer tumour microenvironment
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Background & objectives: Tumour microenvironment in breast cancer has become recently recognised as important for tumour prognosis and response to immunotherapy. We aimed to evaluate tumour microenvironment immune cells of breast carcinoma and their relationship to clinicopathological parameters.
Methods: 54 core biopsies of grade 2-3 ductal NST carcinoma were selected and immuno-stained using multiplex immunofluorescence for CD4, CD8, CD20, CD68 and FOXP3. Cases included were of luminal (n=28), HER2 positive (n=14) and triple negative, TNBC (n=12) molecular subtypes. Detailed quantitative tumour microenvironment immune cell count and density were correlated statistically with patient and tumour characteristics and overall survival.
Results: The most frequent immune cell phenotype was CD4 (35/54;64.8%), followed by CD68 (11/54;20.4%) and CD8 (5/54;9.3%). TNBC & grade-3 cancers had higher total median counts than other molecular subtypes & grade-2 cancers, respectively. In luminal cancers; CD20, CD4 (stromal/total), tumoral CD8 & FOXP3 positive cells correlated positively with survival, whereas CD68 & FOXP3 (stromal/total) positive cells, correlated negatively with survival in HER2 positive tumours. A statistically significant negative correlation was found between tumour FOXP3 and number of positive axillary lymph nodes ($p=0.036$) and between intratumoral cellular density and age at diagnosis ($p=0.026$). Stromal cellular density correlated positively ($p=0.018$) with survival.
Conclusion: CD4 was the dominant immune cell phenotype, followed by CD68 and CD8. The profile of microenvironment and its correlation with survival, varied according to the molecular subtype. Triple negative & grade 3 cancers had the highest median counts of all immune cells. Tumour microenvironment immune-cell characterization could therefore provide prognostic information. The work is being applied to a larger sample to further elucidate the role of microenvironment in breast cancer.

PS-02 Gynaecological Pathology

PS-02-002
Quality of pathology reports for epithelial ovarian cancers at a university teaching hospital in Nigeria, West Africa: an audit of the surgical pathology reports
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Background & objectives: Ovarian cancer is a major cause of morbidity and mortality among women. Therefore, pathology reports must contain important diagnostic and prognostic information. The objective of this study is to assess the quality of pathology reports for epithelial ovarian cancers.
Methods: Pathology reports for the years 2006-2019 were assessed for their conformity with standard universally accepted pathologic diagnostic and prognostic features sign-out checklist. This involved assessing for the presence of the following quality indicators on the pathology reports: histologic type, size, grade, state of the ovarian capsule and stage of disease.
Results: Majority of the tumours (77.8%) were serous carcinomas. The histologic type was stated on 96.3% of the reports while information on the grade of the tumour was also available on 66.7% of the reports. However, information on size, state of ovarian capsule (intact or ruptured) and stage of disease was available for only 14.8%, 7.4% and 3.7% of the reports respectively.

Conclusion: This audit on surgical pathology report of epithelial ovarian cancers shows that a substantial number of reports lacked information on important diagnostic and prognostic indicators. This can have negative consequences on quality of care offered to patients. The use of synoptic reporting can lead to improvement in quality of surgical pathology reports. A follow up study to evaluate quality of the pathology reports after adoption of synoptic reporting is necessary.

PS-02-003

Lymphoepithelioma- like carcinoma of the uterine cervix; tumour microenvironment, tumour budding and p16 expression

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Background & objectives: Lymphoepithelioma-like carcinoma (LELC) of the uterine cervix is a rare tumour of the cervix composed of poorly defined islands of undifferentiated squamous cells in a background intensely infiltrated by lymphocytes. It has striking similarity with its counterpart in the nasopharynx and studies have shown that LELC of the cervix has a good prognosis. We retrospectively study three cases of LELC of the uterine cervix over a three years period (2016-2018) with immunohistochemistry (IHC).
Methods: Three cases of LELC of the uterine cervix were retrieved from our departmental archives. H&E blocks were cut and (IHC) using CD3,CD20, AE1/AE3 and P16 antibodies were done. CD3 and CD20 for IM. Tumour buds were defined according to ITBCC, counted at x20 magnification at the invasive front. P16 stain was defined according to 8Th edition of AJCC guidelines.
Results: The patient's ages were 50, 60 and 65 years respectively. Histology showed a tumour composed of polygonal cells with prominent nucleoli and moderate eosinophilic cytoplasm. Intersperse these cells are numerous lymphocytes. IHC analysis shows the lymphocytes were both intratumoral and peritumoral CD3+ T cells, while CD20+ B cells were mainly peritumoral. Tumour budding was less than 5 buds in all cases which were also P16 positive.
Conclusion: LELC of the uterine cervix good prognosis may be explained by its low level of tumour buds, tumour microenvironment and P16 expression

PS-02-004

BCOR immunohistochemistry is a useful tool to evaluate high-grade endometrial stromal sarcomas but BCOR negative high-grade ESS cases are also present

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Background & objectives: High grade endometrial stromal sarcoma (HG-ESS) is a malignant mesenchymal tumour of uterus which frequently demonstrates YWHAE-NUTM2 fusion. Previous studies identified HG-ESS cases with BCOR gene translocations. Therefore, immunohistochemistry for BCOR could be useful in identifying such HG-ESS cases.
Methods: One hundred seventy-two uterine sarcomas diagnosed between 2000-2019 were re-evaluated. Tissue microarray blocks were constructed from 3 HG-ESS, 19 LG-ESS and 15 uterine sarcomas with high-grade morphology which were included in this study. Fluorescent in situ hybridization (FISH) studies using YWHAE and BCOR brake-apart probes and immunohistochemical studies for BCOR were performed. Patients' files were used for clinical information.
Results: Five patients, 4 of which had tumours extending beyond uterus, had translocations involving YWHAE or BCOR. Four tumours showed high-grade morphology and revealed YWHAE translocation. One patient with myxoid morphology revealed BCOR translocation. In immunohistochemistry, all YWHAE translocated tumours showed BCOR positivity, however, BCOR translocated tumour was negative. One patient is alive after 18 months, three patients died 4, 18 and 34 months after diagnosis, one was lost to follow-up.
Conclusion: HG-ESS is an aggressive tumour with poor clinical outcome. Our study showed that BCOR immunohistochemistry could be a useful diagnostic tool to identify HG-ESS cases with translocation of YWHAE gene. However, FISH analysis is essential for definitive diagnosis. We also report that molecular analysis and conspicuous myxoid morphology can help identifying HG-ESS with translocation of BCOR gene which also seems to have aggressive clinical behaviour. Another important finding is that BCOR translocated HG-ESS was negative with BCOR immunohistochemistry.
This research was supported by Hacettepe University - Coordination Unit of Scientific Research Projects.

PS-02-005

Mismatch repair protein deficiency in the endometria of the general population: an immunohistochemical study

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Background & objectives: There is little literature looking into mismatch repair deficiency in endometrial biopsies of women from the general population. This study aims to assess the frequency of mismatch repair protein deficiency in this group within non-neoplastic and hyperplastic endometrium by immunohistochemistry.
Methods: 200 biopsies of polypoid and flat endometrium were anonymised and allocated to four different diagnostic groups (n = 50 each) for analysis of mismatch repair protein deficiency: non-hyperplastic, disordered proliferation, hyperplasia without cytologic atypia and hyperplasia with cytologic atypia. Each biopsy was assessed by immunohistochemistry for MLH1, PMS2, MSH2 and MSH6.
Results: One (2%) biopsy within the hyperplasia with cytological atypia group showed glandular MSH2 and MSH6 deficiency in areas of atypical hyperplasia and adjacent carcinoma. In the complex hyperplasia group, two (4%) showed glandular MLH1 and PMS2 deficiency, one with focal and the other with widespread loss of staining. The disordered proliferation group contained one biopsy with focal glandular loss of MLH1 and PMS2. The non-hyperplastic group contained no cases of mismatch repair protein deficiency.
Conclusion: Mismatch repair deficient glands are observed in morphologically benign endometrium from women not known to have Lynch syndrome. Glandular loss of mismatch repair protein expression may be an early event in endometrial carcinogenesis and its detection may identify high-risk women in whom endometrial surveillance and/or progestin treatment is justified.
Funding: BDIAP Glasgow 2020 Educational Fellowship

PS-02-006

L1 cell adhesion molecule expression in endometrioid endometrial carcinoma, its prognostic significance, and correlation with survival

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Background & objectives: L1 cell adhesion molecule (L1CAM) is a biological marker that can help identify endometrial cancers with poor prognostic features, and worse survival. This study aims to analyse the relationship between L1CAM expression, clinicopathological parameters, and survival in endometrioid endometrial carcinoma.
Methods: Patients diagnosed with endometrioid carcinoma were selected. Grade, presence/depth of myometrial invasion, invasion patterns, lymphovascular invasion, cervical stromal invasion were re-evaluated. Age, stage, lymph node metastasis, peritoneal cytology positivity,

recurrence, overall and disease-free survival were recorded. Risk classification was made according to ESMO-ESGO-ESTRO consensus. The relationship between L1CAM expression and clinicopathological parameters and its effect on survival was calculated statistically.
Results: A total of 264 cases were included in the study. L1CAM positivity was observed in 22 cases (8.3%). A statistically significant relationship was found between L1CAM expression and advanced age, high grade, deep myometrial invasion, high-intermediate with high-risk cases and pelvic recurrence. Kaplan-Meier survival analysis showed that L1CAM positive patients had poorer overall survival and disease-free survival. L1CAM expression was found to affect overall and disease-free survival in univariate analysis.
Conclusion: L1CAM expression was significantly associated with advanced age, high grade, deep myometrial invasion, high-intermediate, and high-risk cases. Moreover, L1CAM expression predicts pelvic recurrence and poorer survival. Although L1CAM is not routinely used in treatment management algorithms, it seems to be a promising marker for managing patient follow-up algorithms.

PS-02-007
Myoinvasion pattern evaluation in endometrioid endometrial carcinoma
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Background & objectives: Endometrioid endometrial carcinoma has variable five-year survival rates in FIGO stage I, suggesting the involvement of other factors related to tumour behaviour. Our study is evaluating the immunoexpression of epithelial-mesenchymal transition markers (EMT) in different types of myoinvasion patterns.
Methods: The study has been performed on a study group of 20 cases selected from the files of "Elena Doamna" Obstetrics and Gynaecology University Hospital of Iasi, between 2013 and 2017, in patients of 43-78 year-old. The hysterectomy specimens have been evaluated by routine histology and immunohistochemistry for CK7, E-cadherin, N-cadherin, β-catenin, and Vimentin.
Results: Clinicopathological parameters have been evaluated. The myoinvasive pattern has been identified as: MELF (multicystic, elongated and fragmented glands) (45%), diffusely infiltrative (25%), broad front (expansile, pushing border) (15%), adenomyosis-like (10%), and adenoma malignum (5%).The evaluation of different myoinvasive patterns of endometrioid endometrial carcinomas has been challenging, mainly in appreciation of the depth of myometrium invasion in adenomyosis-like and adenoma malignum patterns. MELF pattern has been correlated to age >50 years, deep myometrium invasion (>50%), recurrences (22.22% of cases), and partial immunoexpression of EMT markers.
Conclusion: The evaluation of myometrium invasion types may open new perspectives for endometrioid endometrial carcinoma prognosis. Although our study had been limited, our results are supporting the possibility of EMT phenomena in MELF. Further studies would validate our preliminary results.

PS-02-008
Prostatic metaplasia of the vagina and uterine cervix: an androgen-associated glandular lesion of surface squamous epithelium
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Background & objectives: Prostatic-type differentiation in the lower female genital tract is rare and its causes not well established. Herein, we characterize a distinctive form of prostatic-type differentiation that primarily involves surface squamous epithelium and is associated with androgen exposure.
Methods: Superficial prostatic glandular proliferations involving the vagina or cervix were sought over a 26-year period (1993 – 2019). Cases were also identified from patients clinically suspected to have either exogenous or endogenous androgen excess. Clinicopathological features were reviewed and immunohistochemistry was performed for PSA, NKX3.1, CK7 and AR.
Results: Fourteen cases were identified involving the vagina (n=13) and exocervix (n=1). The most common clinical context was gender dysphoria with long-term testosterone therapy (7/14). Five other patients had congenital disorders of sexual development associated with endogenous androgen excess. Two had no known exposure to androgen excess. Immunohistochemically, glands stained for NKX3.1 (93% of cases), androgen receptor (92%), CK7 (92%), and PSA (64%). Follow-up (median: 11 months) showed no masses or neoplasia.
Conclusion: We propose the designation 'androgen-associated prostatic metaplasia' for this distinctive form of prostate tissue not previously described within the vagina. It is strikingly prevalent among patients undergoing gender-affirming surgery. Recognition is important to distinguish it from other glandular lesions.

PS-02-009
A proposed prognostic panel of immunohistochemical markers for endometrial carcinoma
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Background & objectives: Histopathological prognostic parameters in endometrial carcinoma (EC) include tumour grade, stage and depth of myometrial invasion. This study aimed to assess the value of immunohistochemistry (IHC) "ER, PR, HER2, Ki67 and p53" in assessing the prognosis of EC.
Methods: Archival material of 105 EC were retrieved. Sections were IHC stained and data were evaluated in relation to 3-year overall survival (OS) and disease-free survival (DFS). Analysis were done using Kaplan Meier test and log rank Chi-Square test to detect effect of measurements on survival duration. Cox regression analysis was to detect predictors of survival using forward wald technique.
Results: The median follow-up duration for the included patients was 38 months (range, 1 - 87 months). Twenty-six patients (24.8%) died during the 3-year follow-up period. Fourteen patients had local recurrence in the rectal wall (5 patients), vagina (4 patients) and bladder (2 patients) with distant metastasis in 3 patients. It was found that PR, HER2 and P53 expression had significant effect on the overall survival, unlike ER and ki-67. Regarding disease-free survival, PR is the only marker found to have significant effect on DFS.
Conclusion: ER, PR, HER2, Ki-67 and p53 are not independent prognostic factors in endometrial carcinoma regarding OS and DFS. However, a combination of low ER and PR expression together HER2 overexpression, high ki-67 and aberrant P53 expression are associated with more aggressive behaviour of endometrial carcinoma.

PS-02-010
Cross talk between TP53, MDM2 and CDKN1A expression and progression-free survival in patients with ovarian cancer after platinum-based chemotherapy
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Background & objectives: The goal of the investigation is to assess the link between multiform markers of cell cycle control genes (Arg72Pro of TP53, T(-410)G of MDM2 and Ser31Arg of CDKN1A) and progression-free survival (PFS) in ovarian cancer patients after platinum-based chemotherapy (CT).
Methods: we analysed 49 tumour tissue samples from ovarian cancer patients (high-grade serous carcinomas) obtained before platinum-based CT. All patients were treated with standard protocols and examined till disease progression. Multiform markers of cell cycle control genes were investigated with Полиморфные маркеры генов были исследованы методом Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) and real time PCR.
Results: Results We demonstrated the trend to decrease of PFS median in allele G of T(-410)G MDM2 carriers. We also have shown the increase of PFS median in allele Pro of TP53 ($p = 0.045$). This phenomenon was more prominent in minor homozigota Pro/Pro carriers in compare to patients with Arg/Arg genotype ($p = 0.007$). In group of patients with optimal or total debulking minor allele Arg of Ser31Arg CDKN1A carriers had the decreased PFS mediana ($p = 0.004$).
Conclusion: Thus, we revealed the interconnection between investigated multiform gene markers and remission duration after platinum-based CT. Further investigation should be conducted to assess prognostic value of these markers for ovarian cancer patients before CT application.
The investigation was supported by RFF grant 18-08-01258

PS-02-011
Steroid receptors isoforms disbalance in endometrial polyps pathogenesis
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Background & objectives: Steroid receptors directly impact on endometrial polyps (EPs) development, although the role of their isoforms play even more significant role. The goal of our investigation was to assess the proportion between proliferative and anti-proliferative steroid receptors in endometrial polyps
Methods: We assessed ER-alpha, ER-beta, PgR-A and PgR-B immunohistochemically in 20 EPs and 20 proliferative endometrium. We also calculated ER-alpha/ER-beta and PgR-B/PgR-A.
Results: We demonstrated higher PgR-B expression in EP in compare to normal endometrium (NE) ($p=0.003$).We shew the decrease of glandular and stromal ER-beta expression ($p=0.01$ and $p=0.04$ respectively) and stromal PgR-A expression ($p=0.003$) in EPs in compare to NE. The ER-beta/ER-beta was higher in glands of EPs glands then in NE (1.4 and 1.2 respectively, $p=0.006$). We did not reveal difference in ER-beta/ER-beta in stromal components of EPs and NE ($p>0.05$) . The PgR-BE/PgR-A was higher in glands of the EPs then in NE (1.2 and 1.1 respectively, $p=0.04$) and in stroma of the EPs then in stroma of NE (1.4 и 1.1 $p<0.001$).
Conclusion: In endometrial polyps we revealed the increase of PgR-B expression which accelerate the proliferation. In addition we demonstrated the decrease of ER-beta and PgR-A expression (these isoforms facilitate decidualization and atrophy of the endometrium). This disbalance can promote the proliferation, angiogenesis, apoptosis deactivation, cell cycle disturbance leading to endometrial polyps growth.

PS-02-012
Ovarian morphology in patients treated with one-step surgical procedure for ovarian function activation
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Background & objectives: Patients with primary ovarian insufficiency (POI) have few remaining follicles, their only chance for pregnancy is through egg donation. We tried to reveal morphological features of ovarian in patients treated with surgical procedure for ovarian function activation using ovarian fragmentation.
Methods: We histologically investigated 52 samples of ovarian cortex obtained during surgical operation from 33 patients (19 with POI and 14 with 'poor' response to ovarian stimulation. We assess from 1 to 11 fragments of ovarian tissue 0,2x 0,4 to 1,5x1,5 cm in size.
Results: in 26,9% we demonstrated primary or secondary follicules, in 15,4% - follicle cystic atresia, in 53,8% - corpus fibrosum. Totally we revealed any of folliculogenesis signs in 82,7% samples. This date proved that operated patients had functional active ovaries and supposed an efficacy of ovarian surgical activation. In addition, we revealed serous surface proliferation (in 7,7%) and two types of inclusion cysts (ovarian surface epithelium (OSE)-type and fallopian tube-type). Moreover, we demonstrated samples with preserved OSE so we can suppose that POI can result in fibrous stroma of ovarian cortex and in basal membrane changes leading to tighter junction between these two histological structures.
Conclusion: Detailed assessment of a deliberately reduced ovarian reserve is required to overcome infertility in patients with POI who are resistant to standard f treatment strategy (including assisted reproduction methods). The histological examination ovarian cortex let us characterize the follicular apparatus and surrounding tissue, which is of undoubted significance in patients stratification and their effective treatment.

PS-02-013
The immunoexpression of COX2, HIF-1α , and VEGF-C in the cervical cancer with neoadjuvant therapy (NAT)
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Background & objectives: Cervical cancer can be clinically staged prior to surgery, chemoradiotherapy being the elected treatment for locally advanced disease. Our study aims to assess key biomarkers in NAT cervical cancer, in order to evaluate their diagnostic and prognostic potential.
Methods: We evaluated 20 patients with IIB to IVA cervical carcinoma diagnosed and treated with NAT and subsequent surgery at the Regional Institute of Oncology of Iasi, between 2016 and 2018. The preNAT cervical biopsies and postNAT hysterectomy specimens have been assessed by routine histology and immunohistochemistry for COX2, HIF-1α, and VEGF-C, the results being correlated with clinicomorphological parameters.
Results: The histological type of the tumours included in our study were as follows: keratinized and nonkeratinized squamous cell carcinoma (16/80%), mucinous adenocarcinoma (1/5%), mixed tumours, as carcinosarcoma (1/5%), as well as mixed neuroendocrine and mucinous adenocarcinoma (2/10%). Of all patients, none presented a complete response to chemotherapy, the majority presenting a partial response (19/95%) and a single one (5%) not responding at all to NAT. The imunoexpression of VEGF-C was found significantly higher in preNAT carcinoma (16/80%) than in postNAT malignant cells (11/55%). HIF-1α positivity was higher in preNAT cervical carcinoma (17/85%) than in postNAT patients (13/65%). COX-2 expression was more significant in preNAT carcinoma (18/90%) than in postNAT (9/45%).
Conclusion: The validation of these elements will enable adjusted therapeutic strategies to improve the prognosis and reduce the morbidity of uterine cervical patients, and will identify the molecular variables that predict either sensitivity or resistance to chemotherapy.

PS-02-014

Seromucinous cystadenomas and adenofibromas: first report of a case series

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Background & objectives: In the 2014 WHO Classification of Tumours of the Female Reproductive Organs, a category of seromucinous cystadenoma/adenofibroma was introduced as a benign counterpart of seromucinous borderline tumours and carcinomas. However, there is minimal literature regarding such benign ovarian neoplasms.
Methods: The cases were derived from the Department of Pathology, Belfast Health and Social Care Trust archives between 1/1/2010 and 19/11/2019 (n=18). Additional prospective cases were added from 20/11/2019 till 7/1/2020 (n=3). Most (n=19) were reported by the second author (W.G.M). All the reports and slides were retrieved and reviewed. Clinical information was obtained from the electronic care record.
Results: 21benign ovarian seromucinous neoplasms. Mean age 61years. 19unilateral and 2bilateral. 18cystadenomas and 3cystadenofibromas. Mean tumour size 9cm. The epithelium was predominantly single layered and consisted of admixture of cell types:serous and mucinous(14cases)and serous, mucinous and endometrioid (7cases).12had endometriosis, most commonly in the same ovary. 3had an ovarian borderline tumour or carcinoma; a grade1 endometrioid adenocarcinoma within the same ovary and a contralateral serous borderline tumour and borderline clear cell adenofibroma.
Conclusion: This represents by far the largest case series of benign ovarian seromucinous neoplasms and we show a close relationship with endometriosis and endometrioid differentiation.

PS-02-015

Role of six levels in cervical biopsy - is it really required?

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Background & objectives: Currently, there is no consensus as to the optimum number of levels that should be examined in cervical biopsies. We therefore investigated whether it is necessary to take six levels or taking three would be sufficient
Methods: We collected prospective data over a four month period at Leeds. The parameters included: the last smear result, colposcopy impression, HPV status, histological abnormality. Six pathologists independently recorded on which level abnormality was noted and which was the worst level.
Results: Majority of cases (72.67%) showed abnormality in all six levels. No particular worst level was seen in 54% (81/150). The level showing worst changes was L6 - 36.2% (25/69). Level 1 was worst in a single case (0.67%). Level range with worst changes were L4-6 - 71% (49/69). Levels 1-3 were worst in only a minority (2.67%) of cases (4/150). L1-3 were shallow in 12.6% (19/150) in decreasing order from 1 to 3 (12.6, 10.6 and 8% respectively). Abnormality is seen in increasing order from L1 to 6 (78%, 82%, 86%, 94%, 94 and 94% respectively).
Conclusion: No significant benefit is seen in examining all six levels as majority of cases show similar changes in all levels. Three levels may be sufficient to examine. Although worst levels are more seen in later levels (L4-6), the range needs to be wide as minority of cases had worst changes even in earlier levels (L1-3). It may be optimal to cut L1-7,examine alternate HE keeping coated spares for further work

PS-02-016

Cytology versus endocervical curettage for the detection of HSIL persistence after loop electrosurgical excision procedure (LEEP)

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Background & objectives: Endocervical curettage (EC) and cytology are the common methods to determine the risk of persistence/recurrence after LEEP procedure for high-grade squamous intraepithelial lesions (HSIL) of the uterine cervix, but there is controversy on which method provides more accurate information.
Methods: Prospective study that included 307 women treated for HSIL by LEEP between 2013 y 2018. In all cases, EC and liquid-based cytology (LBC, Thinprep) were obtained immediately after the procedure. The follow-up controls were scheduled every 6 months for at least 24 months and included LBC, HPV testing and colposcopy with biopsy if indicated.
Results: Mean age of the patients was 40.3 ± 10.1. HPV testing was positive in 128 (41.7%) women, cytology in 46 (15.0%) and EC in 18 (5.9%) of the patients. The samples obtained after LEEP were insufficient/inadequate in18 (5.9%) of the LBC and in 71/307 (23.1%) of the EC. HSIL persistence/recurrence was identified in 24/307 patients (7.8%). The sensitivity and specificity of the LBC were 23.9% and 95.0%, respectively. The sensitivity and specificity of the EC were 16.7% and 92.7%, respectively.
Conclusion: Conclusions:
Cytology provides more accurate information on persistent/recurrent than EC.

PS-02-017

Application of the promise molecular classification in endometrial carcinomas: clinical, pathological, metabolical and molecular characterisation

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Background & objectives: ProMisE molecular classification recognizes four groups of endometrial carcinoma (EC), improving morphological and treatment approaches. The objective of the study is to confirm the contribution of ProMisE in EC, adding metabolical analyses and test pyrosequencing (PSQ) in POLE gene study.
Methods: 54 EC diagnosed in our institution were evaluated: histological type, pathological stage, "MELF" and vascular invasion, metabolical activity by PET/TAC and clinical behaviour. Molecular classification was performed in ProMisE sequential order (MMR-D, POLE-EDM, p53abn and p53wt): MMR and p53 proteins by immunohistochemistry and codons 286/411 POLE by PSQ. p53 mutational status was analysed by NGS (TST15) in 7 selected cases.
Results: We collected 21 MMR-D, 1 POLE-EDM, 13 p53abn and 19 p53wt CE: 10 serous carcinomas and 2 carcinosarcomas in p53abn; 3 in/dedifferentiated carcinomas in MMR-D and 2 clear cell carcinomas in p53wt. MMR-D and p53wt harboured 34/35 endometrioid carcinomas. POLE-EDM exhibited high-grade histology. Vascular invasion: 6/21(28,6%)MMR-D, 6/13(46,2%)p53abn, 8/19(42,1%)p53wt. "MELF" invasion: 1/21(4,8%)MMR-D, 1/13(7,7%)p53abn, 5/19(26,3%)p53wt. Extrauterine disease: 4/21(19%)MMR-D, 4/13(30,8%)p53abn, 6/19(31,6%)p53wt. POLE-EDM was IA and disease free survival(DFS). 14/21(66,7%)MMR-D, 5/13(38,7%)p53abn and 17/19(89,5%)p53wt are DFS. SUVmax/SUVpic were higher in MMR-D than p53abn. p53abn MTV and TLG were the lowest

(p<0,005). Only one p53abn(negative pattern) did not correlate with NGS results. PSQ was restricted to two codons, with frequent contaminations, but easy and quantitative interpretation.
Conclusion: ProMisE classification exhibits pathological correlation that improves diagnoses in ambiguous cases, displays strong prognostic value, above classical ones, and guides treatment. p53 immunohistochemistry correlates with molecular status of the gene. Paradoxically, the lowest metabolical activity is observed in p53abn group. PSQ is a sensitive technique, allowing an easy interpretation and quantitative results. However it exhibits some technical limitations. A comparative study with Sanger approach would have to be carried out.
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PS-02-018
Possible etiologic role of human papillomavirus in vulvar seborrheic keratosis: a study combining whole tissue section-PCR, immunohistochemistry (p16 and e4), and laser capture microdissection-PCR
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Background & objectives: HPV-DNA has been previously detected in vulvar seborrheic keratosis (VSK) by performing polymerase chain reaction (PCR) on whole-tissue sections (WTS). However, this has been refuted as evidence of an etiologic involvement of HPV, as WTS-PCR does not inform on HPV-integration.
Methods: We explored the association of HPV and VSK by performing WTS-PCR, immunohistochemistry with p16 and E4, and laser capture microdissection (LCM)-PCR. p16 and E4 are surrogate markers of HPV-oncogene expression, and LCM-PCR allows HPV-detection from specific lesional cells, with a higher precision than WTS-PCR. VSKs were selected following strict histologic criteria to avoid including the common differential, HPV-related condyloma acuminata.
Results: HPVs were detected in 73% (11/15) of VSKs through WTS-PCR (SPF10-PCR-DEIA-LiPA25); these included HPV44 (n=4), HPV6 (n=4), HPV42 (n=2), HPV53 (n=1), and an untypable genotype (n=1). p16-positivity was noted in 82% (9/11), and E4-positivity was noted in 36% (4/11) of HPV-positive VSKs. LCM-PCR was performed on six lesional areas (two p16+/E4+ and four p16+/E4-) and one area of adjacent normal epithelium (p16-/E4-) selected from four HPV-positive VSKs. HPVs were detected from all lesional areas by LCM-PCR and the results were concordant with WTS-PCR. HPV could be detected in the basal/intermediate epithelial layers of the lesional areas, thereby ruling out surface contamination. The area from normal epithelium was negative for HPV.
Conclusion: These results imply a pathogenic involvement of HPV in a proportion of VSKs. p16 and E4-positivity indicated HPV-integration, and through LCM-PCR, HPVs could be localized to the lesional cells. The natural of history of these VSKs deserves further study.

PS-02-019
Analysis of endometrial carcinoma with subclonal P53 expression
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Background & objectives: To study endometrial carcinoma (EC) cases showing subclonal p53 expression on immunohistochemistry (IHC) to determine which molecular category these should be assigned to; in addition, to develop practical guidance for the interpretation of this novel and poorly understood expression pattern.
Methods: 278 EC's were classified into molecular categories using p53 and MMR IHC on whole sections, together with pathogenic POLE mutation testing using targeted next generation sequencing (NGS). Cases with subclonal p53 IHC expression involving ≥5% of tumour underwent directed sampling [a single 1mm core for each differentially staining area] and TP53 sequencing through NGS.
Results: Subclonal p53 expression was observed in 19/278 (6.8%) cases at levels ranging from 0.5% to 95% (median 11%). 7/19 cases (37%) were classified as MMRd EC. An additional 5/19 cases (26%) harboured pathogenic POLE mutations (POLEmut). The remaining 7/19 tumours (37%) were MMR proficient (MMRp) and POLE wild type (POLEwt). Of these, 6/7 contained a TP53 mutation in both the areas with mutant pattern and wild type p53 expression, the only exception being a tumour where the subclonal loss was only present in 3% of the tumour cells, and below the limit of detection of the assay used.
Conclusion: Subclonal p53 IHC reflects underlying TP53 mutation. In MMRd and POLEmut EC this is secondary and unlikely to show adverse prognosis. In MMRp and POLEwt EC, however, this pattern appears to indicate a driver TP53 mutation, ie p53 abnormal EC.

PS-02-020
An audit of histopathology reports of carcinoma endometrium: assessment of different histology parameters from specimens operated at a cancer centre in india, between January 2013 and March 2018
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Background & objectives: To review histopathology reports of patients operated for carcinoma endometrium, at our institute between Jan 2013 to March 2018, and to see our compliance to minimum data sets.
Methods: -After obtaining approval from the Institutional Review Board (IRB), our hospital records showed a total of 457 reports of carcinoma endometrium, operated between January 2013 to March 2018. Various parameters from the reports were noted, and their frequencies were calculated with the help of SPSS software (version 21).
Results: The mean age was 57.5 years, mean tumour size was 3.78 cm. The depth of myometrial invasion and tumour type was mentioned in 100% reports, commonest tumour type being endometrioid-87.3%. The tumour was stage pT1a in 63.9%, stage pT1b in 36.1% cases. Distance of tumour from uterine serosa was mentioned in 86.4% cases. The FIGO tumour grades were grade II- 56.2%; grade III- 28.7%; grade I-14.9%; mentioned in 99.8% cases. Lymphovascular invasion was present in 15.5% cases. The cervix was reported in 99.8% cases, involved in 10.7% cases. Lymph nodes were removed in 78.6% cases (mean lymph node yield 14.01). TNM stage was mentioned in only 56.2 % cases.
Conclusion: -Overall compliance to minimum data sets in carcinoma endometrium reports by our team is good. pTNM stage, distance to serosa need to be mentioned.

PS-02-021
MYB rearrangement is frequent in adenoid cystic carcinomas of the Bartholin's gland: a series of 5 cases
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Background & objectives: Primary vulvar adenoid cystic carcinoma(ACC) is very rare. In most anatomic locations, MYB-NFIB and MYBL1-NFIB fusions are oncogenic drivers in ACC. In two prior series, MYB was rearranged in 2/9 and 3/3 vulvar ACC cases.
Methods: We report the clinicopathologic features of five vulvar ACCs diagnosed between 1963 and 2020, and we describe the prevalence of MYB and MYBL1 rearrangements in this series.

All HE slides from these cases were reviewed, as well as their medical records. FISH using MYB and MYBL1 BAC-clones break-apart probes was carried out.
Results: Patients' mean age at diagnosis was 52 years. Tumour size ranged from 0.5-5cm. Microscopic examination revealed tubular and cribriform patterns. A minor solid component was identified in one case. No high-grade components were detected. Perineural invasion was seen in all cases. All patients were treated with surgery, followed by postoperative radiation in one of them. Positive surgical margins were reported in four patients. During follow-up (median:21 years), three patients (all with positive margins) developed local recurrences treated with surgery and radiation. Currently, all patients are disease-free.
FISH analysis was successful in 4/5 cases. MYB rearrangement was present in 3/4 cases, including one with concurrent MYB amplification. No MYBL1 rearrangements were found.
Conclusion: We corroborate the histological and genetic similarity between vulvar ACC and ACCs elsewhere. We also confirm that MYB rearrangement is frequent in vulvar ACC.

PS-02-022
Prognostic role of mismatch repair protein defect in endometrioid type of endometrial carcinoma
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Background & objectives: Microsatellite instability, associated with mismatch repair proteins deficiency, is a frequent alteration in endometrial cancer(EC) that has been associated with prognosis.
evaluate the state of MLH1 and MSH2 as a potential prognostic factor in endometrioid type of endometrial cancer(EEC).
Methods: the current work was carried out on 80 cases of EEC retrieved [with clinical data] from the department of Pathology, Faculty of Medicine, Tanta University in the period from June 2017 to December 2018. H&E staining and immunohistochemical staining with MLH1and MSH2 was done for each case.
Results: among 80 cases, 29 (36.3%)showed abnormal MMRP expression (loss of MLH1 expression was detected in 19 cases (65.5%) and loss of MSH2 expression was detected in (34.5%) of cases. Loss of MMRP expression was closely related to some clinicopathologic features (patient's age, histopathological tumour grade, and tumour stage) with a statistically significant relation . No significant relation was found with myometrial and lymphovascular invasion (p value= 0.054 and 0.028)
Conclusion: a subset of endometrioid type demonstrates MMRP defect; the MMRP deficient EEC often displays adverse clinicopathological parameters as poorly differentiated or undifferentiated histology as well as advanced stage with early age of onset at presentation.

PS-02-023
Non squamous malignancies of vagina and vulva: 33 year experience at a tertiary centre in UK
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Background & objectives: Under 10% of gynaecological cancers are diagnosed in the vulva and vagina; mostly squamous cell carcinomas. Melanoma, Paget disease, basal cell carcinomas and other cancers can present with vulval/vaginal symptoms.
Methods: The pathology information system of a tertiary referral centre for vulvo-vaginal cancers was searched for cancers of the vulva and vagina from 1996 to 2019. Squamous carcinomas were excluded and the remaining entities were catalogued.
Results: 135 vaginal and 86 vulval cases of non-squamous cancers were found. 108 cases of metastatic carcinomas from endometrium, cervix, ovary, bowel, bladder, kidney and breast formed the largest category. Basal cell carcinomas constituted the 2nd largest category. Others included melanomas, Paget disease, and adenoid cystic carcinomas. Primary adenocarcinomas included porocarcinoma, mammary type carcinoma, enteric type carcinoma, clear cell carcinoma, Bartholin gland adenocarcinoma and malignant transformation of hidradenoma papilliferum.
Conclusion: The vulva and vagina can harbour a wide range of non-squamous malignancies. The most challenging of these are adenocarcinomas which can be metastatic from other sites. The dominance of metastatic carcinomas in this series is likely to reflect consultation practice of specialist pathologists

PS-02-024
Vulva carcinoma: an overview of a rare disease and summary of experience from King Hussein Cancer Center (KHCC)
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Background & objectives: Carcinoma of the vulva constitutes only 5% of female genital malignancies, of which the most common type is squamous cell carcinoma (SCC). There is global variation in the prevalence, with only few epidemiologic studies were conducted in the Arab world.
Methods: This is a retrospective chart review of all vulva SCC cases referred to KHCC between 2004-2018. Phase 1; demographic data, changes in the trends over the years, pathology findings, treatment and outcome are summarized. Phase 2 (in progress); include immunohistochemical testing for (P16, P53, Ki-67), for detection of Vulvar intraepithelial neoplasia (VIN), and RFLP-PCR for detection of HPV infection/serotyping, respectively.
Results: The total number of patients is 62.There is a dramatic increase in the number of cases (59.7%; 2016-2018). The mean age at diagnosis was 56 years. The average tumour size and depth of invasion were 30.1mm and 7.73mm, respectively. According to FIGO staging, stage I, II, III and IV were 46.2%, 5.8%, 28.8%, and 19.2%,respectively. Surgical resection was offered to 82.8% of cases, with or without chemotherapy/radiotherapy. With mean follow up duration of 18.4 months, 64.5% are alive; 90% of them are in complete remission. The 5 years event free survival, and overall survival rates are 67.65% and 55.51%, respectively. At this time, prevalence of VIN and HPV infection are under investigation.
Conclusion: Carcinoma of the vulva is a rare disease that is witnessing an increased trend in the last few years. It is associated with a favourable outcome when treated properly. The underlying predisposing and/or associated risk factors need to be further indicated.
Funding: Phase 2 of this project is currently funded by King Hussein cancer centre-Jordan.

PS-02-025
Plexiform tumourlets of the uterus: clinicopathological and molecular analysis of a series
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Background & objectives: Plexiform tumourlets of the uterus (PTU) are extremely rare, tiny, multifocal epithelioid mesenchymal lesions thought to represent variants of epithelioid leiomyoma. They are detected as incidental histological findings in hysterectomy specimens for other diseases. However, their pathogenesis remains unknown.

Methods: Seven cases of PTU were identified in routine pathology files at the Institute of Pathology, Erlangen (2012-2017), and in consultations files of two authors. Clinical and pathological characteristics were reviewed. Four cases with sufficient material were investigated for gene fusions using TruSight-RNA Fusion Panel (Illumina® Inc., San Diego, CA, USA) and three were assessed for FOXL2 mutations by direct sequencing.
Results: Age at diagnosis ranged between 44 and 56 years. Patients received curettage (1 case) or hysterectomy due to perimenopausal bleeding, endometrial carcinoma, symptomatic adenomyosis uteri or uterine leiomyomas. PTUs presented as solitary lesions (n=2), multiple tiny nodules (n=3) or as tiny lesions extensively involving the myometrium (size range: 0.15-0.5 mm). None of three cases each successfully tested for gene fusions by RNA testing or FOXL2 mutations revealed positive results.
Conclusion: The molecular pathogenesis of uterine plexiform tumourlets remains elusive.

PS-02-026
PD-L1 expression in different molecular subgroups of endometrial carcinomas
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Background & objectives: New oncological treatment guidelines for endometrial carcinomas (ECs) are constantly evolving with the recent emphasis on immunotherapy options for distinct subsets of ECs. Our purpose was to identify specific molecular categories and analyse PDL-1 expression on these different subtypes.
Methods: We included in our study 50 cases of ECs in a Romanian cohort over 5 years (2014-2019). For each case, we evaluated a vast set of pathological parameters and tested p53, MSH6 and PMS2 for MMR status. PDL-1 expression was quantified in four distinct molecular groups: MMR-D, MSS, CNH (abnormal expression of p53) and CNL (wild-type p53).
Results: According to our findings, the mean age for diagnosis was 63 years, with endometrioid subtype being the most frequent. We identified 34 cases - MMR-D, 16 cases - MMR-S, 13 cases - CNH and 37 cases - CNL. PDL-1 positivity was more than 50% in two MMR-D cases and one CNH,1-49% in 7 MMR-D cases, 4 CNH cases and 6 CNL cases and negative in 30 cases.Five-year OS was 84%.
Conclusion: Recent advances in immunotherapy have opened options for women with the MSI subset of tumours and current trials are attempting to expand the benefits of immune checkpoint inhibition to a wider group of patients with ECs. For that reason, we set out to define the molecular landscape of ECs in Romania and establish what other molecular groups would be suitable for PDL-1 testing. To our knowledge, this is the first attempt in our country.

PS-02-028
PD-L1 expression in high grade serous carcinoma of the female genital tract correlates with favourable prognosis - experience within an immunohistochemically re-classified large clinical cohort
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Background & objectives: High-grade serous tubo-ovarian carcinoma (HGSC) is the most lethal carcinoma of the female genital organs. In recent studies, PD-L1 expression correlates with prolonged overall survival. We investigated a large consecutive cohort of immunohistochemically re-classified HGSCs for PD-L1 expression status.
Methods: A consecutive series of 420 cases diagnosed as HGSC and treated at the Womens' Hospital of the University Tübingen from 2000 until 2016 was reviewed by two independent pathologists. Tissue microarrays (TMAs) were stained for a panel of four markers including WT1, p53, progesterone receptor and Napsin-A. PD-L1 expression was analysed using Combined Positivity Score (CPS).
Results: In 94.0% of cases (n= 395/420), the diagnosis of HGSC was confirmed. Within the re-classified 395 (100%) HGSCs, 131 presented PD-L1 expression (36.7%), 250 were negative (63.3%). Median overall survival (OS) for mean CPS showed significant differences: 906 days for patients with PD-L1-negativity (n=250, 63.3%), 1347 days for CPS <1 (n=85, 21.5%) versus 1412 days median OS for CPS 1-25 (n=60, 15.2%)($p<0.001$). We found significant association with complete resection ($p=0.049$).
Conclusion: Within our cohort of re-classified HGSCs of the female genital tract, PD-L1 expression was found in 36.7%, whereas the majority showed negative results (63.3%). In summary, PD-L1 is expressed in a subgroup of HGSCs associated with a favourable prognosis and presents a significant overall survival benefit. These results suggest an important role in the tumour microenvironment and provide a potential therapeutic target.

PS-02-029
Tumour budding and cell nest size did not prove useful as prognostic factors in a series of 121 squamous cell carcinomas of the uterine cervix
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Background & objectives: Squamous cell carcinoma of the cervix (SCCC) grading has no prognostic value. Recently, Jesinghaus, M. et al, proposed a new grading system based on the evaluation of tumour budding and cell nest size, that could help in prognostic patient stratification.
Methods: Two pathologists reviewed a series from 2002 to 2016 of H&E whole slides from SCCC, radical hysterectomies. The clinical files and tumour grading were evaluated accordingly to the parameters proposed by Jesinghaus, M. et al. This grading score was correlated with the staging, treatment and overall survival of the patients.
Results: We studied 121 cases of SCCC. Patients' mean age was 47 years-old (29-80yrs). Tumour stage was pT1(n=99), pT2(n=21) and pT3(n=1) and 31%(n=37) had regional lymph node metastases. 77 patients received adjuvant therapy. Average follow-up was 112 months (5-210mo). 81% of the patients are alive without disease, 8% died of the disease or are alive with disease. 11% of the patients died from other causes or were lost for follow-up. 5%(n=6) had recurrence. Accordingly to the proposed grading system, 11 cases were grade 1, 35 grade 2 and 75 grade 3. We found no correlation between the new grading scores and metastasis, staging, follow-up or recurrence.
Conclusion: In our series, the new grading system showed no correlation with the patient prognostic factors (recurrence, metastasis or follow-up). Poor reproducibility or different patient characteristics might explain this. Although the proposed system seems promising and is useful in other topographies, our results imply that it must be validated in other SCCC cohorts and institutions.

PS-02-031
Clinical and pathologic variables associated to cervical conizations without high grade intraepithelial lesions: a series of 399 cases
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Background & objectives: Between 10-34% of conizations lack ≥CIN-2 (conization without disease, CWD). Our aims are to estimate our CWD

rate, to evaluate the usefulness of deeper morphological reassessment plus p16 to ensure a CWD and to assess clinic-pathologic variables associated to CWDs.
Methods: All conizations and colposcopy biopsies from 2010-19 were reviewed. In CWDs, three deeper extra hematoxylin-eosin slides and one p16 were performed.
The association of clinical (age, colposcopic extension of lesion, only or multiple colposcopy biopsies) and pathological variables (lesion size, lymphocytic reaction in the colposcopy biopsy, conization size; rate of CWD initially and after extra levels) to CWD were studied.
Results: A total of 399 conizations were performed, with a mean age of 38.59 years. 96% of colposcopic lesions were ≥CIN-2, with mean size of 3.23 mm, occupying in a 60.55% of cases a single quadrant. In a 60.55% the colposcopy biopsy was unique.
The initial 81 (20.40%) CWDs were reduced to 63 (15.79%), a decrease of almost a quarter, after applying deeper hematoxylin-eosin levels and extra p16. Six cases (7.41%) were reclassified as low grade dysplasia after reviewing the colposcopy biopsies.
CWD was significantly associated to younger age, single quadrant lesion and a smaller lesional size.
Conclusion: 1.- Our CWD rate is within the published range.
2.- Performing extra hematoxylin-eosin levels and p16 would be a recommended practice to ensure a CWD diagnosis.
3.- There are scarce clinic-pathological variables associated to CWD.

PS-02-032
Uterine rhabdomyosarcomas: 8 cases, a 10-year retrospective study in a tertiary institution
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Background & objectives: WHO defines rhabdomyosarcoma as a rare and malignant, heterologous mesenchymal tumour showing evidence of skeletal muscle differentiation. The cervix is the most common localization, followed by the uterine corpus.
Methods: We conducted a 10-year-retrospective transversal study at Coimbra University Hospital, a tertiary hospital in Portugal (2009-2019) and reviewed all uterine and cervix sarcomas (n=45). Relevant clinical and pathological data was extracted from the hospital database.
Results: A total of 8 cases of rhabdomyosarcomas were found, representing 17.8% of uterine and cervix sarcomas. The tumours consisted of 6 pleomorphic and 2 embryonal rhabdomyosarcomas. No spindled and alveolar variants were found. In this cohort, 2/8 of the cases were diagnosed in a biopsy and 6/8 in the surgical specimen. The most common site was the uterine corpus with 62.5% of cases; the remaining arose in the cervix.
In our cohort, the median age at diagnosis was 69 years (range:40-86years) and the median survival was 21.8 months (range:1-86,7 months). Tumour size ranged from 4 to 13 cm.
Conclusion: Uterine rhabdomyosarcoma is a rare entity. In our series, pleomorphic rhabdomyosarcomas were the most common subtype followed by the embryonal variant.

PS-02-033
First presentation of Mullerian serous carcinoma as nodal metastases: a case series
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Background & objectives: More than of 50% women with serous carcinoma of Mullerian origin present at advanced stage. Dissemination typically occurs via transcoelomic spread. Tubo-ovarian carcinoma presenting as nodal metastases in the absence of clinical features of pelvic disease is rare.
Methods: We present a summary of findings in a series of serous carcinomas of Mullerian origin, diagnosed on lymph node biopsies. These cases were seen as a part of the diagnostic and consultation service of a specialist gynaecological pathology department.
Results: 12 women, 4 each with enlarged axillary and neck nodes, 1 each with enlarged nodes in the supraclavicular fossa, inguinal, peripancreatic and retroperitoneal sites; were diagnosed with metastatic serous carcinoma of Mullerian origin (10 high grade and 2 low grade). 9 presented with mass related symptoms, others with nausea, backache and dysphagia. Pelvic masses were found in 6 cases, 3 patients had lymphadenopathy only, 3 were lost to follow up.
Conclusion: This case series demonstrates that Mullerian serous carcinomas can present as distant nodal metastases in the absence of presenting symptoms of pelvic disease. It is postulated that malignant cells gain access to lymph nodes via peritoneal lymphatics or that carcinomas can arise from Mullerian nodal inclusions. Investigations may demonstrate a pelvic mass in some cases. Accurate and confident diagnosis of Mullerian origin can be made by a combination of morphology and immunohistochemistry.

PS-02-034
Evaluation of spontaneous abortion samples following the Amsterdam Placental Workshop Group consensus statement: study in a single tertiary hospital centre
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Background & objectives: In daily clinical practice, the study of spontaneous abortion is usually limited to the morphological confirmation of pregnancy. In this study we investigated whether the Amsterdam Placental Workshop Group (APWG) recommendations could provide relevant information concerning placental lesions, in comparison to routine study (RS).
Methods: We carried out a 9-month retrospective study of spontaneous abortion samples collected in our institution. All samples coded as "spontaneous abortion" and/or "product of conception" were selected from the Pathology Department database. Maternal clinicopathological and demographic variables were collected from the electronic records. All histopathological samples were reviewed a second time by two pathologists simultaneously using the APWG criteria.
Results: 408 samples were analysed. Mean age 35.5 years (17-48 years), mean gestational age 9.2 weeks (4-18 weeks). Samples were normal in 405 cases in the RS compared to 352 following our systematic revision. Relevant data were identified in 3(1%) cases of the RS [mola(1), acute inflammation(2)] vs. 56(14%) cases with APWG criteria [mola(1), distal villous hypoplasia(1), accelerated villous maturation(1), infarction(12)]. Fibrin was identified in the intervillous space in 41 samples.
Conclusion: The use of the APWG recommendations for the study of spontaneous abortion or placental samples resulted in our identifying 18.6 times more pathology than the RS. Most findings suggest poor placental perfusion, but the intervillous fibrin has uncertain significance.

PS-02-035
Complement system involved in endothelial injury in preeclamptic placenta
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Background & objectives: Preeclampsia is a potentially severe condition of pregnancy, characterized by severe hypertension, proteinuria and

vascular placental lesions. Links between preeclampsia and oxidative stress in trophoblast and endothelium were described and have investigated the role of complement system in these placenta

Methods: 34 placentas from patients with severe preeclampsia (PE) diagnosed before week 32 of pregnancy were obtained. The control group was 10 placentas of women without a diagnosis of hypertension or preeclampsia. Placental specimens obtained were processed and microscopic section were stained for H&E and PAS, as well as for immunohistochemical stains for CD61 (platelet thrombi) and C4d (complement component).

Results: PE group revealed thickened wall of foetal blood capillaries, crowded degenerating villi with decreased intervillous spaces, intravillous and perivillous fibrinoid deposition. Numerous syncytial knots and there was thickened layer of subchorionic fibrinoid. In addition, PE group showed atherosis, swollen endothelial cells and intracapillary thrombi with CD 61 immunomarking and C4d deposit.

Conclusion: Our results show a relationship between PE, lesions in vascular lesions with activation of the complement cascade and C4d deposit. Identification of mechanisms involved in the triggering of endothelial dysfunction may be a promising therapeutic approach in management of PE.

PS-02-038

Co-expression of GATA-3 and PAX-8: a diagnostic pitfall

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Background & objectives: Immunohistochemistry is invaluable in establishing the origin of a poorly differentiated primary tumour or metastatic carcinoma. Overlapping/atypical staining patterns are a common pitfall. Our objective was to ascertain the frequency of tumours co-expressing Müllerian marker PAX-8 and breast/urothelial marker GATA-3.

Methods: We performed a search on our internal pathology I.T. system (CoPath) for all specimens from 2015-2019 on which PAX-8 and GATA-3 immunostains were performed. We then collated the cases which expressed both markers and reviewed the final diagnoses on the pathology reports.

Results: PAX-8 and GATA-3 immunostains were performed on 228 surgical and cytological specimens. 22 tumours expressed both markers. The final histological diagnosis in 12/22 cases (54.5%) favoured tumours originating in the gynaecological tract; most of these were high-grade (8/12) and of tubo-ovarian origin (6/12), while 2/12 were uterine, 1/12 was cervical and for 3/12 the particular site of gynaecological origin was uncertain. 8/22 cases (36.5%) were diagnosed as poorly differentiated/high grade carcinoma where the site of origin could not be determined; 3/8 of these cases had a background history of previous ovarian or endometrial cancer. 1/22 (4.5%) was diagnosed as high-grade urothelial carcinoma and 1/22 (4.5%) as malignant epithelioid tumour.

Conclusion: Immunohistochemistry is commonly used to establish the origin of poorly differentiated or metastatic tumours. PAX-8 is positive in approximately 80% of Müllerian tract-derived carcinomas. GATA-3 is positive in 94% of breast and 86% of urothelial carcinomas. Our study highlights potential diagnostic pitfalls when both markers are positive, particularly in the diagnosis of gynaecological tract malignancy, and supports previous findings of GATA-3 positivity in a subset of endometrial and ovarian carcinomas.

PS-02-039

Mismatch repair deficiency in uterine carcinosarcoma - a 20 year retrospective review: 18 cases tested

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Background & objectives: Immunohistochemistry for mismatch repair (MMR) proteins is recommended in endometrial carcinomas as a screening test for Lynch Syndrome. Carcinosarcomas are staged and treated like other epitelial malignancies, however few studies have evaluated the rate of MMR loss in uterine carcinosarcomas.

Methods: A 20 year retrospective database search of uterine carcinosarcomas was performed at our institution. The histologic diagnoses were confirmed by a gynaecologic pathologist. One tissue section from each case was stained with the 4 MMR proteins (MLH1, PMS2, MSH2, MSH6) and p53.
Heterologous elements and lymphovascular invasion were noted if present.
Clinical features were collected.

Results: 18 cases of uterine carcinosarcoma were identified. 16 cases showed intact expression and 2 mismatch repair deficiency (MMRd) with loss of MSH6 and aberrant p53 expression. 12 of the total number of cases showed aberrant p53 expression. 3 cases showed wild-type p53 expression. 2 cases of Lynch Syndrome were identified among carcinosarcoma patients. Nowadays 17 patients are alive and 1 dead and 1 patient with loss of MSH6 had colorrectal carcinoma.

Conclusion: The rate of MMRd is lower in uterine carcinosarcoma when compared with endometrioid carcinoma. In the setting of MMR loss, a diagnosis of dedifferentiated carcinoma should be considered. Understanding how MMRd contribute to carcinosarcoma pathogenesis is relevant not only for identifying Lynch síndrome and prevent the development of colorectal cancer but also for identifying candidates for immunotherapy, as defects in MMR have been shown to impart vulnerability to checkpoint inhibition.

PS-02-040

Peculiarities of vascularisation of serous adenocarcinoma of fallopian tubes

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Background & objectives: Sometimes it is difficult to estimate the degree of neoplastic vascularization. It can be achieved by using the immunohistochemical studies of CD31 receptors.
To study the peculiarities of the serous adenocarcinoma of fallopian tubes (SAFT) vascularization.

Methods: The study was carried out on 66 samples of tumour tissue of serous adenocarcinoma of fallopian tubes. For study the CD31 expression, the rat monoclonal antibodies 1A10 were used.

Results: In well-differentiated tumours, the structured focal localization of the vessels in papillary formations, which were observed gradually disappeared in the papillae branched. While neoplasia dedifferentiation, the disorders of tumour tissue vascularization with chaotic vessels localization were found. Despite the data on the degrees of microvascular density in different types of carcinoma in case of malignant process development, areas with pronounced microvascular density as well as non-vascular tumour lesions were observed.

Conclusion: The tissue of SAFT is characterized by the structured vascularization of neoplastic tissue with its gradual disorganization under carcinoma dedifferentiation. These results can be used to predict the tumour course, considering the influence of the increased angiogenesis on cancer metastasis and the possibility of using the vascular-suppressant treatment in antitumour therapy.

PS-02-041

Antenatal foetal vascular malperfusion is a placental factor for term preeclampsia

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Background & objectives: Currently, there is evidence that late preeclampsia (PE) in full-term pregnancy is more due to metabolic and

cardiac dysfunction of the mother's body than to placenta pathology, therefore PE in full-term pregnancy should be considered as a pathological condition different from early preeclampsia.
A comparative histopathological evaluation of the foetal-placental and uteroplacental compartments of term and preterm placentas from pregnancies with preeclampsia was performed.
Methods: Retrospective histological examination of 81 placentas from abnormal pregnancies complicated by preeclampsia at 32-35 weeks (n-52) and full-term (37-41 weeks, n-29) gestation was performed. Histopathological criteria of maternal vascular malperfusion follows: acceleration of villi development and placental infarction (more than 10% the placenta volume); criteria for foetal vascular malperfusion follows: fibromuscular sclerosis, vascular ectasia and thrombosis of placental stem villi.
Results: Histopathological signs of maternal vascular malferfusion in all placentas with preeclampsia were detected in 71 cases (88%). Among them, with preterm PE in 52(100%) cases, in term gestation - in 19 (66%) cases. Histopathological signs of FVM were detected in 27 (93%) placentas with term preeclampsia and only in 11(21%) placentas with preterm preeclampsia.
Conclusion: We hypothesize, that FVM is important feto-placental factor in the development of PE. PE in a full-term pregnancy may be associated with compensatory activation the tone of feto-placental large vessels in conditions of clinically latent fetoplacental blood flow disturbance (FVM).

PS-02-042
MRI investigation in preeclampsia for severity diagnostic purposes
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Background & objectives: Over the past 5 years, the number of brain haemorrhages in patients with hypertensive pregnancy disorders has increased 6-fold in the world.
MRI usage prospective in patients with preeclampsia (PE) complaints of headache for reducing the frequency of its complications.
Methods: 36 delivery cases in patients with preeclampsia that had undergone brain MRI were studied.
Results: Brain MRI indications: headache – 35 (97.2%), ophthalmic lesion – 1 (2.8%). PE intensity before the MRI: severe – 24 (66.7%), mild – 12 (33.3%). MRI done during pregnancies – 16.5 (31.3%) of which have revealed abnormalities that prohibit continuing pregnancy: 3 (60%) – posterior reversible encephalopathy syndrome (PRES), 2 (40%) – vascular focal lesions in the brain; a patients (68.7%) had no pathology.
Conclusion: According to MRI data, changes were revealed in 58.3% patients with PE and complaints of headache. Data obtained from the objective assessment of the brain condition helped to avoid unreasonable pregnancy continuation and contributed to the timely therapy correction, which helped reducing the frequency of complications. in 2 patients with PRES and 1 with vascular focal lesions arterial blood pressure and proteinuria levels matched mild PE, but regarding all the revealed changes, all the patients undergone emergen c-section;

PS-02-043
To evaluate the presentation and time of diagnosis of cervical cancer and its precursor lesions in a tertiary care hospital of a low resource country like Pakistan lacking a national screening programme
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Background & objectives: The purpose of the study is to evaluate the most common presentation and diagnosis of cervical cancer and its precursor lesions in a tertiary care hospital of Pakistan in the absence of a local or national level screening program.
Methods: A retrospective descriptive study was carried out in which all the cases of cervical cancer and cervical intraepithelial lesions received in the Histopathology Department of Foundation University Islamabad (FUI) were retrieved from January, 2010 to December 2014. All the surgical specimens were included including biopsies and hysterectomy specimens. The data was then analysed for clinical presentation and age of diagnosis.
Results: A total of 47 cases of cervical cancer and precursor lesions were identified in the 5 year study period.out of which 7 patients were diagnosed with cervical intraepithelial neoplasia(14.89%)while the rest of the women were diagnosed with different types of cervical carcinoma(85.1%).the most common clinical presentation was postmenopausal bleeding(90%) followed by dysfunctional uterine bleeding.(10%).the most common colposcopic findings were cervical growth/mass(89%).the mean age of diagnosis of CIN1,CIN2 and CIN3 was 44.57 and the mean age of diagnosis of carcinoma was
Conclusion: The burden of disease will continue to increase with more frequent presentation with invasive carcinoma therefore education of the public,political support and awarenes is important to combat the disease

PS-02-044
Association of CCL2 (monocyte chemoattractant protein-1) expression with obesity in endometroid endometrial cancer
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Background & objectives: Despite the epidemiological association between endometrial cancer and obesity, the underlying pathophysiological link remains ill-defined. We investigated the potential association between obesity and the tumour-associated inflammatory microenvironment.
Methods: 48 cytokines were profiled by multiplex immunoassay in endometrial cancer (N=93, including 53 endometroid endometrial cancers (EEC) and 40 non-EECs). Sample-matched cytokine mRNA expression data were obtained by microarray analysis of laser-captured microdissected tumour cells. Patient demographics including BMI were also collected for these women. Non-parametric statistical tests were carried out with Benjamini-Hochberg correction for multiple comparisons, as appropriate.
Results: There was no significant difference in BMI between patients with EECs and non-EECs. No significant association between cytokine profiles and BMI were identified in the non-EEC group. However, in the EEC group, there was a significant association between CCL2 expression and obesity, where CCL2 mRNA was higher in patients with BMI >30 (corrected P=0.008). There was a trend for increased CCL2 protein expression (uncorrected P=0.008). CCL2 mRNA and protein levels significantly correlated with each other (SRC=0.551, P<0.00001), as well as positively with BMI (SRC=0.518 and 0.336; P=0.0001 and P=0.017, respectively). There were no significant differences in CCL2 expression between EECs and non-EECs.
Conclusion: We identified an association between tumour epithelial CCL2 expression and BMI in EEC. These findings suggest a potential link between obesity-associated systemic inflammation and its localised effects in the tumour microenvironment.
Funding: Wellbeing of Women (RG1210), Yorkshire Cancer Research (LPP053), Pathological Society of Great Britain and Ireland (Career Development Fellowship awarded to NMO; 1090)

PS-02-046
Pap smear and primary HPV tests results over a recent 3-year period from a routine laboratory setting in Kenya
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Background & objectives: Cervical cancer is a leading cancer in Kenya where a National Cancer Screening Guideline was recently released

recommending HPV Testing as the primary screening method. We hereby share experience on Pap smear and HPV tests done at our laboratory.
Methods: We retrospectively retrieved data from our laboratory information system (LIS) focusing on conventional cervical cytology done over a recent 3-year period from July 2016 to June 2019 corresponding to the period HPV test on Cobas 4800 platform (Roche) was introduced in our laboratory, which is ISO15189 accredited for both tests and one of the busiest laboratories in the country.
Results: A total of 27,447 Pap smears were reported with a median age of 38 years, of whom 97.31% had NILM,1.58% HSIL, 0.57% LSIL, 0.33% ASC-H, 0.02% ASCUS and 0.04% SCC. Up to 43.3% had significant cervicitis on conventional Pap smear and 13.6% had bacterial vaginosis, while 8.9% had atrophic changes.
During the corresponding period, a total of 3523 HPV tests were done, with an over two-fold year-on-year increase in numbers tested. High-risk HPV (HR-HPV) was detected in 26.6% of the cases, of whom 24.5% tested positive for HPV non-16/18 type, 6.2% type 16 and 3.9% type 18. Infection with multiple HPV types was noted in 6% of cases.
Conclusion: The rate of HR-HPV is noticeably high in these women tested in a routine setting. ASCUS seems unusually, low likely due to dual reporting by cytologists and pathologists; HSIL and LSIL rates are comparable to the published literature from Africa

PS-02-047
Clinicopathological features, including immunohistochemical profile of 14 malignant peritoneal mesotheliomas diagnosed at a single institution
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Background & objectives: Malignant peritoneal mesotheliomas (MPMs) are rare tumours with overlapping clinical and histopathological features, especially with epithelial ovarian carcinomas (EOCs). There is no substantial documentation on these rare tumours from our country.
We studied clinicopathological features, including the immunohistochemical profile and clinical outcomes of 14 MPMs, diagnosed at our Institution.
Methods: This was a retrospective study, wherein, 14 cases of MPM in female patients,diagnosed at our Institution, between January 2008 and May 2019 were included, after critical review.
Results: Median age was 54.5 years. Microscopically,most cases(11, 78.6%) displayed epithelioid morphology, followed by biphasic(2, 14.3%) pattern.Sensitivity and specificity of calretinin was 100%(13/13) and 85.%; HBME1 was 100%(5/5) and 100%, and of podoplanin(D2-40) was 60%(2/5) and 100%. Other positively expressed immunomarkers were EMA (n=2/5, 40%) CK5/6 (n=4/4, 100%) and WT1 (n=9/10, 90%). Most patients(5/12)(41.7%) were treated with chemotherapy.The 3-year disease-free and overall survival rates were 25.7% and 54%, respectively.
Conclusion: MPMs can be diagnosed with a combination of clinicopathological features and optimal immunohistochemical markers. Their differentiation from EOCs and other metastatic carcinomas is imperative in view of significant treatment implications.

PS-02-048
Hypoxic damage and endometrial cell antiapoptosis in endometrial hyperplasia
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Background & objectives: Hypoxia stabilizes hypoxia inducible factor-1 alpha (HIF-1 alpha) leading to cell hyperproliferation and antiapoptosis. However, hypoxic damage and antiapoptosis in endometrial hyperplasia (EH) remain little studied. The aim was to compare hypoxic damage and endometrial cells antiapoptosis in EH.
Methods: Endometrial biopsy was obtained from 25 patients with EH without atypia and 25 healthy women. Expression levels of HIF-1 alpha and Bcl-2 were determined by monoclonal antibodies (Epitomics, Clone EP118 and Dako, Clone 124). Videotest - Morphology 5.2 (Russia) was used for morphometric analysis, and nonparametric statistical methods were applied.
Results: In the group of patients with EH, the mean area of HIF-1 alpha immunopositive structures was 41.7% (35.8%; 47.1%). The mean area of Bcl-2 expression was 68.6% (58.4%; 76,2%). In endometrial samples of healthy patients, HIF-positive cells were not recorded, and the average area of immunopositive structures was 0%. The average area of Bcl-2 positive structures was significantly lower in this group compared to patients with EH and was 22.53% (15.6%; 29,8%).
Conclusion: Significantly increased HIF-1 alpha and Bcl-2 expression in EH samples indicates hypoxic damage and raised antiapoptotic activity of intracellular endometrial systems. Increased antiapoptotic activity and HIF-positive cells presence may be an adverse factor leading to endometrial oncotransformation.
The reported study was funded by RFBR, project number 19-315-90101.

PS-02-049
Vitamin D receptors as an additional marker of implantation in ART programmes
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Background & objectives: Vitamin D receptors (VDR) play an important role in endometrial receptivity and implantation. The objective is to assess the impact of VDR expression levels in stroma and endometrial glands on the outcomes of ART programs.
Methods: A prospective study of IVF outcomes was performed in 70 women of advanced reproductive age with tubal-peritoneal infertility. An endometrial pipe-biopsy was taken during the supposed implantation window. The endometrial samples were formalin-fixed and embedded in paraffin. For immunohistochemistry, rabbit polyclonal Vitamin D receptor antibodies were used. The percentage of VDR-positive stromal cells was calculated.
Results: VDR expression in the endometrial stroma was significantly higher in the case of successful implantation. The threshold value was 8.7%, since clinical pregnancy was not observed if the percent of VDR positive cells was equal to or higher than 8.7%. Therefore, the endometrium was favourable for implantation in values of less than 8.7%. There were no significant differences in VDR expression in the endometrial glands.
Conclusion: The obtained results expand the range of endometrial receptivity markers. The identified reference value of VDR expression in the endometrial stroma may optimize the preparation of the endometrium for blastocyst implantation.

PS-02-051
The role of epithelial-to-mesenchymal transition in the development of deep endometriosis
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Background & objectives: Pathogenesis of endometriosis (EM) is not completely studied. According recent researches epithelial-mesenchymal transition (EMT) is involved in progression of EM. Purpose. Identifying the role of epithelial-to-mesenchymal transformation in the development of endometriosis.
Methods: Materials and methods. The study was performed on the surgical materials and from 70 women with deep endometriosis: The control group consisted of 20 women with local peritoneal endometriosis.

Expression levels of panCK, E-cadherin, Vimentin, CD34, SMA were identified by immunohistochemistry analysis of epithelium and stromal cells of heterotopic endometrium. Semi-quantitative assessment of the immunohistochemical results was done.
Results: EMT was found in foci of vascular invasion of deep EM in 47 patients. A hallmark of EMT were the loss of E-cadherin and panCK expression together with arising of vimentin and SMA in epithelial cells.
Conclusion: Progression of deep EM may be associated with EMT. Identifying and understanding the signalling mechanisms, promoting EMT may lead to novel therapeutic strategies, which will inhibit this cellular transformation

PS-02-052
Study of the effect of gestabutonoil on endometrial proliferation in female rats
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Background & objectives: Progesterone analogues are used to preserve pregnancy, treat endometrial hyperplastic processes and endometriosis in combined oral contraceptives. Objective: to evaluate the effect of gestabutonoil on endometrial proliferation in female rats when taken orally.
Methods: All groups included 15 female Wistar rats. Microcapsules with 0.002 g gestobutanoil were intragastrically administered to the experimental groups for 30 days: group 1 at a dosage of 2.5 mg/kg, group 2 - 25 mg/kg. 10 rats made up the control group. Endometrial sections were stained with H&E. Endometrial decidualization was evaluated.
Results: In the first group, the endometrium was in the phase of secretion, an increase in the number, size and tortuosity of the glands, vacuolization of the gland epithelium, loosening of the subglandular zone with pronounced decidualization of the cells was noted. In group 2, the proliferation of glandular epithelium was too intense until the appearance of glandular hyperplasia in 4 females of this group.
Conclusion: Gestabutonoil in small doses causes a therapeutic effect, but at high concentrations it contributes to the development of hyperplastic processes in the endometrium. The use of high doses of gestobanoyl can provoke further proliferation of glands and melignation against the background of endometrial hyperplasia

PS-02-053
Expression of mismatch repair proteins, hormone receptors, and HER2 in metastatic/recurrent endometrial carcinoma
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Background & objectives: Endometrial carcinoma is the most common uterine corpus cancer. Recurrence/metastasis occurs in 1/5 of cases. Molecular markers tailor adjuvant therapies. We aimed to characterize therapy-related marker expression including mismatch repair (MMR) proteins, hormone receptors, and HER2 in metastatic/recurrent endometrial carcinoma.
Methods: A retrospective search in our pathology archive for metastatic/recurrent endometrial carcinoma subsequent to a staging surgery from 2008 to 2019 was performed. Tumours of epithelial origin including carcinoma and carcinosarcoma were included. Slides were retrieved for morphology review. Cases with sufficient formalin-fixed paraffin embedded materials were constructed into tissue microarray for immunohistochemical stains.
Results: Thirty-six cases were identified. The median age at diagnosis was 60 years (34-76) and the median interval to 1st metastasis was 76.4 weeks (1.1 to 795.6). Loss of MMR protein expression was found in 22.2% of cases (seven paired loss of MLH1 and PMS2 and one paired loss of MSH2 and MSH6). Oestrogen receptor, progesterone receptor, and HER2 was positive in 65.6%, 43.8%, and 6.3% of cases, respectively. Thirteen had more than one metastatic event, and paired specimens were available in seven. Four had discrepant marker expression, with one developing MMR protein loss, one oestrogen and progesterone receptor loss, one HER2 gain and one HER2 loss at the last metastasis.
Conclusion: Expression of therapy-related molecular markers is common in metastatic/recurrent endometrial carcinoma. More than half may benefit from hormone therapy and some from immune checkpoint or HER2 inhibitors. Marker expression alters in consecutive metastasis, warranting re-assaying each time to guide treatment.
Funding: Institutional funding

PS-02-054
Case series: p57 discordant hydatidiform moles, case report series
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Background & objectives: Diagnosis and subclassification of hydatidiform moles (HM) is critical to assess the risk of gestational trophoblastic neoplasia (GTN). Rare cases of HM with aberrant p57 immunohistochemistry necessitate genotyping for diagnosis. Here, we present a case series of p57 discordant villi.
Methods: 675 cases of possible HM referred to the Scottish HM service between 2016 and 2019 were analysed using haematoxylin and eosin (H&E) light microscopy examination, ploidy analysis and p57 immunohistochemistry. DNA from 5 cases with discordant p57 staining pattern in cytotrophoblasts and stromal cells were extracted by laser microdissection and genotyped for further characterisation.
Results: Three cases showed aberrant morphology in keeping with HM and a discordant p57 pattern being negative in villous stromal cells while being positive in cytotrophoblasts. Flow cytometry showed a diploid DNA complement. Stromal cells and cytotrophoblasts were separately genotyped using laser microdissection and molecular genotyping which showed mosaicism. Two further cases demonstrated a homozygous and heterozygous complete mole.
Conclusion: This study emphasizes that a multidisciplinary approach using light microscopy, immunohistochemistry and molecular studies is invaluable in subclassifying HM. In particular, rare cases of mosaicism were identified using such approach which is necessary for understanding their risk of developing GTN.

PS-02-055
Immunohistochemistry of P16 and P53 in vulvar cancer
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Background & objectives: Squamous cell carcinoma of the vulva may develop in association or independently of HPV infection. We aim to confirm the association of keratinizing carcinomas with absence of HPV infection, and warty and basaloid carcinomas with presence of this virus.
Methods: We reviewed clinical manifestations, histological morphology and immunophenotype of 39 cases. We performed immunohistochemistry for p16 and p53, and PCR to evaluate HPV status. Statistical analysis was performed using Fisher´s exact test and t/ANOVA test. Histologically we determined 30 classic keratinizing squamous carcinomas, 5 warty and 4 basaloid carcinomas.
Results: In the statistical analysis, diffuse expression with p16 was significantly associated with younger age ($p = 0.0025$), presence of high-grade intraepithelial lesion ($p < 0.0001$), koilocytosis ($p = 0.02$), and morphological subtype ($p = 0.02$), and was inversely associated with

the expression of p53 ($p < 0.0001$) and the presence of lichen sclerosus ($p = 0.0051$). It is curious that 4 keratinizing carcinomas of the cases studied presented coexpression of p16 and p53. Only 1 warty tumour was negative for p16 and positive for p53, and 9 keratinizing tumours were positive for p16 and negative for p53. Four of them were PCR positive for high risk HPV.
Conclusion: Although these findings show that the use of hematoxylin and eosin could correctly define tumours associated with HPV, we strongly suggest the performance of immunohistochemistry, especially in squamous keratinizing classic carcinomas in young patients with a history of HPV.

PS-02-056
Cross-talking of two apoptotic molecules in ovarian cancer
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Background & objectives: Objective: Our study aimed to analyse the immunoexpression of p53 and c-FLIP in ovarian carcinoma in relationship with the clinicopathological features.
Methods: The study group consisted of 63 cases of ovarian carcinomas histopathologically diagnosed as serous (44 cases), and non-serous (19 cases); 24 cases were classified as stage I-II and 39 as stage III; 12 cases were assessed as G1, 24 cases as G2, 27 cases as G3 and G4. Tissue fragments were immunohistochemically processed by using anti-p53 and c-FLIP antibodies.
Results: c-FLIP+/p53+ expression was noted in 15 cases and negative in 14 cases. 17 cases exhibited c-FLIP-/p53+ and c-FLIP+/p53- respectively. Cases with c-FLIP+/p53- profile had the following distribution according to tumour stage: 8 in stage I and 9 in stage III, and tumour grade: G1 in 6 cases, G2 in 8 cases and G3 in 3 cases. Cases presenting c-FLIP-/p53+ profile were framed as follows: 2 in stage I, 2 in stage II and 13 in stage III; 1 case was graded as G1, 6 cases as G2, 9 cases as G3 and 1 case as G4. Statistical analysis revealed significant differences between c-FLIP+/p53- and, respectively, c-FLIP-/p53+ expression, and tumour grade.
Conclusion: The study of FLIP and p53 molecules provides integrated images of the apoptotic mechanism based on a cross-talk between the intrinsic and extrinsic pathways

PS-02-057
Hsp70 and Hsp90 expression in normal and tumour endometrial tissues
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Background & objectives: Endometrial cells acquire new peculiarities during malignant transformation and progression, which plays a significant role in the behaviour of neoplastic cells.
The objective of our study presented here was to characterize hsp70 and hsp90 expressions in normal and tumour endometrium.
Methods: The investigation was conducted on 50 samples with different types (endometrioid, serous and clear-cell) endometrial carcinoma. Ten cases of normal endometrium were used for comparison. The presence of hsp70 and hsp90 was detected by the immunohistochemistry utilizing the mouse mAb W27 and rabbit pAb (0.1μg/ml), respectively.
Results: Normal endometrium is characterized by the focal nuclear-cytoplasmic expression of hsp70. Endometrial carcinomas showed an increase in its expression in tumour cells with the appearance of hsp90. The de-differentiation of tumours was accompanied by increase chaperone response. Both were found in a high proportion of cancer cells. It should be noted, that most neoplasias had a heterogeneous expression of chaperons in tumour tissue.
Conclusion: The occurrence and progression of endometrial carcinomas are accompanied by the change hsp70 and hsp90 expression in tumour cells. They acquire additional resistance due to the synthesis of chaperones which increase their survival.

PS-02-059
A histological analysis of the placenta for the diagnosis of chronic abruption-oligohydramnios sequence
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Background & objectives: Chronic abruption-oligohydramnios sequence (CAOS) is characterized by diffuse chorioamniotic hemosiderosis (DCH). We compared the degree and distribution pattern of hemosiderin deposition (HD) on the chorionic plate (CP) and free membrane (FM).
Methods: We selected 20 CAOS patients, 21 non-CAOS patients as control group A (CA) matched by gestational weeks and 21 non-CAOS patients as control group B (CB) with bloody amniotic fluid. Iron staining of CP and FM was performed for every case. HD was evaluated by a histological score (HS) determined as positivity (0-3) multiplied by the staining area extent (0-4).
Results: HD was found in 100% (20/20) of CAOS patients and 14% (3/21) of CA and 9.5% (2/21) of CB patients. In both FM and CP, CAOS patients showed a significantly higher HS than control patients (CAOS, HS=4-12; CA, HS=0-1, $p<0.0001$; CB, HS=0-3, $p<0.0001$). In three CAOS patients, HD was seen only in the CP. The HS of the CP was significantly higher than that of the FM ($p=0.0003$).
Conclusion: CAOS was histologically characterized by DCH with an HS ≥4. The CP was better suited for the evaluation of DCH than the FM.

PS-02-060
A review of cases submitted for molecular genotyping by the Scottish Hydatidiform Mole Service over a 3-year period
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Background & objectives: In Scotland, suspected molar pregnancies are referred by the local pathologist to the Scottish Hydatidiform mole service (SHMS) in Dundee. This is a review of those cases that were diagnostically challenging and were submitted for molecular genotyping.
Methods: Submitted slides and blocks are booked in and ploidy analysis undertaken on all cases. If diploid, P57 immunohistochemistry (IHC) performed. Slides are reviewed by the pathologist and a final diagnosis of complete or partial mole or non-molar pregnancy reported. Molecular studies were undertaken if the diagnosis was equivocal. Genotyping was performed on DNA extracted from chorionic villi and maternal decidua.
Results: 689 cases received between 2017 and 2019. Histology, ploidy analysis and p57 IHC sufficient for diagnosis of 95% of referrals. The remaining 5% (34/689) were submitted for molecular genotyping to confirm the diagnosis. Where required, specific populations of chorionic villi or regions of discordant P57 expression were microdissected. Results showed, 56% (19/34) of cases were associated with a molar genotype including complete heterozygous or homozygous complement, or diandric triploidy. This included 5 cases of complex results including mosaicism and triandric tetraploidy. Biparental inheritance was reported in 15% (5/34) of cases. 18% (6/34) of cases were uninterpretable and the remaining 12% (4/34) of cases were associated with trisomy 21 or digynic triploidy.
Conclusion: Only a small number of cases submitted to the SHMS required further investigation by molecular genotyping with several cases showing complex results that could not be reliably established by other methods. This work reviews the range of diverse and complex cases seen by a national referral centre.

PS-02-061

Correlation of core needle biopsy to diagnose breast phyllodes tumours – experience of a tertiary hospital

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Background & objectives: A retrospective study of diagnosis was performed in patients with phyllodes tumours (PT) of the breast who were submitted to preoperative core needle biopsy(CNB) and had breast surgery at Centro Hospitalar e Universitário of Coimbra, comparing accuracy of both diagnosis.
Methods: Data from 13 patients with PT who underwent preoperative CNB and breast surgery were retrospectively analysed. We reviewed the CNB and surgical specimen diagnostic data. A diagnostic test was used to evaluate the sensitivity and specificity of CNB in diagnosing benign, borderline, and malignant phyllodes tumours.
Results: All patients were female with a mean age of 50.3 years (range 27-70 years). The accuracy of CNB for diagnosing PT was 38.5% (5/13). Of the remaining patients, were diagnosed with fibroadenoma or high-grade sarcoma. The sensitivity of CNB to diagnose benign, borderline, and malignant phyllodes tumours were 50% (2/4), 25% (1/4), and 20% (1/5), respectively, whereas the corresponding specificity were 40%, 100%, and 100%, respectively.
Conclusion: CNB provides a pathological basis for the preoperative diagnosis of PT of the breast, but it's accuracy is poor and guidance is limited for surgical decisions. Considering CNB along with multiple histologic features may improve the ability to accurately diagnose PT. Literature recommends an integrated assessment using CNBs in combination with clinical data and imaging features as a reliable strategy to assist PT diagnosis.

PS-02-062

Predictive assessment and follow-up strategy for patients with CIN 1 based on the use of colposcopic indices and immunohistochemical markers

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Background & objectives: There are currently no clear criteria for patient management with CIN 1. It is important to find diagnostic tests and approaches that can predict the following development of CIN and justify the choice of patient management tactics.
Methods: 84 biopsy specimens from patients with a histologically verified diagnosis of CNS 1 were examined: HPV 16/18 status, colposcopic features, routine histopathology with koilocytosis evaluation, expression of Ki-67, P53 and P16INK4a by immunohistochemistry. The control study was carried out 12 months later. The patients were divided into 3 groups according to the results: regression, CIN permanence, progression to CIN 2.
Results: Differences in the colposcopic characteristics using Reid and Coppleson indexes have been identified. In the group with CIN persistence a well-established increase in the number koilocytosis changes were revealed, as well as differences in the level of P16ink4a expression ($p<0,05$). .After calculation of the quantitative influence of factors and using the Wald test (non-uniform serial analysis) diagnostic coefficients for these factors were calculated with the following validity parameters: sensitivity - 92,7% and specificity - 86,1%. Immunohistochemical detection of Ki-67 and P53 correlate with the dynamics of morphological changes but was not relevant to the prediction for the evolution of CIN 1.
Conclusion: CIN 1 is a heterogeneous group with different colposcopic characteristics and parameters of cell renewal which determine the prognosis. The following characteristics are significant for the forecast: colposcopic indexes Reid and Coppleson, detection of koilocytosis after haematoxylin and eosin stain of fixed tissue, evaluation of expression level of P16ink4a. The proposed method of CIN 1 prognosis assessment with estimation significant colposcopic, morphological and immunohistochemical indicators is effective.

PS-02-064

Evaluation of PTEN protein expression in normal endometrium and endometrioid carcinoma surgical specimens

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Background & objectives: In the present study, we examined PTEN protein expression patterns in normal endometrium (NE) and endometrioid carcinoma (EC).
Methods: Thirty cases each of FFPE NE and EC samples were examined by immunohistochemistry for PTEN expression. Specimens were evaluated manually by scoring the staining intensity of the strongest stained part for glands and stroma separately. The score was 0 to 4; negative, very weak, weak, medium, and strong. For statistical analysis, Wilcoxon rank-sum test was used.
Results: Distribution of gland score in NE was 76.6%, 20%, 3.3%, 0%, 0%, (average: 0.266). While, the one in EC was 50%, 16.7%, 20%, 10%, 3.3% (average: 1.000). The average gland score of EC were significantly higher than that of NE ($P = 0.0104$). Distribution of stroma score in NE was 10%, 0%, 60%, 30%, 0% (average: 2.1). While, the one in EC was 20%, 0%, 60%, 20%, 0% (average: 1.8). The stroma score was not significantly different in both groups. In both NE and EC, the stroma score was significantly higher than the gland score (NE: $P<0.0001$, EC: $P = 0.0065$).
Conclusion: PTEN expression in NE is supposed to be weak because PTEN is not mutated. Indeed, in our analysis, PTEN expression was mostly negative or very weak, which results were identical to the previous report. While, in EC, strong expression and no expression was sometimes observed in the same specimens. Our results indicated that heterogeneous PTEN gene mutation would happen during progression to cancer and resulted in a patchy staining pattern.

PS-02-065

Histological pattern of endometrial biopsies in women with abnormal uterine bleeding in a hospital in North Central Nigeria

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Background & objectives: Varied morphological patterns have been reported in Endometrial biopsies in various parts of our country. We aim to document fnding from a one-year review of cases seen in a community group private practice.
Methods: The study is a retrospective cross-sectional study carried out in the Department of Pathology of Premier Hospital, Abuja, on specimens received over a one-year period. Four hundred and eighty-six samples of endometrial biopsies and curettings from women presenting with abnormal uterine bleeding sent to the histopathology laboratory were analysed.
Results: Four hundred and eighty-six samples of endometrial biopsies and curettings from women presenting with abnormal uterine bleeding sent to the histopathology laboratory were analysed. The most common biopsies were those of product of conception which accounted for 304 cases (62.6%). Most of the cases of endometrial hyperplasia were typical. Endometritis and chorioamnionitis were the infammatory conditions seen. Twenty-three women had molar pregnancies. The most common cause of abnormal uterine bleeding in this population is retained products of conception.
Conclusion: The most common cause of abnormal uterine bleeding in this population is retained products of conception. There may be need to retrain some of the staffs involved in the management of pregnancy related complications. There is need to further evaluate pregnancy related

complications to ascertain the causes and circumstances responsible for them so as to appropriately direct interventional protocols.

PS-02-066

High risk HPV detection in formalin fixed paraffin-embedded (FFPE) cervical tissue with Aptima HPV assay

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Background & objectives: High risk-HPV(HR-HPV) is implicated in the development of intraepithelial neoplasia and carcinoma of uterine cervix. Several liquid based HPV detection techniques are available, and approved by FDA, however there are no FDA approval and enough experience for HPV detection in FFPE tissues.
Methods: One hundred and ninety-six cervical tissue specimens, each from a patient, were retrieved for HR-HPV detection. One-hundred and fifteen of these samples were diagnosed as HSIL and 46 as cervical squamous cell carcinoma (SCC). 36 of these FFPE cervical samples were normal. Histopathologic diagnosis was accepted as the golden standard.
Results: 189 of the assays provided informative results. HR-HPV was detected in 99.35% of the HSIL and cervical SCCs. Only one tissue sample was resulted as false negative and there were no false positive results. Sensitvity and specifity of the test were 99.35% and 100% (95%CI: 96.41%-99.98% and 90.26%-100% respectively). Positve predictive value and negative predictive value was 100% and 97.30% (95%CI: 83.62%-99.61%). Accuracy for this technique was 99.47% (95%CI: 97.09%-99.99%)
Conclusion: This HPV detection technique with Aptima HR-HPV Assay provides a reliable method for HR-HPV testing in FFPE tissue specimens however there is still need for larger studies.
Funding: HPV detection test cost covered by Hologic

PS-02-067

New approaches in study of pathomorphological aspects of diabetes on background of pregnancy

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Background & objectives: About 422 mln. people are suffered from diabetes. The birth of children in women with such pathology is very important question. In this connection, the aim of our research is the exploration of pathomorphological features of diabetes in pregnant.
Methods: The pregnant with diabetes of 1 type (25), diabetes of 2 type (22), gestational diabetes (20) were explored. The way of modelling of pancreatogenic diabetes with relevant insulin insufficiency at partial resection of pancreas in rats was designed. The samples of placenta and uterus of rats and women of line "Wistar" (30) were studied in light and scanning electron microscope.
Results: Plethora, diapedesis, thrombosis, fibrin were revealed in vessels of miometrium. Their extension at gestational diabetes was 1,9±0,6μm, at diabetes of 1 type was 1,4±0,2μm, at diabetes of 2 type was 1,7±0,6μm (3,0±0,4). The surface of endotheliocytes was altered. Villi of intermediate type were prevailed in placenta. The vast majority of blood vessels are full-blooded, with area 33,6±4,3, 40,2±5,0, 49,3±6,6μm (28,7±2,4). The sites of sclerosis were revealed in stroma.
Conclusion: Necessary correction for improving of pregnancy and childbirth indexes' may be conducted by clinicians due to received data

PS-02-068

Analysis of intraoperative consultation in ovarian tumours: an 11-year retrospective study of 321 cases

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Background & objectives: The intraoperative consultation evaluation in ovarian tumours is crucial for surgical management. Our purpose was to assess the concordance, discordance, and deferred rates of intraoperative diagnosis, along with the agreement in the behaviour of the tumour.
Methods: A retrospective, 11-year review of consecutive intraoperative consultations done between January 2009 and December 2019 at the Department of Pathology, Prof. Doutor Fernando Fonseca Hospital, was compared with definitive histology reports. The sensitivity, specificity and predictive values of each category (benign, borderline/uncertain behaviour and malignant) were determined.
Results: On a total of 321 intraoperative consultations, 261 reports (81.3%) were concordant with the definitive histology, 34 reports (10.6%) had minor discordances, 3 reports (0.9%) had major discordances and 23 cases (7.2%) had a deferred report to paraffin sections. The diagnosis that resulted in most inconsistencies were borderline tumours that turned out to be carcinomas and benign mesenchymal lesions, highlighting the importance of some limitations, including the sampling errors. Agreement between the behaviour of the tumour in the frozen section and definitive histology was observed in 98.3%, yielding a sensitivity and a positive predictive value for malignant tumours of 94.9% and 98.2%, respectively.
Conclusion: This retrospective study shows that frozen section evaluation of ovarian tumours represents a highly sensitive and specific technique that can be used to guide the surgeon to perform the appropriate surgical procedure. The authors present the main diagnostic challenges.

PS-02-069

Histopathological spectrum of ovarian tumours- a prospective study at CMS-TH - Bharatpur - Chitwan - Nepal

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Background & objectives: Ovary is the third most common site of neoplastic lesions in female genital tract. Ovarian tumours occur in any age group. Ovarian neoplasms have become increasingly important because they have gradually increased mortality rate due to female genital cancers.
Methods: This study was carried out on 75 cases of surgically resected ovarian tumour specimens fulfilling inclusion criteria at Department of Pathology in CMS-TH, from January 2016 to June 2017. Clinical data was recorded in predesigned proforma. The specimens were grossed, processed, embedded and stained using standard procedures and were analysed using light microscopy. Statistical analysis was done using SPSS 20.0
Results: Age range of the patients was from 10 to 70 years with maximum cases 32.0 in the age group of 21-30 years. Histopathological diagnosis was mature cystic teratoma 38.8%, serous cystadenoma 29.4%, mucinous cystadenoma 8.0%, borderline mucinous tumour 5.3%, serous cystadenocarcinoma 4.0%, dysgerminoma 4.0%, steroid cell tumour 2.7%, and borderline serous tumour, mucinous cystadenocarcinoma, mature cystic teratoma transforming into SCC, immature teratoma, Sertoli Leydig cell tumour and fibroma 1.3%.
Conclusion: Benign tumours were more common than malignant tumours for all age group. Most of the tumours were of surface epithelial cell origin. Mature cystic teratoma was the most common ovarian tumour as well as the most common benign tumour. Serous cystadenocarcinoma and dysgerminoma were most common malignant tumours. Malignant surface epithelial tumours usually occurred in older age whereas malignant germ cell tumours occurred in younger age. There was significant statistical Clinico-pathological correlation.

PS-02-070

Clinicopathological features, immunohistochemical profile and clinical outcomes of 27 primary peritoneal carcinomas: a single institutional study

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Background & objectives: Primary peritoneal carcinomas (PPCs) are rare tumours, with overlapping clinic-pathological features with epithelial ovarian carcinomas(EOCs) and mesotheliomas. We studied clinicopathological features, including immunohistochemical profile and clinical outcomes of PPCs diagnosed at our Institution.
Methods: This was a retrospective study, wherein 27 PPCs, diagnosed between January 2008 and May 2019 were included, after review, as per established criteria. Various clinicopathological features were analysed with Median and average age of patients being 60 and 55 years, respectively.
Results: Microscopically, 93% tumours (25/27) were of high-grade serous type. Sensitivity and specificity of PAX8 was 100% (13/13) and 87.5%, and for oestrogen receptor (ER) was and 100% (7/7) and 100%. Most patients (14/23, 60.9%) were treated with neoadjuvant chemotherapy (NACT), interval debulking surgery (IDS) and adjuvant chemotherapy. Median disease-free survival (DFS) was 32 months. Estimated 3 year-DFS and overall survival was 47.3% and 69.8%. There were lesser recurrences in cases of NACT and IDS (4/14) vs. surgery and adjuvant CT (4/8) (p=0.59).
Conclusion: This constitutes the largest series on clinicopathologic profile of PPCs from our subcontinent. PAX8, ER and calretinin constitute as useful diagnostic immunostains. It is crucial to differentiate these tumours from their mimic, mesotheliomas, in view of associated treatment implications.

PS-02-071

CEACAM1 expression in the normal uterus of rats

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Background & objectives: The carcinoembryonic antigen-related adhesion molecules (CEACAM) play a significant role in numerous physiological processes, such as cell-cell and cell-ECM adhesion, angiogenesis, proliferation, etc.
The objective is characterization of the CEACAM1 expression pattern in normal tissues of rat uterus.
Methods: Uterus sections were taken from intact female wild-type Wistar rats. The immunohistochemical investigation was performed utilizing mAb Be9.2 (α-rat-CEACAM1, N domain binding, mouse IgG1 kappa), mAb 11-1H (α-rat-CEACAM1, not-N domain binding, mouse IgG1 kappa) and isotype matched control antibodies kindly provided by B.B.Singer. Goat anti rat-HRP coupled antibody and a DAB substrate were used for visualization of the CEACAM1 expression.
Results: CEACAM1 expression was found on the apical cellular polarity of the luminal and glandular columnar cells along the surface of normal endometrium and endocervix. This localization was coinciding with the location of the cellular microvilli. Interestingly, the use of mAb 11-1H allowed to detect week CEACAM1 expression only in the luminal and single glandular epithelium, although mAb Be9.2 was expressed by all endometrium. As expected, single leukocytes diffusely scattered in the underlying stroma were CEACAM1-positive as shown by Be9.2 and 11-1H binding and thus served as internal staining control for both antibodies.
Conclusion: The luminal and glandular epithelium of normal endometrium and endocervix express significant amounts of CEACAM1 on the apical cell surface. However, mAb Be9.2 showed a higher sensitivity for CEACAM1 in uterus epithelial cells during immunohistochemical investigation than mAb 11-1H.

PS-02-072

Differential proteomic analysis between low grade, early stage endometrioid endometrial carcinoma and benign endometrium

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Background & objectives: Low grade, early stage endometrioid endometrial carcinomas are the major proportion of endometrial carcinomas. As a previous step to identify diagnostic biomarkers, we aimed to elucidate the differences at the proteomic level between tumour tissues and matched uterine non-tumour tissues.
Methods: Tumour and non-tumour tissue including endometrium and myometrium from 16 patients was analysed. Proteins were extracted from formalin-fixed paraffin-embedded tissue. Quantitative proteomic analysis was done by isobaric labelling with tandem mass tags (TMT). Tryptic peptides were performed using a Q Exactive mass spectrometer coupled to a nEasy-nLC 1000 nano system (ThermoScientific). MS data were analysed with Maxquant using standardised workflows.
Results: A total amount of 3,113 proteins were quantified and 730 were differentially expressed between both conditions. Relevant pathways affected included integrin signalling and inflammation mediated by chemokine and cytokine signalling. The main biological processes altered were cellular and metabolic processes.
Conclusion: Integrin signalling and inflammation mediated by chemokine and cytokine signalling pathways are promising pathways to identify diagnostic biomarkers in low grade, early stage endometrioid endometrial carcinomas.
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PS-02-073

A morphological and immunohistochemical comparison of primary low grade, early stage endometrioid endometrial carcinomas and their relapses

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Background & objectives: Low grade, early stage endometrioid endometrial carcinomas fall into copy number low and microsatellite unstable molecular groups. Our main objective was to analyse concordance between morphological features and immunohistochemical markers used for molecular classifying in primary tumours and their relapses.
Methods: A total of 19 relapse biopsies from 16 patients were identified from a single hospital cohort comprising 258 low grade, early stage endometrioid endometrial carcinomas. Morphological features such as grade, squamous and mucinous differentiation were evaluated in primary and relapses. Tissue microarray were constructed and immunohistochemical markers for mismatch repair proteins (MLH1, PMS2, MSH2 & MSH6) and p53 were performed.
Results: There were 16 biopsies from locoregional relapses and 3 from lung metastases. Concordance was poor for morphological features such as grade (kappa=0.023), squamous (kappa=-0.203) and mucinous differentiation (kappa=0.215). Tumour grade at relapse was the same in 8 cases, upgraded in 8 and downgraded in 3. Microsatellite instability interpretation derived from mismatch repair proteins expression and p53 expression had a perfect concordance (kappa=1).

Conclusion: There is a perfect surrogate molecular group concordance between relapses and primaries low grade, early stage endometrioid endometrial carcinomas. Morphological features of primaries are poor predictor of their relapses.

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PS-02-074

HPV-independent intraepithelial lesions of the vulva mimicking HPV-positive squamous intraepithelial lesions

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Background & objectives: There are two etiopathogenic types of vulvar squamous cell carcinoma (VSCC), HPV-associated and HPV-independent, each one associated with a specific intraepithelial lesion. However, unusual patters have been described. We aimed to explore these unusual histological patterns of intraepithelial precursors.
Methods: We analysed 779 DNA HPV negative, p16-negative VSCCs, with at least 1 cm of skin adjacent to the invasive tumour available. We evaluated the neighboring skin and performed p53 immunohistochemistry.
Results: 254 tumours (33%) had adjacent intraepithelial lesions. Of them, 22 (9%) had vulvar acanthosis with abnormal differentiation /differentiated exophytic intraepithelial lesion, and 232 had differentiated vulvar intraepithelial neoplasia (dVIN), which was of conventional type in 184 cases (72%), and mimicked squamous intraepithelial lesions (SIL) in 48 cases (19%)). Four of these SIL-like lesions resembled LSIL and 44 simulated HSIL (24 basaloid-like, 13 warty-like and 7 mixed basaloid/warty features). Thirty-five of 48 (73%) of these HPV-negative intraepithelial lesions mimicking HSIL showed p53 abnormal staining.
Conclusion: A small, but significant percentage of intraepithelial precursors associated with HPV-independent VSCC mimic SIL, mostly HSIL. Approximately one-third of these lesions will arise in absence of TP53 mutations.

PS-02-075

An audit of histopathology reports of carcinoma cervix: assessment of different histology parameters from specimens operated at a cancer centre in India, between 2013 and 2018

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Background & objectives: To review histopathology reports of patients operated for carcinoma cervix, at our institute between 2013 to 2018, and to see our compliance to minimum data sets.
Methods: After obtaining approval by institutional review board (IRB), our hospital records showed a total of 243 reports of carcinoma cervix, operated between 2013 to 2018. Various parameters from the reports were noted down, and their frequencies were calculated with the help of SPSS software (version 21).
Results: The mean age was 50.5 years (range 15-82). The mean tumour size being 3.03 cm. The depth of cervical stromal involvement was mentioned in 98.8% cases; It was more than half In 67.5% cases. Distance of tumour from cervical stromal adventital margin was mentioned in 94.2% cases.The vaginal cut margins were mentioned in all but one case (99.6%). Right and left parametria were free in 96.7% and 96.3% cases respectively. The commonest tumour type was squamous (74.5%), followed by adenocarcinoma (17.6%) followed by adenosquamous carcinoma (5.35%). Lymphovascular emboli present in 40.3% cases.The mean lymph node yield was 18.54. The stage was not mentioned in 127 cases (52.3%).
Conclusion: Compliance to minimum data sets for carcinoma cervix reports in our hands was generally good. Lymph node yield improved comparative to previous audit. Stage need to be mentioned.

PS-02-076

Tumour size and mTOR pathway activation assesed by immunohistochemistry as predictor of Silva pattern of invasion in biopsies of HPV-associated endocervical adenocarcinomas (HPVA)

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Background & objectives: We aimed to use small cervical biopsies to determine whether markers of mTOR pathway activation and tumour size associate with aggressive Silva patterns of invasion B and C.
Methods: 34 HPVA biopsies were evaluated for size and expresion of pS6, pERK and HIF1a. Immunohistochemical stains were scored semiquantitatively, ranging from 0-4+ with scores 2-4+ considered positive, and Silva pattern was determined in follow-up excisional specimens.
Results: 8 cases were pattern A, 4 pattern B and 22 pattern C. Statistically significant associations were found comparing pS6 and pERK immunohistochemistry with Silva pattern (p=0.034 and 0.05, respectively). pERK was the most powerful for distinguishing between patterns A and B/C (p=0.026). Large tumour size (≥2 cm) correlated with Silva pattern (p=0.027) with a moderate association when comparing pattern A with B/C (r: 0.404, p=0.027, R square: 0.163).
Conclusion: Both tumour size and pERK immunohistochemistry can be used to predict Silva pattern using only small biopsies of HPV-associated endocervical adenocarcinomas.

PS-02-077

Comparison between P53 immunohistochemical staining pattern and molecular characteristics of tubo-ovarian high-grade serous carcinoma by next-generation sequencing examination

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Background & objectives: Strong p53 immunohistochemical staining is one of the hallmarks of tubo-ovarian high-grade serous carcinoma (HGSC). The aim of this study was to compare between the p53 staining patterns and the molecular characteristics of HGSC cases identified by next-generation sequencing (NGS).
Methods: A commercial NGS cancer panel comprising 143 genes, including TP53, was used to analyse the genetic profiles of tubo-ovarian HGSC cases. Eleven HGSC cases were sequenced using formalin-fixed paraffin-embedded (FFPE) sections. Immunohistochemical stain for p53 was performed for each case.
Results: Among 11 HGSC cases, nine novel TP53 somatic mutations from nine patients (81.8%) were identified; missense mutation in 3 cases, frameshift mutation in 5 cases, and nonsense mutation in one case. Among 9 TP53 mutant cases, p53 IHC staining revealed strong nuclear overexpression in 3 cases and complete absence in 6 cases. The remaining 2 cases showed no TP53 mutation; p53 overexpression in one and complete absence in the other.
Conclusion: Genomic sequencing in the tubo-ovarian HGSC cases revealed mutations of TP53 in 81.8%. p53 immunohistochemical staining revealed overexpression in 4 cases (36.4%) and complete absence (abnormal/aberrant/mutation-type) in 7 cases (63.6%). The p53 IHC staining patterns should be considered in diagnosis of HGSC cases.

PS-02-078

Reproducibility of interpretation of P53 immunostaining in vulvar squamous cell carcinomas using a pattern-based approach

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Background & objectives: p53 immunostaining is a surrogate for *TP53* mutation assessment in vulvar squamous cell carcinoma (VSCC) and allows biomarker-based subclassification into prognostically significant subtypes, with HPV-independent/p53abn VSCC having the worst prognosis. We assessed the reproducibility of p53 interpretation in VSCC.
Methods: p53 immunostaining (N=69) was performed and evaluated independently at two institutions, by five pathologists, and classified as **abnormal** (basal overexpression, basal and parabasal overexpression, absent expression, or cytoplasmic staining), **wild-type**(scattered or midepithelial staining with basal sparing) or **indeterminate**.
Results: In 51/69 cases (73.9%) there was complete agreement between all 5 raters. In 12 cases (17.4%) one or more raters considered the p53 staining indeterminate, while the remaining observers agreed that it was either abnormal or wild-type. In 5 cases (7.2%) there was disagreement regarding whether the p53 staining was aberrant or wild-type and in the final case the range of opinions included abnormal, wild-type, and indeterminate. The overall Fleiss' kappa for the five observers was 0.78. If all indeterminate results were to be resolved by performing sequencing of *TP53*, there were only 6 cases with a disagreement (Fleiss' kappa = 0.91).
Conclusion: There was excellent inter-observer agreement in the interpretation of p53 immunostaining in VSCC, with staining performed independently at two different laboratories. The main issue identified was variability in the number of cases considered to show indeterminate staining i.e. not possible to conclude whether it was abnormal or wild-type. Although such cases can be resolved through *TP53* sequencing, refined p53 interpretation criteria may help reduce the frequency of indeterminate results.

PS-02-079

P53 immunohistochemical patterns in HPV-related neoplasms of the female lower genital tract can be mistaken for TP53 null or missense mutational patterns

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Background & objectives: We recently encountered cases where p53 IHC in HPV+ tumours were confused with mutational-pattern staining. Herein, p53 IHC were assessed in a cohort of HPV+ invasive and in-situ squamous cell carcinomas (SCC) and adenocarcinomas (EDAC) of the cervix and vulva.
Methods: Only cases with block-like p16 staining were included. p53 was scored as "wild-type", "overexpression" (strong diffuse staining), "null" (absent staining), "markedly reduced" (reduced staining, >70% of cells, mimicking null staining) and "midepithelial (basal sparing)" (absent staining in basal cells juxtaposed with strong staining in parabasal cells). *TP53*sequencing and HPV in-situ hybridisation (ISH) were performed in select cases.
Results: "Markedly reduced" staining was present in 14/25 SCCs, 7/14 HSIL and 18/20 EDACs. This mimicked null-pattern staining. There was "mid-epithelial (basal sparing)" in 10/25 SCC and 7/14 HSIL. This mimicked overexpression-pattern staining. Wild-type was seen in 1/25 SCC and 2/20 EDAC. No cases showed overexpression. One EDAC had a *TP53* missense mutation and markedly reduced staining. HPV ISH results showed an inverse association with p53 immunoexpression, cells positive for HPV mRNA were negative for p53.
Conclusion: p53 IHC patterns in HPV+ neoplasms can mimic the null mutational patterns ("null-like") and overexpression mutational patterns ("overexpression like"). Knowledge of these patterns can help pathologists avoid misinterpreting p53 status in the setting of HPVA cancers.

PS-02-081

Role of epigenomics in ovarian serous carcinomas

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Background & objectives: We aimed to determine the difference in terms of epigenetic modifications between the primary tumour cells, ascites tumour cells and metastasis tumour cells of patients with high-grade and low-grade serous ovarian cancer (HGSOC and LGSOC) by bioinformatic analysis.
Methods: GSE73168 gene's microarray data were downloaded from the "Gene Expression OmniBus" data base to investigate the association of serous ovarian carcinomas with epigenetic modifications. Differentially expressed genes were generated by re-analyzing them RNA transcripts from tissues obtained from 5 HGSOC patients and 3 LGSOC patients. "Biobase", "Limma" and "Geoquery" libraries were obtained with bioinformatics analysis and R program.
Results: Cytoscape with Search Tool for the Retrieval of Interacting Genes and Molecular Complex Detection plug-in was utilized to visualize protein-protein interaction of these differentially expressed genes. In comparing the expression profiles of transcripts, "log2 fold change >1" and $P \leq 0.05$ were considered statistically significant. Statistically significant differences were found in genes related to DNA methylation and histone modifications (acetylation, methylation, phosphorylation, ubiquitination, sumoylation) by using the DAVID (Database for Annotation, Visualization and Integrated Discovery) functional annotation system.
Conclusion: A greater understanding of the role of epigenetics in high grade and low grade serous ovarian carcinomas will provide for improved therapeutic interventions. Moreover, this study can shift the focusing on the K-RAS, B-RAF and p53 mutations to genes involved in epigenetic modifications.

PS-02-082

Concerns of the histological phenotype of the placenta during physiological pregnancy and antenatal foetal death of unknown aetiology

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Background & objectives: Unfavourable conditions for foetal development are associated with the development of diseases in the postnatal period. Cause of perinatal death is latent or clinically expressed placental dysfunction, which developed under the exposure of various damaging factors at any stage of pregnancy.
Methods: A prospective histological study of 106 placentas (37-42 weeks) during physiological pregnancy (n-82) and prenatal death of the foetus (n-24) was carried out. All placentas were examined in accordance with Vogel principles (1996). The relative number of immature forms of villi in 100 peripheral grooves of the representative placental area was determined.
Results: In 28 placentas, the delayed development of chorionic villi was determined. Of these, 22 placentas (79%) showed expressed (> 50% immature villi) and 6 placentas (21%) moderate delay (30-50% of immature villi) of the development of chorionic villi. In 92% of the placenta, with antenatal asphyxia of the foetus and in 15% of the placenta during physiological pregnancy was found an immature histological phenotype ($54.2 \pm 12\%$ and $34.3 \pm 5.8\%$ of immature villi, respectively). Therefore,

postnatal evaluation of placental phenotype can help in the timely identification of adverse foetal conditions and early stratification of the heterogeneous population of new-borns, with identification of individual risk of disease in post-natal life.
Conclusion: Physiological pregnancy may be accompanied by a delay in the maturation of chorionic villi and thereby latent chronic placental insufficiency. In the case of antenatal foetal death,the placenta becomes the main reliable source of information for making a diagnosis.

PS-02-083
Dedifferentiated endometrioid adenocarcinoma of uterus
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Background & objectives: Dedifferentiated endometrioid adenocarcinoma is recently described and rare uterine neoplasm which contains both low grade(FIGO grade 1 or 2) endometrioid adenocarcinoma and undifferentiated carcinoma. This tumour is a new entity and may pose diagnostic challenges.
Methods: We discuss a case of 28-year old women who had severe stomach ache with palpable mass in abdomen. By the surgical examination we learned that the tumour was mainly located in uterus and invaded colon, bladder, liver, paraaortic lymph nodes. Hysterectomy specimen showed polypoid tumour filling endometrial cavity, invading full thickness and exceeding serosa.
Results: Tumour was described by the coexistence of undifferentiated carcinoma(%85) and low grade endometrioid adenocarcinoma(%15).Undifferentiated component was characterized by the proliferation of noncohesive, medium size, monotonous epithelial cells growing in a patternless solid fashion. The transtion between the two tumour components was abrupt with a sharp border. Undifferentiated cells were negative for epithelial markers, oestrogen, and progesterone receptors although others were positive. There were no loss of mismatch repair gene proteins. Metastases contained only undifferentiated component.
Conclusion: Dedifferentiated endometrioid adenocarcinoma has poor prognosis and aggressive behaviour. It can be misdiagnosed as grade 3 endometrioid adenocarcinoma. Accurate diagnosis requires more awareness of this entity. Morphological, immunohistochemical and molecular features should be considered for better clinical outcome and patient survival.

PS-03 Head & Neck Pathology

PS-03-001
Ladinin-1, overexpressed in oral squamous cell carcinoma adjacent to non-cancerous epithelium, is involved in cell motility by mediating actin and focal adhesion dynamics
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Background & objectives: Oral squamous cell carcinomas (SCCs) often form the interface against non-cancerous epithelium. We identified several proteins, including ladinin-1 (LAD1), overexpressed in cancer tissue at the interface by tissue proteomics. This study aimed to examine LAD1 functions in oral SCCs in-vitro.
Methods: Oral SCC cell lines, HSC-2, 3, and 4, were used for in-vitro functional and immunofluorescence analyses with siRNA knockdown methods.
Results: LAD1-knockdown cells showed decreasing of cell proliferation in MTS assay and increasing of numbers of migrated cells in the transwell migration assay. Morphologically, LAD1 was localized in the peripheral area of the cytoplasm. High-resolutional morphological analysis using structured illumination microscopy revealed that LAD1 was co-localized with actin filaments forming "actin arc". LAD1-kockdown cells showed decreasing of elongated filopodial filaments and ruffling of cell borders compared with controls. In addition, LAD1-kcockdown cells overexpressed WNT5a and showed prominent accumulations of phosphorylated focal adhesion kinases in the cytoplasm.
Conclusion: LAD1 is potentially involved in cell motility by modulation of actin dynamics and focal adhesion formation in oral SCC cells and the non-canonical WNT pathway may play a pivotal role in LAD1 functional association.

PS-03-002
Effectiveness of rapid onsite evaluation of thyroid fine needle aspiration cytology
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Background & objectives: FNA is the first line diagnostic modality in the evaluation of the thyroid lesions. However, the specificity is variable which can be improved by the implementation of ROSE, thus, to evaluate the improvement in adequacy of thyroid cytology with ROSE.
Methods: A comparative cross-sectional study was conducted on 166 patients with thyroid masses (83 in each of the two groups). After the standard FNA procedure, ROSE was performed by staining the slides with rapid stains. For inadequate smears, repeat FNA was done at the same time thus improving the adequacy and reducing the number of patients' visits to the hospital for repeated attempts.
Results: RESULTS: The study showed that there was no dramatic increase in the diagnostic rate of thyroid FNA with ROSE (86.7%) as compared to that without ROSE (72.3%). However, ROSE assisted to reduce the rate of false negative cytology and the degree of patients' inconvenience due to delay in the diagnosis ,owing to repeated visits.
Conclusion: Rapid Onsite Evaluation of thyroid cytology smears enhances the effectiveness of Fine Needle Aspiration by reducing the rate of false negative cytology and alleviating the degree of inconvenience to the patients.

PS-03-003
Assessment of tumour-infiltrating lymphocytes (TILs) in head and neck squamous cell carcinoma: inter-observer agreement and visual versus digital image analysis comparison
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Background & objectives: TILs correlate with patient outcome in many cancers. The evaluation of TILs in HNSCC has not been yet standardized. The aim was to evaluate the inter-observer agreement of visually-assessed TILs and a visual-versus-digital image analysis (DIA) evaluation comparison.
Methods: 40 samples from HNSCC patients from the Colombian cohort of the InterCHANGE study (IARC) were included. TMAs were constructed and Hematoxylin and eosin (H&E) and Immunohistochemistry for CD3, CD4 and CD8 were performed. TILs average score was assessed independently by three pathologists. Their scores were compared to DIA-scores using QuPath.
Results: The inter-observer agreement coefficients were 0.64, 0.71, 0.55 and 0.70 (ICC p=0.0001) for H&E, CD3, CD4 and CD8, respectively. When the DIA-scores were compared to visual estimates, the average

scores of the pathologists (H&E: 0.71, CD3: 0.73, CD4: 0.4, CD8: 0.68, weighted-kappa) had better agreement than comparing individual scores (H&E: 0.52-0.66, CD3: 0.54–0.79, CD4: 0.33–0.39, CD8: 0.5–0.66, weighted-kappa). When scores were grouped into categories (low-moderate-severe) the agreement decreased compared to evaluation as continuous parameter.

Conclusion: We show a substantial inter-observer agreement between pathologists, these scores have moderate agreement with DIA ones, but improve when evaluated as an average. We consider that visual estimation can be used with an acceptable level of agreement in routine practice and research. However, in cases when the scores are close to a limit of a category/range, DIA can be very useful to proper classify the density of the infiltrate.

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PS-03-004

PIK3CA gene mutations in human papilloma virus 16 head and neck scamous cell carcinoma

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Background & objectives: Human Papillomavirus (HPV)-associated head and neck squamous cell carcinomas (HNSCC) typically arise in the pharynx. HPV active infection may lead to alterations in key signalling pathways that promote carcinogenesis. Different studies identified PIK3CA mutations more commonly in HPV positive tumours (37%).

Methods: We evaluated PIK3CA gene mutations associated with HPV16+HNSCC patients from the Portuguese Institute of Oncology between 2007 and 2019. HPV DNA status was evaluated by PCR and genotyped (INNOLIPA/ALLPLEXHPV28). PIK3CA mutation analysis was performed by real-time PCR for the qualitative detection of four mutations (H1047L; E542K, E545K, E545D) in human genomic DNA extracted from tumour tissue (AmoyDx).

Results: PIK3CA mutations were evaluated in 50 squamous cell carcinomas, all HPV16 positive. Co-infection with HPV18, HPV53, HPV58 was present in 2 cases. Ten cases harboured PIK3CA mutations (20%). Three different mutations H1047R (10%), E545D (50%), E545K (20%) were identified. Combined E545D/E545K mutations were present in 20% of cases. Mutations in PIK3CA gene were present in cases from the oral cavity (20%) and the oropharynx (80%).

Conclusion: In our series, a lower frequency of PIK3CA gene mutations was found among HPV16+ HNSCC compared with other series. These results may be related to the method used and to clinical aspects and should be confirmed by other series in Portugal. Multiple PI3K/AKT/mTOR inhibitors are under investigation as potential therapeutic options for HNSCC, adding relevance to regional variations in PIK3CA mutations and their identification methods.

PS-03-005

The effect of E6 and E7 knockdown and PARP inhibition on cisplatin sensitivity in oropharyngeal squamous cell carcinoma

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Background & objectives: Clinical outcomes in HPV- OPSCC are poor, with a 3-year survival of 57.1%. Although HPV+ has an improved response to therapy, a subset of patients suffer from loco-regional recurrences and distant metastases, with a poor prognosis.

Methods: The effect of E6 and E7 on cisplatin sensitivity in HPV+ OPSCC was investigated by knockdown of E6 and E7 using siRNA in a HPV+ cell line. A HPV+ and HPV- cell line were exposed to long term cisplatin treatment to generate resistant models. Immunofluorescence and MTS assays were used to assess DNA double strand breaks and cell viability respectively.

Results: Knockdown of E6 and E7 in a HPV+ cell line did not significantly effect cell viability in response to cisplatin. Following long term treatment with cisplatin, the HPV+ and HPV- resistant cells had a significantly higher half maximal inhibitory concentration (IC50) compared to the parental cells (HPV- resistant cells IC50: 47.5 compared to 10.3 and HPV+ resistant cells IC50: 84.9 compared to 40.0) and showed fewer DNA double strand breaks following cisplatin treatment. Treatment with Olaparib partially resensitised both HPV+ and HPV- resistant cells to cisplatin.

Conclusion: Although knockdown of E6 and E7 did not appear to sensitise HPV+ cells to cisplatin, Olaparib was able to resensitise both HPV+ and HPV- resistant cells to cisplatin. These findings have implications for future research in this area.

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PS-03-006

Status of HPV-16 in cervical lymph node metastatic squamous cell carcinoma of unknown origin - a study of three cases

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Background & objectives: In head and neck pathology 5% of malignancies present as lymph node metastasis of unknown origin. In up to 45-80% of cases the primary site can be identified. In identifying the origin, the study of HPV-16 status can be useful.

Methods: We have studied three patients that presented cervical lymph node metastases of unknown origin. All three of them were middle-aged women with no relevant medical history. The lymph node study was done with hematoxylin eosin slides and immunohistochemistry techniques including CK5/6, p63 and p16. The HPV status was studied through DNA-PCR amplification and microarray hybridization.

Results: All cases showed infiltration in the lymph node of poor-differentiated squamous cell carcinoma. Two of the three cases showed positivity for p16 and also for HPV-16. The third case was negative for p16 and HPV. Gynaecological exams were performed in all these women, with absence of cervical dysplasia. In one of the patients the origin was identified, being oropharyngeal. The other two patients still remain with no primary tumour detected.

Conclusion: The presence of HPV seems to be important in this patients but appears to not have direct relationship with cervical dysplasia or anogenital origin. Also, in oropharyngeal carcinomas it has been associated with a more favourable prognosis. This shows that identifying the presence of HPV should be a routine procedure in all cervical lymph node metastases.

PS-03-007

PD-L1 expression in head and neck squamous cell carcinomas (HNSCC) and its correlation with clinical variables

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Background & objectives: Immune checkpoint inhibitors have created a revolution in oncology. Despite a higher likelihood of response to immunotherapy in PD-L1 positive tumours, the cut-off remains unclare. The objective is to describe PD-L1 expression related to clinical variables, disease-free survival and toxicity.

Methods: Case reports of HNSCC diagnosed between 2014 and 2019, treated with immunotherapy. PD-L1 IHC using the 22C3 antibody was performed. The scores were compared at both the

1% and 20% cutpoints, using the CPS result obtained from core biopsy or resected specimen. Information regarding clinical characteristics was retrieved as documented by the treating physicians.
Results: 67 patients were identified, both in clinical trials and assistance. PD-L1 expression was related to gender, smoking, age and histologic status. Only 11 of them were women. 48 of them received nivolumab alone, 3 pembrolizumab alone, 7 durvalumab alone. 3 patients received durvalumab in combination with tremelimumab, another 3 nivolumab with ipilimumab and 3 combination chemotherapy with pembrolizumab.
Conclusion: To identify more suitable HNSCC cases for anti-PD-1/PD-L1 therapy, PD-L1 expression in HNSCC should be combined with clinicopathologic features.

PS-03-009
Small round blue cell tumours of the sinonasal tract: histopathological evaluation of 34 cases
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Background & objectives: Histopathology of the small round blue cell tumours of the sinonasal tract (SRBCT-SN) remain challenging because they consist of diverse malignancies including epithelial, haematolymphoid, neuroectodermal and mesenchymal origin. We aimed to evaluate the histopathological and immunohistochemical characteristic of these tumours.
Methods: All the patients who were diagnosed with a SRBCT-SN between January 2006 and January 2020 in our department were evaluated retrospectively. The demographical, clinical, radiological, histopathological and immunohistochemical findings were recorded.
Results: There were a total of 34 cases with 13 females and 21 males. The mean age was 58 years. Histopathologically, there were 10 sinonasal undifferantiated carcinoma, 9 malignant melanoma, 3 rhabdomyosarcoma, 3 olfactor neuroblastoma, 3 lymphoma, 2 plasmocytoma, 2 ectopic pituitary adenoma, 1 Ewing sarcoma and 1 sinonasal neuroendocrine carcinoma cases. Twenty-two of these cases were located inside the nasal cavity, whereas 6 were in the paranasal sinuses and 6 were in the nasopharynx. When diagnosing these challenging lesions, clinical and radiological findings should be taken into account since they have overlapping histologic and immunohistochemical findings.
Conclusion: With the help of newly described entities and increased usage of molecular testing,these tumours can be diagnosed better.A precise diagnosis is importat especially because some of these tumours behave aggresively and the pathological diagnosis will help identifying the correct treatment.

PS-03-010
Metastatic, non-cutaneous squamous cell carcinoma to the salivary gland: a cases series observed at the Royal Surrey Hospital
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Background & objectives: Metastasis to the salivary glands tends to occur from primary squamous cells carcinoma (SCC). Rarely metastases may be from more distant sites or of non squamous cells cutaneous tumour. Given the histological variety of salivary tumours, diagnosis can be difficult.
Methods: Tumours of salivary gland origin discussed at Head and Neck MDT meeting at the RSH have been reviewed searching from metastasis versus primary neoplasms with the exception of squamous cell carcinoma of skin origin. Here we present our experience and differential diagnoses.
Results: Metastasis to the salivary glands included basal cell carcinomas, a rare merkel cell carcinoma and distant neoplasm such as renal cell carcinoma and Upper GI tract adenocarcinoma. A metastasis from an undiagnosed olfactory neuroblastoma to the submandibular gland was initially interpreted as unusual primary neuroendocrine malignancy. The primary manifested 6 months after submandibular gland resection. All cases were diagnosed and confirmed by appropriate immunohistochemistry and additional clinical information.
Conclusion: Non squamous cell cutaneous carcinoma metastasizing to salivary glands is uncommon and difficult to diagnose especially without sufficient clinical history and familiarity with the long list of primary malignant tumours of salivary glands.
We propose a high index of suspicion in cases with unusual histological or immuno-histochemical features and inadequate clinical information when assessing salivary gland neoplasms.

PS-03-011
The tumour immune microenvironment and its implications for clinical outcome in patients with oropharyngeal squamous cell carcinoma
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Background & objectives: To analyse the PD-L1 expression on tumour cells (TC) and immune cells (IC), and densities of CD3+ and CD8+ tumour-infiltrating lymphocytes (TILs) in oropharyngeal squamous cell carcinoma (OPSCC), and to correlate them with radiotherapy treatment outcomes and clinicopathological parameters.
Methods: The study included 65 OPSCC treated by definitive intensity-modulated radiotherapy (IMRT) in curative intent. Immunohistochemical analysis of PD-L1 expression on TC and IC, and TILs subtyping was performed on primary biopsy tumour tissues, followed by prognostic evaluation of these immune response related parameters including classification into four tumour immune microenvironment (TIM) types. To evaluate HPV status, p16 immunohistochemistry was performed.
Results: Densities of CD3+ and CD8+ TILs and PD-L1 expressions on TC and IC were significantly higher in p16+/HPV-mediated OPSCC. Patients with high densities of stromal CD8+ T cells displayed significantly better overall survival (OS) and progression-free survival (PFS). PD-L1 expression neither on tumour cells (TCs) nor immune cells (ICs) affected survival outcomes. Distribution of TIM types based on combination of PD-L1 expression on TC and densities of CD8+ TILs is significantly different in p16+ compared to p16- OPSCC. In type III TIM OPSCC (TC-PD-L1+/low CD8+ TIL density), significantly better OS was showed in p16+ group compared to p16- OPSCC.
Conclusion: The role of tumour immune microenvironment was confirmed and combining HPV status with evaluation of densities of CD8+ TILs and PD-L1 expression including TIM classification might provide valuable predictive and prognostic information for patients with OPSCC.

PS-03-012
Perineural invasion of squamous cell carcinoma of the head and neck – ten years of experience
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Background & objectives: Perineural invasion has been defined as the ability of cancer cells to invade through, in or around nerves and is clinically associated with elevated recurrence and diminished survival.

It is morphologically described in many solid tumours (head and neck, prostate)
Methods: We have retrospectively analysed cases of 532 patients with squamous cell carcinoma of head and neck in age from 33 to 86 years. In all cases, cervical block dissection was also perfomed with the resection of the main tumour. Patients without cervical block dissection were excluded. All cases were paraffin embedded and 3 um sections were stained by the hematoxylin/eosin.
Results: The tumour size, depth of invasion, the presence and morphology of perineural invasion and the presence of lymfangioinvasion and hemangioinvasion were evaluated. From the total number of 532 cases, 70 (13,15%) cases with perineural invasion, 22 (4,13%) with hemangioinvasion and 60 (11,27%) with lymphangioinvasion were encountered. Metastases in ipsilateral lymph nodes were found in 249 (46,80%) cases, contralateral metastases were present in 39 (7,33%) cases. These factors were further compared to other morphological features (depth of invasion, tumour budding).
Conclusion: We focused mostly on perineural invasion, which is probably based on the chemotropism of tumour cells, that can be stimulated by nerve tissue to further growth. The interactions between tumour and neural cells is not only limited to cell migration and tumour growth from the primary location but such interaction can also stimulate axonogenesis or extend the nerves themselves together with increasing number of axons.
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PS-03-013
Variants in SDHAFx genes in vagal paragangliomas
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Background & objectives: *SDHAFx* encode assembly factors of the succinate dehydrogenase (SDH) complex; variants in these genes are associated with the SDH complex deficiency. The objective of this study was to analyse the pathogenic/likely pathogenic variants in *SDHAFx* genes in vagal paragangliomas (VPGLs).
Methods: In the study, we used a set of eight VPGLs collected in the Vishnevsky Institute of Surgery, Ministry of Health of the Russian Federation. Exome libraries were prepared using the TruSeq DNA Exome Kit (Illumina, USA) and were sequenced on the Illumina NextSeq 500 System in pair-read mode (76x2). Immunohistochemistry (IHC) was performed using anti-SDHx antibodies (Abcam, USA).
Results: We revealed two patients with VPGLs characterized by likely pathogenic mutations in *SDHAFx*genes. Variant NM_145267 (*SDHAF4*): c.C223T, p.P75S (chr6:71298323, rs146446063) in *SDHAF4*was detected in both patients. In one patient, the variant co-occurred with a pathogenic mutation in *SDHB*(NM_003000 (*SDHB*): c.541-2A>G (chr1:17350571, rs786201161)), in another patient – with likely pathogenic variant in *SDHFA3*(NM_020186 (*SDHAF3*): c.T157C, p.F53L (chr7:96747192, rs62624461)). IHC revealed negative and weak diffuse expression of SDHB protein in these cases.
Conclusion: Variants in *SDHAFx* are less frequent than mutations in *SDHx* in paragangliomas. We revealed likely pathogenic variants in *SDHAF3* and *SDHAF4* genes in two patients with VPGLs. According to the IHC results, we revealed changes in *SDHB* protein expression in patients with *SDHB*/*SDHAF4* and *SDHAF3*/*SDHAF4* variants. Thus, co-occurring variants in *SDHAFx* genes or present mutations in *SDHAFx* and *SDHx* together can lead to disruption of SDH complex stability and function.
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This work was performed using the equipment of EIMB RAS “Genome” centre (http://www.eimb.ru/ru1/ckp/ccu_genome_c.php).

PS-03-014
Germline mutations in metastatic carotid paraganglioma
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Background & objectives: Carotid paraganglioma (CPGL) is a rare neuroendocrine tumour of the head and neck that is characterized by the variable metastasis potential. Mechanisms and biomarkers of this process are unclear. In the study, we performed a genetic analysis of metastatic CPGL.
Methods: We carried out the exome analysis of tumour, lymph node and metastatic tissues derived from a patient with metastatic CPGL. Exome libraries were prepared using the TruSeq DNA Exome Kit (Illumina, USA) and were sequenced on an Illumina NextSeq 500 System (paired-end reads, 76x2). We performed the search for pathogenic/likely pathogenic germline variants in the patient using GATK HaplotypeCaller.
Results: Base on in silico prediction tools (PolyPhen2, LRT, SIFT, and others) and ClinVar database, we analysed the pathogenicity of germline variants identified in the patient. We found germline pathogenic variants in *ALDH7A1*and *CBS*genes. Likely pathogenic variants were determined in a wide range of genes, including *HK2*, *HYDIN*, *GALC*, *ZNF717*, *MMP28*, *EIF2AK3*, and others.
Conclusion: We revealed a number of germline pathogenic/likely pathogenic variants that can be associated with the metastatic CPGL. Interestingly, no variants were found in any genes, which are frequently associated with paragangliomas/pheochromocytomas (*SDHx*, *RET*, *NF1*, etc.). However, likely pathogenic variant was identified in the *HK2* indicating alterations in glycolysis. Mutation in *HYDIN* can also play an important role because a high mutation frequency of this gene in CPGLs was previously shown.
This work was financially supported by the Russian Science Foundation, grant no. 17-75-20105.
This work was performed using the equipment of EIMB RAS “Genome” centre (http://www.eimb.ru/ru1/ckp/ccu_genome_c.php).

PS-03-015
Immunohistochemical expression of programmed death ligand-1 (PD-L1) in oral squamous cell carcinoma and its clinicopathological correlation
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Background & objectives: Oral squamous cell carcinoma is responsible for tremendous cancer related deaths and tumour load in the Indian subcontinent. To assess the immunohistochemical expression of programmed death ligand-1(PD-L1) in oral squamous cell carcinoma and correlation of PD-L1 expression with clinico-histopathological parameters.
Methods: All 106 cases histopathologically and programmed death ligand-1(PD-L1) expression in tumour cells were evaluated separately by two observers. Only membranous positivity was considered as positive. Immunoreactivity score for PD-L1 expression was calculated based on staining intensity as well as percentage. The statistical analysis was done using SPSS version 21.0 statistical analysis software. P value of <0.05 was considered statistically significant.
Results: Age group 40 to 60 years was most affected. Tongue was the most commonly involved site. Tobacco smoking was reported in 86.8% of cases. No statistically significant association of histological grade, ulceroproliferative pattern, and patient survival could be seen with PD-L1 immunoexpression scores, however, tumour stage, lymph node metastasis, tumour size (p=0.030), depth of invasion(p=0.005),

lymphovascular and perineural invasion (p=0.008) were found to be statistically significantly associated with immunohistochemical scores.
Conclusion: We conclude that total of 106 cases were included in this study. PD-L1 expression was evaluated in tumour cells by two observers, interobserver agreement of 97.1% was present which is in the acceptable range.PD-L1 pathway plays a significant role in tumour immune evasion in oral SCC patient. Role of targeted therapy can be predicted by evaluating PD-L1 expression and suggesting the OSCC patients that may be benefited by immunotherapy.

PS-03-017
P62/sequestosome1(SQSTM1) and GATA3 expression in salivary duct carcinoma: in comparison with pleomorphic adenoma
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Background & objectives: SDC is immuno-phenotypically akin to mammary apocrine carcinoma (MAC), due to the expression for AR and GCDFP-15. GATA3 is a well-known biomarker for breast and urothelial cancers. We aim to elucidate the status of SQSTM1 and GATA3 expression in SDC.
Methods: We collected 53 cases of SDC, including 30 cases of carcinoma ex pleomorphic adenoma (CXPA), and 30 cases of pleomorphic adenoma (PA), and performed the immunohistochemistry for SQSTM1 and GATA3 on their FFPE sections, adding GCDFP-15 and AR. Finally, we estimated the positive rates and the pattern for these molecules in SDC and PA cases, respectively.
Results: The positive rates for GCDFP-15, AR, SQSTM1, and GATA3 in SDC cases were 91%, 85%, 81% and 89%, respectively. The signals for AR and GATA3 were limited to nuclei (N), whereas the signals for GCDFP-15 were observed in the cytoplasm (CY). The signals for SQSTM1 were seen in N and/or CY. Although approximately 27% of PA cases were positive for GATA3, a few cases of PA were positive for SQSTM1.
Conclusion: SQSTM1 is a molecule related to the autophagy, whereas it was recently reported that its expression was up regulated in MAC. As SQSTM1 is also a marker for apocrine differentiation, it is better that SDC is called "apocrine carcinoma of the salivary gland". Although GATA3 has been also reported the consequential positivity in secretory carcinoma of the salivary gland, it could be one of the sensitive diagnostic markers for SDC, adding to AR, GADFP-15 and SQSTM1.
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PS-03-018
PD-L1 IHC 22C3 pharmDx helps determine first-line pembrolizumab eligibility in head and neck squamous cell carcinoma patients
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Background & objectives: PD-L1 IHC 22C3 pharmDx is a CE-IVD-marked assay intended for use in detection of PD-L1 protein in formalin-fixed, paraffin-embedded non-small cell lung cancer, urothelial carcinoma, melanoma, and recently, head and neck squamous cell carcinoma (HNSCC) tissues.
Methods: For the HNSCC indication, the device has been validated at Dako North America on the performance of precision and robustness using the Combined Positive Score (CPS) ≥ 1 and CPS ≥ 20 cutoffs; external validation studies were performed at three external laboratories. CPS ≥ 1 and CPS ≥ 20 cutoffs were evaluated in KEYNOTE-048, a phase 3 clinical trial.
Results: Analytical validation studies supporting the companion diagnostic indication (CPS ≥ 1) achieved point estimates of > 85% for negative, positive, and overall percent agreement. Clinical validation studies show that patients treated with pembrolizumab as a single agent had an overall survival (OS) of 12.3 months at CPS ≥ 1 (95% CI, 10.8-14.3) compared with patients receiving cetuximab, platinum, and 5-fluorouracil (CPS ≥ 1 OS of 10.3 months (95% CI, 9.0-11.5)).
Conclusion: Analytical and clinical validation studies demonstrate that PD-L1 IHC 22C3 pharmDx is a robust and precise companion diagnostic assay, allowing for selection of eligible HNSCC patients for treatment with pembrolizumab.

PS-03-019
New entities of sinonasal tract tumours: a single centre experience
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Background & objectives: Sinonasal tract tumours have been newly classified according to molecular and immuno-histochemical studies leading to an expansion of the category of sinonasal undifferentiated carcinoma (SNUC). Our goal here is to familiarize the new entities with the pathologists and clinicians.
Methods: We have searched our files to see if there were cases initially called SNUC and now reclassified according to the recent WHO recognized sinonasal tract carcinoma, classification, which include NUT midline carcinoma, SMARCB 1 deficient sinonasal carcinoma and HPV related carcinoma with adenoid cystic like features. Participation to clinical trial and follow up was arranged.
Results: When immunohistochemistry and molecular tests were performed, the new tumour entities were identified. Molecular analysis including the NUT gene (t15 q14) and immunohistochemistry for NUT protein was necessary to identify NUT midline carcinoma. T6:9 translocation, hallmark of adenoid cystic carcinoma, was performed to confirm HPV related carcinoma with adenoid cystic like features which has better prognosis. Deletion of SMARCB1/22q was observed in a case of SMARCB1 deficient sinonasal carcinoma.
Conclusion: Our study confirms that sinonasal carcinoma can be reclassified using immunohistochemistry and molecular testing leading to new entities with prognostic, diagnostic and therapeutic implications. Our reclassification allowed a patient with NUT midline carcinoma to be enrolled in clinical trial for BET inhibition with good clinical response.

PS-03-020
Histopathological processing of sentinel lymph nodes in head and neck cancer
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Background & objectives: Sentinel node biopsy (SNB) can be offered to patients with early-stage squamous cell carcinoma (SCC) of the head and neck. There is currently no agreed protocol for histopathological processing of SNBs – an audit was undertaken to inform local practice.
Methods: Seventy seven SNBs from 2013-2016 were retrieved from our records. We examined each report, recording specimen size, dissection method, and total number of histological levels and immunohistochemical stains requested. The positive SNBs were and the histological level at which metastatic SCC was first seen was recorded. The results and clinical outcomes for the positive and negative SNB cases were compared. **Results:** In all positive SNB cases, metastatic SCC was present on the first H&E level. Additional histopathological levels and immunohistochemical staining did not contribute to the identification of SCC. Histological levels were required in one case to demonstrate conversion from a micrometastatic to a macrometastatic deposit and in one case to demonstrate extracapsular spread. There was no documented clinical recurrence in any of the negative SNBs.

Conclusion: We propose examining a single H&E section of each block without pre-emptive ordering of levels, blanks and immunohistochemistry. When a micrometastasis is identified or extra-capsular spread is suspected, then additional levels may be warranted. In our institution, examining a single H&E as has a potential cost saving of £25 per block.

PS-03-021

Evolutionary epigenetics: DNA methylation modifications in ultra-conserved non-coding elements from squamous cell carcinoma of different species revealed a common epigenetic behaviour

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Background & objectives: Ultra-Conserved-Non-coding Elements(UCNEs) represent genomic sequences that exhibit >95% sequence identity between human, mammals, birds, reptiles, fishes. Recent findings reported their functional role in cancers. Aim of this study was to evaluate DNA methylation modifications in oral-squamous-cell-carcinoma (OSCC) from different species.
Methods: 50 OSCC, 14 feline stomatitis and 63 normal tissue were enrolled in this study. DNA purification followed by bisulfite Next Generation Sequencing protocol were used to quantify the DNA methylation level of each CpG from seven UCNE(uc.160, uc.283, uc.416, uc.339, uc.270, uc.299, uc.328). Bioinformatic data analysis was performed in cloud computing using galaxyproject tools, Methylation Plotter and ClustVis.
Results: 50 OSCC, 26 from human, 17 from cats, 3 dogs, 1 badger, 1 horse, 1 porcupine, 1 bovine, 1 chicken were investigated. Moreover, 14 feline stomatitis and normal tissue from 42 healthy human donors, 7 cats, 5 dogs, 5 horses, 2 caws, 1 badger, 1 iguana were collected as normal controls. DNA methylation analysis revealed consistent epigenetic modifications able to correctly stratify OSCC vs feline stomatitis and vs normal tissue. A common DNA methylation pattern was observed in OSCC of all the species evaluated in this study with an increasing trend of hypermethylation starting from normal mucosa, through stomatitis to OSCC. 57/59 CpGs were statistically significant in Kruskal-Wallis test ($P<0.05$).
Conclusion: Our findings indicate that UCNEs are hypermethylated in human OSCC, and this behaviour is also conserved among different species of mammals and also in reptiles. These similarities at both clinical and molecular level have led to the proposal that feline and other mammal species may serve as a spontaneous model for human disease.
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PS-03-023

The diagnostic utility of RAS Q61R mutation-specific immunohistochemistry in epithelial-myoepithelial carcinoma

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Background & objectives: Epithelial-myoepithelial carcinoma (EMC) is a rare salivary gland tumour characterized by biphasic tubular structures. The *HRAS* Q61R mutation is frequent in and specific to EMC. We evaluated the usefulness of immunohistochemical staining for detecting this genetic alteration in EMC.
Methods: We investigated 74 EMC cases and 63 cases of salivary gland tumours with an EMC-like component, including pleomorphic adenoma, adenoid cystic carcinoma, basal cell adenoma, and myoepithelial carcinoma. Immunohistochemical staining was conducted using the monoclonal antibody specific to the RAS Q61R mutation (SP174; Abcam, Cambridge, MA, USA). Sanger DNA sequencing was also performed for *HRAS*, *KRAS*, and *NRAS*.
Results: The diffuse and membranous RAS Q61R immunohistochemical expression was observed in 51 of 74 EMC cases (68.9%), in which 50 cases (98.0%) harbored the *HRAS* Q61R mutation. The immunoreactivity was largely restricted to the myoepithelial cells in EMC. Conversely, only one of the EMC cases lacking the *HRAS* Q61R mutation and no EMC-like salivary gland tumours showed the abovementioned immunopositivity. None of the cases examined carried *KRAS* or *NRAS* mutations.
Conclusion: Immunohistochemistry for RAS Q61R is highly sensitive and specific for detecting the *HRAS* Q61R mutation in EMC. Further studies will be needed to clarify the molecular mechanisms underlying the differences in the immunoexpression between the ductal and myoepithelial cells in *HRAS* Q61R mutation-positive EMCs. Since significant immunopositivity was exclusively identified in more than two-third of EMCs but not in the histologic mimics, the immunohistochemistry of RAS Q61R is a useful tool for diagnosing EMC in general pathology laboratories.

PS-03-026

BRAF V600E mutations in odontogenic tumours with ameloblastic epithelium: clinicopathological significance and immunohistochemical validation

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Background & objectives: The BRAF V600E mutation is an oncogenic mutation that can be a therapeutic target. We determined the prevalence and clinicopathological significance of BRAF V600E mutations in benign and malignant odontogenic tumours and validated immunohistochemistry using a BRAF V600E-specific antibody (VE1).
Methods: BRAF V600E detection was performed using Sanger sequencing in a total of 20 odontogenic tumours: 5 ameloblastic carcinomas (ACs), 1 metastasizing ameloblastoma, 1 clear cell odontogenic carcinoma, 7 ameloblastic fibromas (AFs), 2 ameloblastic fibro-odontomas (AFOs), and 4 developing odontomas. Associations between BRAF V600E and clinicopathological factors were statistically analysed. VE1 immunohistochemistry was conducted and its validity was evaluated.
Results: BRAF V600E mutations were identified in 40.0% of AC, 42.9% of AF, and 50.0% of AFO, although no clinicopathological factors were significantly associated with the mutation status. VE1 immunohistochemistry showed diffuse cytoplasmic staining in AC, but no VE1 expression was found in BRAF V600E-mutant mixed odontogenic tumours. Compared with the sequencing results, VE1 immunohistochemistry yielded a sensitivity of 33.3% (2/6) and a specificity of 100% (14/14).
Conclusion: Odontogenic tumours with ameloblastic epithelium have BRAF V600E mutations in common, which suggests the utility of BRAF-targeted therapy for AC and supports the notion that AFO is a true neoplasm. Considering the low sensitivity of VE1 immunohistochemistry in odontogenic tumours, molecular tests should be performed to determine the presence of BRAF V600E mutations.

PS-03-027

Orofacial tumours and tumour-like lesions in Birnin-Kebbi metropolis: histopathological analysis

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Background & objectives: Orofacial tumours can occur at any age. An increasing occurrence has made these tumours a significant cause of morbidity and mortality.

Aim
To determine the histopathological pattern of orofacial tumours and tumour-like lesions in Birnin-Kebbi, North-West, Nigeria.
Methods: This is a 9-year retrospective histopathological analysis of orbital tumours diagnosed between 2004-2012 in the Department of Histopathology, Federal Medical Centre, Birnin-Kebbi, Kebbi State, North-West, Nigeria. All the Haematoxylin &Eosin stained slides and paraffin embedded blocks were retrieved and studied.
Results: A total of 23 patients were studied, 11 males and 13 females. The age range is 7-80 years with the mean age of 43.5 years. There is a bimodal peak age at the fourth and fifth decades. The most common benign tumour was pleomorphic adenoma, PA (43.5%), while the most common malignant tumour was adenoid cystic carcinoma, ACC followed by squamous cell carcinoma, SCC.
Conclusion: Orofacial tumours and tumour-like lesions are common in our environment. A very high-index of suspicion, good clinical acumen, adequate histopathologic sampling and reporting can go a long way at making diagnosis.

PS-03-028
The cytokeratin 7/α-smooth muscle actin immunohistochemical combination is sufficient to distinguish adenoid cystic carcinoma from polymorphous adenocarcinoma in small biopsies
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Background & objectives: Adenoid cystic carcinoma (ACC) and polymorphous adenocarcinoma (PAC) represent one of the most troublesome examples of morphological overlap seen in salivary gland pathology. We aimed to demonstrate the combined CK7/α-SMA immunohistochemical combination as a reliable method to make this distinction.
Methods: 100 PACs and 79 ACCs samples diagnosed in small incisional biopsies were submitted to CK7 and α-SMA immunohistochemical reactions. Results were described as positive or negative.
Results: ACC group of patients consisted of 53 women and 26 men, with an overall mean age at presentation of 45.6 years. Cases affected the palate, upper lip, buccal mucosa, retromolar trigone and paranasal sinus. All cases were infiltrative biphasic tumours composed by basaloid cells showing a concordant CK7+/α-SMA+ immunoprofile. The PAC patients were represented by 80 women and 20 men, with a mean mean age of 58.7 years. Cases affected the palate, upper lip, buccal mucosa and retromolar region. All were represented by invasive tumours with diverse architectural growth patterns, displaying a consistently discordant CK7+/α-SMA- profile.
Conclusion: application of the combined cytokeratin 7/α-SMA antibodies is a trustworthy and cost-effective method to separate ACC from PAC, even in small biopsy samples.

PS-03-029
Multi-parametric analysis of interferon γ transcription as assessed by in situ hybridization in head and neck human papillomavirus-related squamous cell carcinomas
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Background & objectives: Patients with Human Papillomavirus (HPV)-related head and neck (HN) squamous cell carcinoma (SCC) have long been considered as having a better outcome. However, they still exhibit variability in their prognosis, that could be linked to micro-environment heterogeneity.
Methods: Sixty-three patients diagnosed with HPV-positive HNSCC and confirmed by HPV DNA PCR, were included. For each of them, one whole slide was stained by Interferon γ (IFNγ) RNAScope® coupled with pancytokeratin, PD-L1 and CD8. Tyramide signal amplification and immunofluorescence revelation followed. IFNγ and/or CD8 expressing cells were quantified in 10 representative high-power fields (distinctively 5 tumoral and 5 stromal).
Results: More than half of HPV-positive oropharyngeal SCC showed IFNγ transcription. The latter was localised in stromal and tumour infiltrating immune cells, as well as in carcinomatous cells. Analysis by log-rank test showed that intra-tumoral IFNγ high expression was associated with a better overall survival (p=0.035), unlike stromal IFNγ expression (p=0.806). Furthermore, HPV-positive oropharyngeal SCC showed enrichment of CD8+IFNγ+ lymphocytes, in both tumoral and stromal compartments (respectively p=0.037 and p=0.048). Of note, the results were independent of PD-L1 expression (positive in 92.1% of all cases).
Conclusion: In conclusion, intra-tumoral IFNγ expression distinguishes two prognostic groups of oropharyngeal HPV-positive SCC. The associated enrichment in CD8+IFNγ+ lymphocytes suggests an underlying mechanism involving the immune micro-environment.
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PS-03-030
Foetal parotid gland morphology in cases of toxaemia of pregnancy
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Background & objectives: Salivary gland's adequate function is important in maintaining an oral environment. Saliva's composition alterations may cause periodontal status and be responsible for the caries development. The aim of the study was to examine the foetal parotid gland morphology under toxaemia of pregnancy,
Methods: 20 foetal parotid glands of 18-22 weeks of gestation were examined after spontaneous abortions in pregnancies complicated by toxaemia of pregnancy. Salivary glands of 15 human foetuses with the same gestational age in cases of induced abortions due to social and psychological reasons were in control group(CG). Histological study of H&E stained slides was followed with morphometry and statistical analysis.
Results: The delay of acini and intralobulae ducts differentiation within the parotid gland tissue were revealed in the study. Dystrophic changes of parenchymal elements of large salivary glands were also determined. Morphometry investigation have shown a reduction of parenchymatous elements volume fraction, decreased vascularity and decline of parenchyma/stroma index. The connective tissue volume fraction in parotid gland tissue increased.
Conclusion: The results of the study present a structural impairments in foetal parotid gland anternatal development in cases of pregnancies complicated with toxaemia. These alterations perhaps cause functional disorders in salivary gland's activities and may contribute to the pathology of the oral cavity in childhood and later life.

PS-03-031
Intraosseous adenoid cystic carcinoma – a case series
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Background & objectives: Intraosseous adenoid cystic carcinoma (ACC) is a rare neoplasm with only a small number of cases described in the literature. This report describes two cases of intraosseous ACC arising in the mandible, and discusses their presentation, imaging, histopathology and management.
Methods: The slides and case reports were examined and data was extracted including demographics, clinical presentation, histological and immunohistochemical features of each case. Further clinical information including radiological findings, clinical management and prognosis was

obtained from our regional electronic patient record system. A literature review was performed.
Results: Both cases are those of middle-aged females, presenting with large lytic lesions involving the mandible. Histopathology of both cases showed the typical features of a solid adenoid cystic carcinoma and immunohistochemical stains and molecular studies were supportive of this. Imaging, including PET CT, highlighted metastatic disease at presentation in both cases. MDT discussion highlighted poor prognosis in each case.
Conclusion: Intraosseous salivary gland neoplasms, although rare, should be considered in the differential diagnosis for tumours within the mandible. They have a propensity for local recurrence and metastasis, and complete surgical resection therefore offers the best outcome. Their clinical and radiological features can be similar to odontogenic tumours. Accurate histological diagnosis is therefore crucial as well as close clinical and radiological correlation to delineate the most appropriate treatment for these patients.

PS-03-032
Protocols of lymph node sampling in 95 cases of head & neck squamous cell carcinoma: is excessive concern for cost control leading to understaging and under treatment?
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Background & objectives: 1. To assess the sampling of large lymph nodes (LN) (>15mm) in Head and neck cancer as per recommendation & evaluate its effect on LN stage and prognostication.
2. Does under-sampling of larger grossly uninvolved LN compromise the patient care.
Methods: 95 cases of head -neck SCC with metastatic lymph nodes(MLN) were categorized into four groups as small nodes(submitted entirely), grossly positive LN, bisected LN and both halves show metastasis and LN which were bisected or trisected and only one slice shows metastatic disease. LN level and the 'N' stage were noted. Retrospective analysis of its impact on staging was done.
Results: Nine cases out of ninety-five revealed that under-sampling of the MLN would have missed the detection of metastasis. Surprisingly, there would have been under-staging of LN stage in five out of these nine cases if the LN were not sampled entirely. This also changes the prognosis of the patient and will lead to false staging.
Conclusion: The gross and microscopic examination provides information about the number of nodes involved, size of the deposit and presence of extracapsular extension (ECE) for staging of the disease. Accurate sampling and thorough examination of LN is perhaps the most important contribution of a pathologist in the management of head and neck cancers. Adequate sampling should be the standard of practice to avoid compromise in patient care.
Larger grossly uninvolved LN should be submitted entirely for adequate staging.

PS-03-033
Focal melanocytic lesions of the oral mucosa: an 18-year retrospective study
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Background & objectives: This study aimed to compile the focal lesions of melanocytic origin diagnosed at the Service of Surgical Pathology of the School of Dentistry of the University of São Paulo and to analyse their respective clinical and histopathological characteristics.
Methods: A cross-sectional study was conducted over an 18-year period. Patient information was collected from medical charts, and all archived histopathological specimens with diagnoses of oral melanocytic lesions were retrieved and reviewed.
Results: We identified 341 melanocytic lesions among 64,695 samples received for histopathological analysis. Of these, 191 were melanotic macule; 112 melanocytic nevi; 14 mucosal lentigo simplex; 12 oral melanomas; nine actinic lentigines and one melanoacanthoma. Lesions occurred mostly in women (n=218; 65.5%), with white skin colour (n=217; 74%). The main reported clinical aspect was macular (n=124; 67.6%). Melanocytic lesions occurred mainly in lip vermilion (n=83; 25.6%), followed by palate (n=74; 22.8%). The age of the patients was higher in melanoma patients and these cases had a shorter average duration until the time of diagnosis. Most lesions were small and only oral melanomas were larger in size when compared to other lesions.
Conclusion: Melanocytic lesions are an uncommon diagnosis in oral pathology routines. The most frequent lesions are melanotic macule and nevus. Patients with these lesions are usually white-skinned women presenting a small, long-lasting, macular lesion on lip vermilion or palate.

PS-03-034
Expression of microRNA-31 in saliva-liquid biopsy of oral squamous cell carcinoma patients
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Background & objectives: Aberrant expression of microRNA-31 in saliva-liquid biopsy has been reported in various cancers. However, little is known about its expression in oral-squamous-cell-carcinoma (OSCC). We aimed to investigate microRNA-31 expression in pre-and post-surgical OSCC patients and its association with clinicopathological features.
Methods: We investigated salivary microRNA-31 expression in pre-surgical and post-surgical (6 weeks after surgery) patients with oral squamous cell carcinoma (n=16) and control (n=2) by quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) after ethical approval from institutional review board (IRB).
Results: Salivary microRNA-31 expression was differentially regulated in pre- and post-surgical patients with oral squamous cell carcinoma and controls. MicroRNA-31 was significantly upregulated in pre-surgical cases ($p<0.05$). However, the expression was significantly reduced after 6-weeks of surgical excision of tumour, indicating that most of the microRNA-31 derived from oral squamous cell carcinoma tissues. Moreover, no significant association was found between pre-surgical microRNA-31 expression level and age, gender, site, habits, pathological TNM staging and grading.
Conclusion: Our findings showed increased expression of microRNA-31 in saliva-liquid biopsy, suggesting microRNA-31 an important player in pathogenesis of oral squamous cell carcinoma.

PS-03-035
HRAS mutation is a surrogate diagnostic marker in challenging cases of epithelial-myoepithelial carcinoma
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Background & objectives: Epithelial-myoepithelial carcinoma (EMC) is a challenging diagnosis for the wide variety of patterns. We analysed HRAS status in 3 cases of EMCs with predominant solid-oncocytic and sebaceous features, as Urano et al (2019) demonstrated HRAS mutation in 82.7% of EMCs.
Methods: Patients were 2 males and 1 female aged 69-75 years. Two cases presented prominent solid oncocytic pattern and 1 was characterized by extensive sebaceous differentiation (initially diagnosed as sebaceous carcinoma). HRAS sequencing were analysed in 3 cases using a single base primer extension approach (SNaPshot assay) on an ABI Prism

3500 genetic analyser. Fragment analysis was performed using GeneMapper software.
Results: All 3 cases analysed for mutations in HRAS showed positive results. The site of mutation was exon 2 (p.Gly13Arg; c.37G>C) in one oncocytic EMC, while the same mutation in exon 3 (Q61R; c.182A>G) was found in the second oncocytic case and in the sebaceous EMC.
Conclusion: EMCs with prominent unusual variants of histologic features can be frequently confused with other entities with different behaviour and prognosis. We demonstrated that HRAS mutations are present in these variant EMCs. Thus assessment of HRAS status is useful in salivary gland neoplasms that do not entirely fulfil clear diagnostic criteria for EMC and cannot otherwise be classified as other entities.

PS-03-036
PD-L1 score and CD8 heterogeneity in head and neck squamous cell carcinomas
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Background & objectives: In an effort to further characterise head and neck squamous cell cancer (HNSCC) phenotypes relevant to the currently applied immunotherapy with checkpoint inhibitors (ICIs), we profiled PD-L1 status, CD8+ lymphocytic infiltrate density and their heterogeneity in these tumours.
Methods: We evaluated p16 protein expression (positive/negative), combined PD-L1 positivity score (CPS, clone 22C3) and CD8+ lymphocyte density/mm^2 in 228 HNSCC (52.5% laryngeal supraglottic/glottic/subglottic; 19.7% oral cavity; 12.2% oro-hypopharyngeal; 15.6% other) informative for all 3 markers. CD8+-density was analysed as continuous variable. Immunohistochemistry was performed on tissue-microarray sections with multiple cores per tumour, allowing for the assessment of intra-tumour heterogeneity.
Results: Out of 228 HNSCC, 16 were p16 positive (7.0%), half of them oro-hypopharyngeal; 37 (16.3%) were PD-L1 positive with CPS ≥1, while 7 of them with CPS ≥20 (high PD-L1 expression level); median CD8+-density was 204.9 (interquartile-range 105.0-437.2). Twenty-two (9.6%) and 48 (26.7%) tumours exhibited heterogeneous PD-L1 status and CD8+-density, respectively. p16-positive tumours demonstrated higher CD8+-density (Wilcoxon rank-sum p=0.0022), but none of them expressed PD-L1 at high levels (Pearson's p=0.0008). PD-L1-positive tumours had higher CD8+-density (Wilcoxon rank-sum p<0.0001); the latter did not differ for PD-L1 scores 1-19 and ≥20. PD-L1-positivity was associated with CD8+-heterogeneity (Fisher's exact p=0.0005), particularly concerning tumours with high PD-L1 expression level (p<0.0001), independently of tumour location.
Conclusion: PD-L1/CD8 profiles may distinguish previously described immunologically "hot" and immunosuppressed HNSCC. CD8+-heterogeneity may be related to different immunological priming by tumour subpopulations. PD-L1/CD8 assessment may further aid in the distinction of tumour immunological classification, particularly for predicting efficiency to ICIs.

PS-03-037
Evaluation of high-risk human papillomavirus mRNA silver in situ hybridisation diagnostic assays in oropharyngeal squamous cell carcinomas
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Background & objectives: Testing is required to distinguish human papillomavirus (HPV) driven oropharyngeal squamous cell carcinomas (OPSCC) with favourable treatment response and prognosis from HPV negative tumours. Recently developed RNA ISH probes complementary to HPV E6/E7 mRNA enable direct visualization of viral mRNA.
Methods: Sensitivity/specificity of high-risk (HR) HPV mRNA silver in situ hybridization (SISH) for HPV16, HPV18 and HPV33 was tested for the first time. 67 FFPE OPSCC and 3 papillomas from 62 patients diagnosed between 2006-2014 were tested with SISH, Abbott RealTime High Risk HPV test, in-house GP5+/6+/68 PCR test and p16 immunohistochemistry (IHC).
Results: Using HR-HPV PCR, 46 (69%) OPSCC were HPV+, with single HPV type in 44/46 (38 HPV16+, 2 HPV33+, 3 HPV35+, 1 HPV58+), 2/46 with co-infections (HPV16/X, HPV16/35). Of HR-HPV PCR+ OPSCC, 45/46 overexpressed p16, 43/46 were SISH+. Others were PCR HPV16+/p16-/SISH-, HPV35+/p16-/SISH-, HPV58+/p16-/SISH-.
Sensitivity/specificity/AUC with 95% confidence interval of combined SISH+ (HPV16/33) and p16 IHC compared to PCRs were 100.0%, 100.0% and 1.00. HPV+ group had favourable overall survival (p<0.001).
Conclusion: mRNA SISH methodology for FFPE tissue reliably detects HPV-driven OPSCCs without need for additional tests in most cases, with clearly positive signals easily detectable at 10x/20x magnification, enabling visualisation of viral transcripts required to recognise clinically relevant HPV infection. Compared to PCR, clear signals reliably exclude false-positivity, but rare/tiny signals require experienced pathologist or a team for consensus interpretation of results.
Funding: Roche Ventana provided mRNA probes for SISH

PS-03-039
An audit to compare the turn-around times of oral and maxillofacial resection specimens including and excluding bone
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Background & objectives: To identify the turnaround times (TATs) for resection specimens and to assess for compliance with The Royal College of Pathologists Key Performance Indicators that 80% of resection cases (excluding those with bone) should be reported within 10 calendar days.
Methods: Two cycles of the audit were completed. All resection specimens (including and excluding bone) over 3 separate and comparable 3-month periods were assessed. The average TATs and percentage of cases reported in both 10 working days and 10 calendar days was recorded.
Results: There have been significant improvements between cycles one and two with the average TAT for resection cases without bone decreasing from 12.9 to 10.4 calendar days. The percentage of resections without bone reported within the recommended timeframe increased from 31.4% to 57%. The average TAT for resections including bone decreased from 29.2 to 20.4 calendar days, although in both cycles 0% of cases were reported within 10 calendar days.
Conclusion: TATs for specimens including bone are significantly higher with decalcification processes being a major contributory factor. To improve patient care, work is required to achieve the target within the recommended timeframe. A possible solution includes use of alternative decalcification techniques.

PS-04 Dermatopathology

PS-04-001
Acral melanomas in Singapore
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Background & objectives: Singapore population has higher incidence of acral melanoma compared with Caucasians, with fewer BRAF mutations compared with cutaneous melanomas. Our Singapore study

correlates molecular findings in acral melanomas with clinicopathological features and compares with other Asian data.
Methods: 195 cases of melanoma with molecular analysis for mutations in exon 15 of the BRAF gene and exons 9, 11, 13, and 17 of the ckit gene in genomic DNA by polymerase chain reaction amplification and direct Sanger sequencing were retrieved from Singapore General Hospital files (2007-2020
Results: Of 195 cases, 72(37%) were cutaneous, 69(35%) acral and 54(28%) mucosal. Of 69 acral tumours, 16/53(30%) were BRAF positive. Of 28 acral cases with ckit mutational analysis, 11/43(26%) were ckit positive. The majority of BRAF positive cases were of Chinese ethnic group (12/16), female (11/16), mean age 59 years, located at acral non-pressure sites (12/16) and foot (12/16). No significant differences in the incidence of ulceration were seen between the BRAF positive (52%) and BRAF negative (42%) tumours, and also ckit positive (55%) and ckit negative (63%) tumours. The incidence of nodal metastasis was markedly different between ckit positive tumours (55%) compared with ckit negative tumours (33%).
Conclusion: The BRAF positive mutation rate in Singaporean ALM was comparable with data from China, Korea, Taiwan and Japan (range 25-42%). Our findings suggest a possible relationship between ckit mutation and the incidence of nodal metastasis.

PS-04-002
Histopathologic features of dermatologic eruptions due to immune checkpoint inhibitors [monoclonal antibodies targeting cytotoxic T lymphocyte-associated antigen-4 (CTLA-4), programmed cell death protein 1 (PD-1) or programmed death ligand 1 (PD-L1)]
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Background & objectives: Checkpoint inhibition induces immune-related adverse events. Skin toxicity is one of the most common, mostly as a maculopapular rash, less frequently as vitiligo, psoriasis and auto-immune diseases. This review describes the histopathologic aspects of dermatologic irAEs induced by checkpoint inhibitors.
Methods: We reviewed19 biopsies, obtained from 16 patients who were referred to the Dermatology Department of "La Paz" University Hospital, a tertiary care hospital. All patients had developed dermatologic toxicity while receiving either anti-PD-1, anti-PDL1, or anti-CTLA4 agents, from January 2017 to January 2020.
Results: Patients were 9 males and 7 females, with a medium age of 64 years. Lung carcinoma was the most common tumour being treated, followed by gastric adenocarcinoma and melanoma. In twelve biopsies the patient was on anti-PD-1 agents, in 4 on anti-PDL1, and in 3 on anti-CTLA4 plus anti-PD1 or anti-PDL-1 treatment.
The most common histopathologic pattern was "interface dermatitis", in 10 biopsies (52,6 %), which was lichenoid in 6 of them. Other patterns observed (sometimes overlapped) were: psoriasiform (15,3%), spongiotic,vesiculobullous (bullous pemphigoid and Grover's disease) and urticarial (10,5% each). One patient with melanoma, showed loss of melanocytes, which was interpreted as vitiligo.
Conclusion: The results reveal that histopathologic features of reactions secondary to check point inhibitors therapy arequite heterogeneous. Clinical correlation is needed for definitive diagnosis. Despite interface dermatitisis the most common pattern, florid lichenoid pattern was observed in just 6 biopsies (31,6%). It is important that doctors are familiar with these increasing adverse effects, quite unknown to date, for the correct management of patients.

PS-04-003
Subcutaneous sarcoidosis: a series of 8 cases
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Background & objectives: Subcutaneous involvement has been described in up to 16% of patients with cutaneous sarcoidosis. It consists of sarcoid granulomas affecting mainly subcutaneous tissue and manifests clinically as erythematous, flesh-colored, violet or hyperpigmented nodules, mostly in upper limbs.
Methods: We reviewed our institutions' archives from 2013 to 2019 and found eight cases. Histopathological diagnosis of subcutaneous sarcoidosis was demonstrated by the presence of non-casefying granulomas in subcutaneous tissue while excluding other causes of granulomatous panniculitis.
Results: Patients' ages ranged between 33 and 76 years old. Six had nodules in limbs, one in scalp and one in face and breast. Seven patients presented with subcutaneous sarcoidosis at the beginning, being the only sign of disease in four of them. Two cases showed other sarcoid cutaneous manifestations and two others, bilateral hilar adenopathies. Two cases had history of dermatomyositis under treatment and another, prostate adenocarcinoma with hormone therapy.
Conclusion: Our series' results are consistent with current literature. It is important to recognize subcutaneous sarcoidosis since this would allow earlier diagnosis and treatment of systemic disease. It is remarkable that three patients had history of immunosuppressive therapy; also reported as cases of subcutaneous sarcoidosis related to this type of treatment.

PS-04-004
Nevus sebaceous with associated uncommon pathologies
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Background & objectives: The obectives were to study clinicopathological features of Nevus Sebaceous and associated other pathologies – benign and malignant, reported from 2010 till February 2020 in the section of Histopathology at our University Hospital.
Methods: We retrieved ten year data from our archives, using our Integrated Laboratory management system software, by using words "Nevus Sebaceous". Demographics including age, gender, site and presence of other pathologies was recorded. Frequencies of benign and malignant lesions were calculated.
Results: 111 cases of Nevus Sebaceous were reported from 2010 till February 2020. Age ranged from 3-85 years (mean age 31.2 years). 74.7% of patients were above 20 years. 57.6% were male and 40.5% females. 45.9% were located on scalp, face (42%), ear (4.5%), back (1.8%) and neck (0.9%). Site was unknown for 8 cases (7.2%). 23/111 cases (20.7%) showed associated lesions. These included Syringocystadenoma Papilleferum (39.1%), Epidermal Nevus (17.4%) and Trichoepithelioma (8.7%). One patient each had Syringoma, Solar Lentigo, Actinic Keratosis, Tumour of Follicular Infundibulum, Intradermal Nevus and Hemangioma. Two showed metaplastic bone formation and Amyloidosis respectively. Two patients (1.8%) had Basal Cell Carcinoma, one of them below 20 years.
Conclusion: Knowledge of the probability of encountering other benign or malignant lesions arising within a nevus sebaceous is essential for correct diagnosis, as they might be missed due to inadequate sampling, which may adversely affect patient management and follow up.

PS-04-005

Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder - the presence of dual lineage rearrangements

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Background & objectives: The Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (PCSMP-TLPD). It is included in the Peripheral T -cell lymphoma with follicular T helper phenotype; which are the providers of T- cell help to B cells for the development of germinal centres

Methods: We have studied the cases diagnosed in our hospital from 2012 until now. We have reviewed 16 cases and analysed them with CD3, CD4, CD8, CD7, CD10, Bcl6, PD-1, CD20, CD38, Kappa and lambda. Polymerase chain reaction (PCR) was performed to analyse clonal expansion of T and B cells.The mean age at diagnosis was 58.6 years (range 31-85).

Results: There was a women predominance (10 women out of 16 cases). Histologically, the lymphoid infiltrated shows nodular arrangement; a very focal epidermotropism and extended folliculotropism. By immunohistochemical analysis, all cases showed a mixed population of T-cells that expressed T helper phenotype, and B cells.

All are cases were positive for TCR gene arrangements, but 4 of 10 cases tested were also positive for IgH gene rearrangements and one was pseudoclonal.

Conclusion: -The mixed nature T and B could make a challenging diagnosis in PCSMPTLPD.

-The presence of dual lineage rearrangements in cutaneous lymphoproliferative disorders is documented but rare phenomenon.

-The presence of two distinct monoclonal populations could confirm the reactive nature.

PS-04-006

A 5-year retrospective study reviewing the histopathological features of cutaneous and subcutaneous malignant melanoma metastases

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Background & objectives: Melanoma can metastasize either by lymphatic or haematogenous route and may develop either satellite, in-transit, regional lymph node or distant metastases. Cutaneous and subcutaneous metastases can be difficult to diagnose in the absence of clinical suspicion or hallmark histopathological characteristics.

Methods: In this study, we reviewed the medical records of 21 patients who presented in our Dermatopathology unit with cutaneous and subcutaneous metastatic melanoma during a period of five years (2014-2019). We thoroughly re-examined clinical photos, Hematoxylin-Eosin and immunohistochemistry slides, aiming to identify characteristic histological features.

Results: Most tumours presented as nodular proliferations of atypical epithelioid cells with abundant clear or eosinophilic cytoplasm, hyperchromatic, atypical nuclei with prominent nucleoli and high mitotic index. Approximately half of them presented with pigment formation. Four of them presented necrosis and only two of them presented epidermotropism. One particular case, had a blue nevus-like appearance, with round-oval and spindle cells, subtle atypia, fibrous stroma, varying pigmentation and extremely rare mitoses. This study included patients with various clinical presentations, from a 24-year-old male with no history of melanoma, to a 74-year-old male with two concurrent metastases.

Conclusion: Although they are a common occurrence in Dermatopathology, up to 10% of melanoma metastases appear in the absence of a previously diagnosed or currently detectable primary tumour. We identified common histological hallmarks and rare features such blue nevus-like metastasis.

PS-04-007

Malignant melanoma arising in tattooed areas: report of two cases

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Background & objectives: Malignant melanoma is an aggressive type of skin cancer, with a high risk of metastasis in late stage disease, making early diagnosis essential. The relationship between melanomas and tattoos is still unclear.

Methods: We report two cases of a 33-year-old and a 35-year-old patient, both males, each presenting with a cutaneous melanocytic lesion on a tattooed area, located on the upper extremity. We examined the Hematoxylin-Eosin slides and clinical photos of the lesions.

Results: We present two extremely rare cases, both from a clinical perspective (tattooed area) as well as a histopathological one (nevoid melanoma and completely regressed melanoma), both of them historically documented with clinico-pathological images.

First case was a naevoid melanoma with 2.9 mm Breslow index (pT3a) and Clark level IV. Low-power appearance was that of an intradermal nevus with hypercellular dermal papillae featuring "puffy-shirt-sign" with 3 mitoses/mm², anisomorphic nuclei, 1-3 nucleoli and no maturation. Second case was a completely regressed melanoma which presented as tumoral melanosis, with dense fibrosis and lymphoplasmacytic inflammation. Breslow maximum depth was of 8.1 mm, corresponding to Clark level V.

Conclusion: Despite paucity of literature data regarding malignant melanoma in tattooed areas, establishing a clinico-pathological connection between the two could increase chances of early detection and therefore, effectiveness of treatment. Both lesions presented in young patients and were challenging to diagnose.

PS-04-008

Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder: one-year experience in one dermatopathology unit

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Background & objectives: Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder is characterized by a solitary cutaneous lesion on the face, neck or trunk, with excellent prognosis. According to 4th Edition of the Blue Books it is a provisional entity, with uncertain malignant potential.

Methods: In this retrospective study, we examined the clinical records of 4 patients diagnosed with Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder in our Dermatopathology unit. We thoroughly reexamined clinical photos, Hematoxilyn-Eosin and immunohistochemistry slides (CD3, CD20, CD4, PD-1, CD 8, BCL6, Kappa and Lambda).

Results: Each patient (median age 44-years-old), presented with a single lesion: three on the trunk and one on the forearm. In two cases, the lymphoid infiltrate featured a lichenoid pattern, predominantly affecting the papillary and upper reticular dermis. In the other cases, the lymphoid infiltrate was nodular and mostly affected the reticular dermis. The lymphoid proliferation was constituted primarily of small-sized lymphocytes, with fewer medium-sized lymphocytes and peripherally situated plasma cells. One of the cases presented with epidermotropism, and in all of them, the infiltrate surrounded cutaneous adnexa. Immunohistochemically, all cases were positive for CD3, CD4, PD-1 and negative for CD20 and CD8.

Conclusion: We highlight the importance of recognizing this entity in order to avoid misdiagnosis as lymphoma and subsequent over-treatment. In the case of Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder, intralesional steroids or simple excision are sufficient, with rare recurrences.

PS-04-009

Slow Mohs micrographic surgery in dermatofibrosarcoma protuberans: 6 years experience in one dermatopathology unit

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Background & objectives: Dermatofibrosarcoma protuberans is a soft tissue sarcoma with aggressive local behaviour and high recurrence risk. Due to its seemingly benign cytological appearance and irregular pattern of invasion, some cases may raise difficulties in determining whether the surgical margins are clear.
Methods: We present 12 cases of dermatofibrosarcoma protuberans which were surgically removed using Slow Mohs micrographic surgery. All surgical specimens were intraoperatively marked by the surgeon and then photographed, inked and sectioned in our pathology lab, according to our slow Mohs protocol. All sections were examined using Hematoxylin-Eosin and CD34 immunolabeling.
Results: Patient age was 15-55 years, with male predominance (58%). Tumours presented either on the torso or head and neck area, apart from one, located on the foot. Two cases presented with clear margins after first excision, the rest having positive deep excision margins. The highest number of interventions was 5, the average being 3. One case presented with fibrosarcomatous transformation, featuring hyperchromatic nuclei and 21 mitoses per 10 HPF.
Our experience to date demonstrates that Mohs microsurgery combined with immunohistochemical evaluation is a reliable method of providing patients with complete surgical excision, especially when facing tumours in challenging locations, which are growing between nerves and/or tendons.
Conclusion: Slow Mohs micrographic surgery offers the surgeon a histological confirmation before closing the wound. If the resection margins are positive, the surgeon can further remove the areas marked by the pathologist, sparing as much healthy tissue as possible.

PS-04-010

Melanocytic nevus and osseous metaplasia: pathological features of 5 cases

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Background & objectives: Wide variety of histopathological changes may be found in melanocytic nevi. Osseous metaplasia represents an unusual finding, sometimes misunderstood or overlooked, characterized by foci of bone formation adjacent to or surrounded by melanocytic nests exhibiting a normal maturation pattern.
Methods: We conducted a retrospective review, using our database from the last 15 years. Clinicopathologic features were gathered: age, sex, location, nevus type, intra or extralesional ossification and presence of dermal inflammation. Five cases were identified, four osteonevi of Nanta and one blue osteonevus.
Results: There were three men and two women. The ages ranged from 32 to 81 with a mean age of 53 years. Of these nevi, only one had congenital features, four showed presence of fatty marrow, three were intradermal and two compound, and all were on the upper part of the body. There were two of them with inflammation associated, and one with foreign-body granuloma. Four cases presented intralesional bone formation.
Conclusion: To our knowledge, this represents the largest series of such cases in Spanish literature, and the fourth example of blue ostenevus ever reported. Bone formation in nevi represents an unusual finding, and only small series have been reported. We confirmed the upper body location, intradermal type predominance and age span, similar to literature. In contrast to previous series, we found a slight predominance in males. The pathogenesis of osseous metaplasia in nevi is not fully understood and requires further study.

PS-04-011

Neuronevus of masson: four cases with typical clinicopathological features

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Background & objectives: The so-called “blue neuro-nevus of Masson” or "Masson neuronevus" (MN) is a benign variant of the cellular blue nevus that due to its cellularity and abundant pigment is sometimes misdiagnosed as melanoma.
Methods: We present four cases obtained from the files of our hospitals.
Results: The patients were three women and a man, whose ages were 8, 19, 35 and 50 years. All lesions were localized on gluteal areas, consisting of asymptomatic, brownish to greenish nodules, one of them presumed to be since birth.
Histologically all cases were circumscribed tumours situated in medium and deep dermis, with intact epidermis, growing in a fascicular pattern, with a “hourglass” configuration.
Cytologically they were composed of ovoid and/or spindled cells, surrounded by fibrous tissue containing sparse dendritic cells and melanophages, without mitotic figures. All of them where immunoreactive for S100, SOX10 and HMB45 (the latter only focally at the periphery). Betacatenin was negative in all of them.
Conclusion: MN can mimic melanoma because of the size, the involvement of deep dermis and the abundance of melanophages. The absence of mitosis (or <1/mm²), necrosis and atypia, without infiltrative margins supports the diagnosis. Unlike deep penetrating nevus, Beta-catenin is absent.

PS-04-012

Blastic plasmocytoid dendritic cell neoplasm: a rare cutaneous lymphoma - analysis of 3 cases

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Background & objectives: Blastic plasmocytoid dendritic cell neoplasm represents less than 1% of cutaneous lymphomas, being more common in males. Although some cases are indolent, the course is often aggressive with involvement of the bone marrow, peripheral blood and lymph nodes.
Methods: We report the cases of three male patients with ages between 57 to 85 years old, with diagnosis from 2013 to 2019, that presented multiple purpuric, painless and non-ulcerated nodules on the trunk, extremities and face. All patients didn't present systemic symptoms.
Results: Histopathological examination revealed a dermal infiltrate by a population of medium-sized cells with nuclear pleomorphism, several nucleoli and a moderate to scant cytoplasm. The mitotic count was high, and the epidermis was spared. In one case there was a lobular pattern extended to the subcutis.
Immunohistochemistry study showed positivity for CD4 and CD56 in all cases; however, in one case it revealed focal positivity for LCA and CD43 that could lead to a differential diagnosis of cutaneous infiltration by myelomonocytic leukaemia. CD3, CD20, TdT, CD138, CD30 and CD8 were negative.
All patients had involvement of the bone marrow and there was affection of the cervical lymph nodes in two cases.
Conclusion: The expression of CD56 and CD4 favoured the diagnosis of blastic plasmocytoid dendritic cell neoplasm in all cases and immunophenotyping by flow cytometry was concordant. The median survival varies from 10 to 20 months. In our study, one patient died three months after the diagnosis and the others showed initial response to chemotherapy; however, advanced age, negative expression of TdT and bone marrow involvement have a negative impact on prognosis.

PS-04-013

Cutaneous leukemic infiltrates: unusual manifestation of haematological diseases - study of 4 cases

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Background & objectives: Leukaemias are neoplastic proliferations in the bone marrow and peripheral blood that rarely involve the skin as non-specific lesions like purpura, vasculitis and vesicular eruptions that may simulate acantholytic dermatoses. Reports of specific involvement have been documented in several subtypes.
Methods: We describe the cases of three males and one female patients with ages between 44 to 78 years old, that had previous diagnosis of chronic myeloid leukaemia and myelomonocytic leukaemia. Now they present multiple non-symptomatic purpuric to reddish cutaneous lesions in the scalp, trunk, arms and legs.
Results: Histopathological examination revealed a diffuse and interstitial dermal infiltrate composed by atypical round to polygonal cells with slight nuclear pleomorphism with dispersed chromatin and small nucleoli; cytoplasm was moderate to scant. High mitotic count, apoptosis and epithelial hyperplasia with mild acanthosis were present in all cases.
Immunohistochemistry study showed positivity for LCA, CD34, CD117 and myeloperoxidase in two cases, favouring the cutaneous involvement by chronic myeloid leukaemia. Diffuse positivity for CD4, CD56, CD68, CD163 and lysozyme with negativity for CD34 and CD117 in the other two patients, suggesting cutaneous infiltrate by chronic myelomonocytic leukaemia. CD3, CD5, CD20, CD79 and CD30 were negative in all cases.
Conclusion: Most cutaneous involvement by myeloid leukaemia follow an aggressive clinical behaviour. In our analysis, two patients died in less than six months following the appearance of the cutaneous lesions despite systemic chemotherapy. Both cases were from elderly patients (>70 years old): one with chronic myelomonocytic leukaemia that had transformation to acute myeloid leukaemia and other with chronic myeloid leukaemia. Advanced age is also associated with shortened survival.

PS-04-014

Kaposi sarcoma: a 3-year retrospective study with emphasis on epidemiology in a non-endemic country

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Background & objectives: Kaposi sarcoma (KS) is a malignant vascular proliferation usually encountered in elderly middle eastern men, young African-American and patients with iatrogenic immunosuppression or AIDS. Patients usually present with multiple coalescent red macules or nodules located on the distal lower extremities.
Methods: This is a retrospective study including 32 cutaneous KS diagnosed in our unit during a period of four years (2016-2019). We aimed to analyse the epidemiologic features and establish clinico-pathological correlations regarding KS diagnosed in Romania. Clinical information was retrieved from the virtual database. We thoroughly re-examined all Hematoxylin-Eosin and immunohistochemically (HHV-8, CD34, D2-40, SMA) stained slides.
Results: Patient age ranged from 25 to 85 years. Lower extremities were frequently involved (55.2%), followed by upper extremities (27.6%), face (10.3%) and buttocks (6.9%). The overwhelming majority of the patients were males (72%) and nodular stages of the disease represented 65.5% of cases. Clinical diagnosis varied from Kaposi's sarcoma (58%), haemangioma (10.3%), carcinoma (20.7%), sarcoma (7%) and melanoma (3.4%). "Promontorium sign" was present in 60% of patches and plaques cases. Clinical diagnosis accuracy increased in patients who already developed nodules.
Conclusion: Most cases in our study consisted of classic Kaposi's sarcoma developing on acral sites, with only one exception encountered on the face of a young male. In our experience, KS should be considered when encountering vascular lesions on acral sites.

PS-04-015

Slow Mohs micrographic surgery in extramammary paget disease: 3-year experience in one dermatopathology unit

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Background & objectives: Extramammary Paget disease (EMPD) is known to have a local recurrence rate of 34-40% after surgical excision, while the recurrence rate after Slow Mohs micrographic surgery is only 12%. This way, the wound is left open, awaiting the pathological report.
Methods: We re-evaluated 4 cases of extramammary Paget disease which were cured in our unit (2016-2019) using this technique. All specimens were received with marking sutures. Excision margins were inked, sectioned, mapped and submitted in separate blocks, in regard to the suture mark. All resulting slides were evaluated using Hematoxylin-Eosin staining and CK7 immunolabeling.
Results: All patients were females in their sixties and most lesions were located on the labia (75%) or in the perianal area (25%). In 50% of cases, the lesion spread in opposite directions, requiring multiple excisions per intervention. The total number of blocks used ranged from 18 to 38. First interventions required larger excisions (40/21/3 mm to 115/85/10 mm), while the last ones were much smaller (16/9/2 mm to 42/8/2 mm). Patients required 3 to 5 reinterventions in order to achieve curability. No case featured dermal invasion or signs of recurrence to date. This technique combined with immunohistochemistry is a reliable technique which increased the curability of EMPD in our unit.
Conclusion: Slow Mohs micrographic surgery allowed the clinician to remove a targeted area with residual tumour located between specific hour intervals, thus sparing healthy tissue. In this manner, many reinterventions can be done, in order to achieve curability.

PS-04-016

The MANIAC: pagetoid spread in benign acral nevi

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Background & objectives: Melanocytic acral nevus with intraepidermal ascent of cells (MANIAC) was first described by LeBoit et al. in 1997. Although the lesion is characterized by suprabasal scatter of single melanocytes, it is considered benign and has good outcome.
Methods: In this study we re-evaluated the clinical records of 8 patients diagnosed with MANIAC in our Dermatopathology unit within the last 3 years. Average age was 20.5 years. Upon follow-up, none of the lesions recurred or progressed. We thoroughly re-examined the slides and analysed the clinical data retrieved from the virtual database.
Results: Most lesions were located on the toes, followed by the lateral aspects of the foot and palms. Histologically, 75% were compound and 25% were junctional nevi. 50% were well-circumscribed, 25% were moderately well-circumscribed, and 25% were poorly circumscribed. No cytological atypia or lymphocytic infiltrate were noted. All lesions

featured intraepidermal ascent of melanocytes throughout the entire epidermis, and 25% of the cases even showed rare melanocytes within the cornified layer as pigmented columns above the sulci or crista profundae intermediae. Well-circumscribed and symmetric lesions occurring in young adults which feature maturation and lack cytological atypia or brisk lymphocytic infiltrate usually manifest as benign nevi.
Conclusion: Practicing pathologists should be aware that suprabasal scatter of melanocytes is not pathognomonic for melanoma in acral nevi without other worrisome features like lateral confluence of junctional nests, cytological atypia or lymphocytic infiltrate.

PS-04-017
Merkel cell carcinoma of an unknown primary origin, 5 case report
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Background & objectives: Merkel cell carcinoma(MCC) is a rare neuroendocrine tumour of the skin. MCC of an unknown primary origin(MCCUP) is much rarer; approximately 200 cases have been reported in literature. In this study,5 patients diagnosed with MCCUP in the lymph node in our hospital between 2015-2019.
Methods: The age distribution was 69-84(mean=75.8),3 were female;2 were male.2 patients had axillary; 3 patients had involvement in the inguinal region lymph nodes. All patients had skin examinations; no primary skin lesion was found. Diagnosis was made from axillary in 2 patients and inguinal lymph in 3 patients. The diameter of the lymph nodes assessed macroscopically was 6.42 cm(average).
Results: In the examination after diagnosis,3 patients were identified as pT0NxM1a Stage 4 and 2 patients as pT0N1M0 Stage 3.2 patients with stage 4 received palliative chemotherapy+radiotherapy,1 patient received palliative radiotherapy.2 patients with stage 3 had definitive surgery. While 3 patients with stage 4 were exitus,2 patients with stage 3 didn't develop locoregional recurrence or distant metastasis, one of them was followed for 3,5 years and the other for 9 months without disease.
Conclusion: Polyomavirus, accused in the aetiology of MCC, was detected more rarely in MCCUP (76% vs 31% P = 0.001), and these two entities were thought to use different biological pathways. MCCUP is a tumour that shows a better progress compared to metastatic MCC and has different views on treatment. We presented our cases reported in a single centre for the purpose of contributing to the literature with clinical, histological and treatment methods.

PS-04-019
Study of the sebostatic effect of retinoic acid on rat sebaceous glands
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Background & objectives: Morphological changes in the skin with acne are characterized by acanthosis, parakeratosis and intercellular oedema in the epidermis, lymphocytic infiltration of the dermis and sebaceous gland (SG) hypertrophy. Using retinoic acid reduces the synthetic activity of SG cells.
Methods: 10 Wistar male rats (ExpG) were applied a 0.05%solution of retinoic acid on the clipped surface of the skin daily, for 10 days in the form of an application. The control group (CG) included 10rats of the same line. Histological sections were stained with H&E. 5 section was examined from each animal, in which up to 30 SG profiles were measured.
Results: The histostructure of SG of ExpG was distinguished by polymorphism. The gland profiles are visually unevenly reduced. The cytoplasm of individual sebocytes loses the cellular structure, the cells look like undifferentiated. Morphometric studies confirmed the results of visual assessment. A retinoic acid solution significantly reduces the average area of SG profiles (3323.42±82.65) in the section compared to CG (3940.19±67.12) ($p<0.001$). The proportion of undifferentiated sebocytes in the area of SG increases($p<0.001$).
Conclusion: Applications with retinoic acid have a pronounced sebostatic effect, manifested in the reduction of sebaceous glands and an increase in the area occupied by undifferentiated sebocytes. Sebaceous gland profiles are visually and morphometrically reduced. This minimizes the etiological factor of acne.

PS-04-020
Pathohistological examination of early detection of skin melanoma by ytterbium porphyrin complex gel
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Background & objectives: The optimum diagnostics is the melanoma development in situ.
The present study considers the potential of melanoma fluorescent diagnostics by ytterbium porphyrin complex (YbPC) and consequent pathohistological examination of its effectiveness.
Methods: The method of using the laser consists in the ability of YbPC to accumulate well in tumour cells, they also have intense luminescence. First the pharmaceutical product containing Yb-2,4-dimethoxyhematoporphyrin IX is applied to the lesions. 30 minutes later we measured the luminescence intensity in the near infrared range (900-1100 nm) using the Onkoflurometer" laser device.
Results: The study involved a group of 28 patients aged from 19 to 67 years with dysplastic naevus as provisional diagnosis. The examinees were examined by means of dermatoscopy, a diagnostic laser with use of fluored gel containing YbPC, with exposure time of 30 minutes and evaluation of the depigmentosus part, the hyperpigmentosous parts in the centre and in peripheral zones.
Among 28 biopsies, 3 melanomas were detected at stages 1 and 2. However, there were no signs of melanoma during dermatoscopic examination
Conclusion: This method is highly sensitive and specific and can be implemented directly into the routine practice of specialists.

PS-04-021
Melanocytic matricoma: report of two cases of a rare entity
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Background & objectives: Melanocytic matricoma is an extremely rare benign tumour derived from the hair matrix and may be misdiagnosed because of its peculiar morphological features.
Methods: We report two cases of melanocytic matricoma: one from a 77-year-old man presented with a pigmented papule, 5 mm across, on the nose and the other from an 85-year-old female presented with an ulcerated dark-brown tumour, 12 mm across, on the right lower leg. We also review the literature.
Results: CASE 1: Microscopically, it was a nodular polypoid dermal proliferation of atypical basaloid cells, with prominent nucleoli. Some shadow cells were present. A conspicuous melanocytic proliferation was colonizing matrical areas. Mitosis: 18/10hpf(400x).
CASE 2: Histology showed a nodular dermal tumour, with prominent shadow cell formation. A conspicuous scattered proliferation of the melanocytes was also seen. Mitosis: 32/10hpf(400x).
Basaloid cells were cytokeratins+, p63+ and β-catenin+. Melanocytes were S-100+ and SOX-10+.

Conclusion: Melanocytic matricoma is a very rare entity with about 25 cases described in the literature. Its morphology can be confused with pilomatricoma, pilomatrical carcinoma with melanocytic hyperplasia or other malignant epithelial tumours. A prominent melanocytic proliferation and melanin in a tumour with cytological atypia and high mitotic count may lead to the erroneous diagnosis of malignant melanoma. Its distinction is important to ensure adequate treatment and follow-up.

PS-04-022

A 3-year retrospective study reviewing the spectrum of orofacial granulomatosis: granulomatous cheilitis and Melkersson-Rosenthal syndrome

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Background & objectives: Granulomatous cheilitis or Miescher cheilitis is a rare condition often related to hypersensitivity or atopy, characterized by protuberant swelling of one or both lips, and is sometimes associated with facial nerve palsy and fissured tongue, condition known as Melkersson-Rosenthal syndrome.
Methods: In this study we examined the clinical records of six patients presenting with granulomatous cheilitis which were examined in our Dermatopathology unit during a 3-year period (2016-2019). We thoroughly re-examined the slides, analysed the clinical data retrieved from the virtual database and correlated all the findings.
Results: Patients ranged from 28 to 60 years. Lower lip and upper lip were equally often involved, and males were slightly more frequently affected (66% males, compared to 33.3% females). One patient also presented with facial nerve palsy, consistent with Melkersson-Rosenthal syndrome. None of the patients had any previous history of Crohn disease. Upon histologic examination, all patients had non-necrotising granulomas, with mild dermal oedema and no sign of epidermal ulceration. If the histologic examination reveals non-necrotizing granulomas in the lamina propria, often protruding into and obstructing the vessels, then also Crohn disease, sarcoidosis or granulomatosis with polyangiitis should also be considered.
Conclusion: Granulomatous cheilitis is a rare entity. Taking into consideration the numerous reports of patients with orofacial granulomatosis and no gastrointestinal symptoms which were discovered with colonoscopic features consistent with Crohn disease, further check-up should be advised in such cases.

PS-04-023

Sentinel lymph node excision in malignant melanoma: 3-year experience from one dermatopathology unit

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Background & objectives: Sentinel lymph node (SLN) technique is used worldwide in patients with invasive breast carcinoma or malignant melanoma. It is recommended for patients with melanoma stage pT2 or pT3 and it could be considered in patients with pT1b or pT4 melanomas.
Methods: In this study we retrospectively analysed 84 patients which underwent SLN excision between 2017 and 2019, after being diagnosed with malignant melanoma. Each lymph node received in our pathology department was sectioned at 2-3 mm intervals and entirely submitted. All resulting paraffin embedded sections were examined at multiple levels in Hematoxylin-Eosin, Melan A and Tyrosinase.
Results: Out of 84 cases, 26.5% had lymph node metastases, and 12.05% had incidental capsular nevi. Positive SLN stemmed from pT2 cases (14.3%), pT3 (52.3%) and pT4 (33.3%). Most of them were axillary (54.5%), followed by inguinal (31.8%). Patients age ranged from 30 to 77 with both genders equally involved. Most cases featured one affected lymph node (75%), while 21.8% had two involved and only 3.2% had more than 2 affected.
Conclusion: This technique can provide important information which should be considered in the follow-up and treatment of patients. In our study size of the metastatic deposit ranged from 0.1 mm to 12 mm and only 4.7 % had extranodal extension. Statistical analysis showed that the number of lymph nodes involved, size of the metastatic deposits and the presence of extranodal extension strongly correlated with more advanced stage of disease (pT4) and presence of ulceration in the primary tumour.

PS-04-024

Nodulotumoral cutaneous involvement in adult T-cell leukaemia/lymphoma: report of two cases

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Background & objectives: Adult T cell leukaemia/lymphoma (ATLL) is a rare lymphoproliferative disorder, encountered in HTLV-1 carriers, which may be associated with cutaneous manifestations, ranging from patches, plaques, nodules to erythrodermia. Patients with the lymphoma-type variant of the disease have a worse prognosis.
Methods: We report two cases of ATLL, one in a 44-year-old male, known with systemic disease and HTLV-1 infection which developed cutaneous nodules, and one in a 66-year-old male, who presented with cutaneous manifestations, without any prior relevant medical history. Both patients had multiple red, tender nodules on the forearms and hands, which were clinically suspicious for cutaneous lymphoma.
Results: Both excision specimens revealed a diffuse intradermic lymphoid proliferation composed of medium-large cells, with marked epidermotropism and angiotropism. The lesions from the patient known with systemic disease also featured central ulceration. Immunohistochemistry revealed CD3, CD4 and CD5 positive cells, which were negative for CD8. Both lesions had a KI67 proliferative index of 50%. Unfortunately, both patients died within the next 4 to 6 months.
Conclusion: We report two cases of cutaneous manifestation in patients with lymphomatous and acute ATLL variants, respectively. The only difference between the two lesions was that the one originating from the patient with systemic disease also had central ulceration and the cells were immunoreactive for CD30. The patient with no prior medical history was positive upon subsequent HTLV-1 testing. Both cases had an aggressive clinical course, associated with nodulotumoral presentation of the disease.

PS-04-025

Dermatomyofibroma: a short series of a great mimicker

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Background & objectives: Dermatomyofibroma is a rare benign neoplasm, first described by Kamino et al. in 1992, histologically composed of spindle cells of fibroblastic/myofibroblastic origin. Patients are typically young females presenting with a plaque on the neck, shoulders and upper trunk.

Methods: In this study we examined the clinical records of five patients diagnosed with dermatomyofibroma in our Dermatopathology Department during a 3-year period. We thoroughly re-examined the slides and analysed the clinical data retrieved from the virtual database. Histologic examination reveals fascicles of spindle cells arranged parallel to the epidermis. Ancillary studies included S100, SMA and CD34.
Results: All patients were females in their thirties, with tender plaques located either on the upper trunk (60%) or proximal extremities (40%). Clinical diagnosis ranged from granuloma annulare (40%) to dermatofibroma (40%) and lymphoma (20%). Histologic examination revealed a diffuse spindle cell proliferation involving the reticular dermis. The neoplastic cells featured abundant eosinophilic cytoplasm and elongated nuclei. All cases featured faint SMA positivity, while S100 and CD34 were completely negative.
Conclusion: Dermatomyofibroma is a rare benign neoplasm, which should always be considered when evaluating a spindle cell proliferation from the upper trunk of young females. Due to inconsistency of immunohistochemical results, one should establish this diagnosis after excluding other benign mesenchymal proliferations, like leiomyoma or dermatofibroma Early lesions tend to show immunoreactivity for SMA, while older lesions are negative for SMA, S100 and CD34. This diagnosis should be kept in mind, even when SMA shows no or only weak positivity.

PS-04-026
Cutaneous involvement by diffuse large B-cell lymphoma: clinical-pathological correlation
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Background & objectives: Cutaneous involvement by diffuse large B cell lymphoma (DLBCL) is uncommon and may be primary or secondary to systemic spread. Skin biopsy leads to diagnosis. Our main objective is to describe clinico-pathological correlation between lesions and the skin infiltrate.
Methods: We report four cases of DLBCL whose initial manifestation was the appearance of distinct cutaneous lesions diagnosed through skin biopsy, describing clinical, histopathological and immunohistochemical findings.
Results: Case 1 - a man with multiple tumour lesions affecting the entire right lower limb; case 2 - a woman with tumoral and ulcerated lesions in the breast, simulating breast carcinoma; case 3 - a man with infiltrative and arciform lesions on the back, with a non-neoplasic appearance; case 4 - a woman with an ulcerated and necrotic lesion in the right leg. All cases were diagnosed as DLBCL through histopathological and immunohistochemical examination of skin biopsy.
Conclusion: Although uncommon, skin lesions can be the first and sole manifestation of DLBCL and may have multiple clinical presentations. We report four cases of cutaneous involvement by DLBCL and describe the clinical-pathological correlation.

PS-04-027
Making mountains out of molehills – a study of possible links between malignant melanoma genotypes and their Royal College of Pathologists dataset phenotypes
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Background & objectives: With the rise of molecular analysis in histopathology, malignant melanoma can be classified based on its genotype to allow for targeted therapy. This study aims to find a link between BRAF and NRAS mutations in malignant melanoma and histological phenotype.
Methods: Data was gathered from 337 cases of metastasizing malignant melanoma occurring between 2015 and 2018 that were tested for BRAF and NRAS mutations. The Royal College of Pathologists core data items were recorded from the primary skin lesions in each case. Data from BRAF positive, NRAS positive and wildtype cases was compared to assess patterns between mutation and histological phenotype.
Results: On comparing each genotype and histological phenotype, several trends have been noted. The most noteworthy of these were seen in the following dataset items: tumour subtype, tumour location and mitotic rate. These trends, as well as those of the remaining dataset items will be discussed further in this poster, as well as an assessment of the statistical significance of the data gathered.
Conclusion: The results generated from this study highlighted trends which could indicate that tumour phenotype can be predicted by genotype testing and vice versa. Future studies could also incorporate non-core data items from the dataset such as age, gender and prognosis.

PS-04-028
Evaluation of histopathologic prognostic variables in cutaneous melanoma in a black African cohort
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Background & objectives: The aim of this study was to evaluate the clinico-pathological prognostic variables in cutaneous melanoma cases in a black population, where it is believed to be rare and to run a more aggressive course compared to Caucasians.
Methods: This was a 20-year retrospective study (1997-2016) in a tertiary institution. Thirty-one H/E-stained tissue slides were reviewed. Microscopic features documented included histologic subtype, tumour thickness, level of invasion, ulceration, mitoses and vascular invasion. The relationship between these variables in addition to patient's age, gender and tumour site were assessed using Spearman rank correlation. Statistical significance was set at $p<0.05$.
Results: The median tumour thickness was 7.00mm (2.1-19.5mm). Twenty-five (80.6%) of tumours had pT4 stage and also had Clark level IV and V. Ulceration was present in 30 (96.8%) cases and 20 (64.5%) had evidence of vascular invasion. Thirteen (41.9%) of the patients had metastasis at presentation. There was significant positive correlation between tumour thickness and level of invasion ($r=0.7$, $p<0.001$), mitotic rate ($r=0.45$, $p=0.01$) and vascular invasion ($r=0.42$, $p=0.02$). Furthermore, level of invasion showed significant correlation with mitotic rate ($r=0.41$, $p=0.02$), and gender ($r=0.37$, $p=0.04$).
Conclusion: The findings of this study showed that cutaneous melanomas in our population are characterized by very poor prognostic histologic factors at presentation. Achieving early detection and treatment of this malignancy is advocated.

PS-04-029
WT1: a useful immunomarker for the diagnosis of dermatofibrosarcoma protuberans
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Background & objectives: The most common malignant soft tissue tumours of the dermis/subcutis is dermatofibrosarcoma protuberans. The aim of the present study was to investigate the immunohistochemical expression of WT1 in primary and recurrent dermatofibrosarcoma protuberans and in its main morphological mimickers.
Methods: The cases were retrieved from Anatomic Pathology of the University of Catania and Santa Chiara Hospital of Trento. The following tumours were collected: 57 cases of dermatofibrosarcoma protuberans; 15

cases of dermatofibroma; 8 cases of dermal scars; 5 cases of deep-seated fibrous histiocytoma. The antibody against the N- terminal portion of WT1-6F-H2, was used.
Results: The majority of dermatofibrosarcomas protuberans (54 out of 57), exhibited cytoplasmic staining for WT1. The immunohistochemical expression was diffuse, heterogeneous or focal, respectively, in 75%, 15% and 6% of cases. With the exception of 4 cases showing a weak to moderate staining in different areas of the same tumour, the staining intensity was diffuse and strong. All recurrent tumours showed diffuse and strong WT1 cytoplasmic immunoreactivity while the fibroblasts of the associated scar tissue were negative. None of the other tumour or tumour-like, bland-looking spindle cell lesions examined, were WT1-positive.
Conclusion: WT1 is an ancillary immunomarker, exploitable in combination with CD34, in confirming the diagnosis of dermatofibrosarcoma protuberans, including in the recurrent tumours.

PS-04-030
The relationship between BRAF mutation status and certain clinical and pathological features in melanoma
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Background & objectives: BRAF mutation in melanoma predicts response to BRAF and MEK inhibitor therapy. This study investigated the relationship between clinicopathological characteristics of primary and metastatic melanomas with BRAF mutation status, in cases sent for testing in the period 2012-2016.
Methods: A total of 519 samples were identified. Patient age, gender and melanoma reporting dataset items were gathered from the histology report. Each variable was analysed against BRAF mutation status.
Results: 58% of patients were male and 42% were female with similar mutation rates for both (37% and 38% respectively). 40% of the samples were primary tumours, 57% were metastases and 3% were recurrences. 74% of mutations were v600E and there was no significant difference in type of mutation between primary and metastatic tumours. BRAF mutations were more common in metastases than primary tumours (41% and 33% respectively). BRAF mutation was significantly associated with superficial spreading and nodular histological subtypes; younger age; and location of metastasis. High rates of BRAF mutation were seen in brain metastases (78% positive). BRAF mutation was not associated with mitotic count, Breslow thickness, or ulceration.
Conclusion: BRAF mutation in our cohort is more common in younger patients and in metastatic tumours, in keeping with the published literature. We found high rates of mutation in metastasis to the brain, the reasons for which are unclear.
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PS-04-032
A case series of granular cell tumour with malignant potential; a rare cutaneous tumour
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Background & objectives: Granular cell tumour (GCT), is an uncommon soft tissue neoplasm of neural in origin. These tumours are usually slow growing and benign. The malignant counterpart is extremely rare in the skin with a potential to metastasize.
Methods: Histologically, this can be diagnosed using the Fanburg-Smith criteria. We report a series of 3 cases with a histological diagnosis of granular cell tumour with malignant potential and evaluate the clinical presentation, investigations and progress.
Results: Case1-7 year-old boy presents a growing lump on his right shoulder. Histology revealed an incompletely excised GCT with atypia. Wider excision was consistent with a malignant GCT. Case2- 67 year-old female with firm nodule on her abdomen. Excised lesion revealed an atypical GCT. Consensus was to manage as a potentially malignant GCT. Case3-72 year-old man presents with a rapidly growing nodule on his right eyebrow. Excision biopsy favoured malignant GCT.
Conclusion: Clinical diagnosis of GCTs are difficult and should be included in the differential diagnoses of head and neck cutaneous lesions. Clinicians should be aware that atypical and malignant variants exist. There is some degree of pathological debate regarding classification of these lesions, especially in borderline atypical/malignant cases. There is a lack of consensus regarding the optimal management of this tumour but in our experience, we recommend a wide local excision for all GCTs and discussion at the multi-disciplinary team level.

PS-04-033
Ultraviolet impact on rat skin
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Background & objectives: The aim of our study was to establish a >model imitating of UV-B (wavelength peak is 311 nm) therapy for rat's skin and to find match macroscopical and following histological skin changes including melanocytes spreading and melanin distribution.
Methods: We used 6 laboratory rats with white and 12 with black coating applying UV-B light source (9 W power) during minimal erythema dose. The changes were studied by macroscopical and histological methods.
Results: In 3 of 18 of observations transitional symptoms looking alike, actinic keratosis occurred (1 black, 2 white rats). Other passing side effects (exfoliation, erythema) occurred and were successfully removed with exposure correction. Typical histological changes (chronic inflammation, hyperkeratosis, epidermal cells dystrophy) are more noticeable in rats with side effects, but still present in the rest of rats. Expected changes of melanocytes and melanin distribution could not be displayed with routine histological staining.
Conclusion: UV-B therapy model is a valid method to investigate it itself or to investigate chronic UV-exposure effects. The typical histological effects following UV-B exposure and their depending on macroscopical changes were found.

PS-04-036
Prognostic value of tumour-infiltrating lymphocytes and mitotic rate in melanoma
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Background & objectives: The use of immunohistochemistry to assess the number of CD3 and CD8 lymphocytes and an objective assessment of mitotic index, using computer-assisted image analysis allows for a more accurate assessment of the values of these parameters.
Methods: Our study included primary tissues from 88 non-consecutive cutaneous melanoma patient who were retrospectively examined at Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice in 2005-2008 years. We used to determine the mitotic index Phosphohistone H3, Rabbit Polyclonal Antibody (PHH3) and to determine TILs :Polyclonal Rabbit Anti-Human CD3 and Monoclonal Mouse Anti-Human CD8.
Results: Statistically significant differences were found in the number of CD8 lymphocytes depending on the depth of the infiltrate ($p < 0.01$), in the number of lymphocytes depending on the stage ($p < 0.05$). Differences in lymphocyte counts between T1 and T3 ($p < 0.05$) and T1 and T4 (p

<0.05) were demonstrated. Analysing the number of abnormal mitoses depending on the stage, differences between T1 and T3 (p <0.05) were found, similarly between T1 and T4, as well as T2 and T4. Statistical differences were found for the number of mitoses depending on the state of the lymph nodes (p <0.05).
Conclusion: Identifying CD3 and CD8 instead of together as TIL allows a better understanding of the significance of these factors as elements of good prognosis, and the use of PHH3 allows a reliable assessment of the mitotic index as a factor of poor prognosis. The use of computer image analysis for routine diagnostics would improve the reliability of the assessment and the associated significance of prognostic factors.

PS-04-037
Persistent late reactions in decorative tattoos: a series of eight cases with immunohistochemical study
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Background & objectives: Persistent late reactions (PLR) in decorative tattoos are difficult to treat and their nature is not completely understood. They show different, poorly characterized histopathological patterns.
Methods: Eight cases of PLR in decorative tattoos have been retrieved form he files of the Department of Pathology, University Hospital of Santiago de Compostela (Spain). Clinical and histopathological features have been reviewed and immunohistochemical study performed in all cases.
Results: Seven women and one man, 21 to 39 years, presented PLR in decorative tattoos. Seven cases were related with red colour and one with black. Lesions started from two weeks until 2 years after performing the tattoo and were refractory to topical treatments.
Biopsies showed dermal lymphoid infiltrate, reaching the reticular dermis. Moderate to severe interface lesion was present in all but one case, the only one with well-formed granulomas. Five cases showed interstitial inflammatory infiltrate, mimicking granuloma annulare, but extensive collagen degeneration was present in only two cases.
Immunohistochemistry demonstrated a clear predominance of T lymphocytes, balanced for CD4 and CD8. CD8 lymphocytes were predominant in the interface lesion.
Conclusion: Decorative-tattoos- related PLR are characterized by a combination of inflammatory patterns, interface dermatitis with CD8 lymphocytes being the most common. Grannuloma annulare.-like lesions are also common, but collagen degeneration is usually limited. Well-formed granulomas are not a usual feature.
- Liver

PS-05 Digestive Diseases Pathology - Liver

PS-05-001
Morphofunctional and histochemical changes in liver tissue with predominant copper (Cu-10%) content in the experiment
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Background & objectives: Liver is a barrier to toxic substance and is primarily affected by pathogenic effect. Xenobiotics are metabolized exactly in this organ.
Evaluation of morphofunctional and histochemical changes in liver tissue at the exposure of polymetallic copper (Cu-10%) content dust.
Methods: The experiment included outbred white male rats weighing 120-170 g for 30 days. The dust was injected once intratracheally (50 mg/1.0 ml of physiological saline). Method of cytophotometry was used for quantitative characterization of the enzymes activity in liver cells. All manipulations, including elimination, were carried out by «Rules for biomedical experiments conducting» of MH RK (12.11.2009 №697).
Results: A histochemical study determined a sudden decrease of hepatocyte glycogen level. Glycogen was absent in cells containing altered nuclei. The activity of the enzymes was reduced – up to a complete absence. The activity enzymes showed the expressed decrease in comparison with control group: acid phosphatase by 54.5% (P<0.001), succinate dehydrogenase by 46.79% (P<0.001), lactate dehydrogenase by 56.96% (P<0.001), glucose-6-phosphate dehydrogenase by 36.48% (P <0.05), glycogen by 46.31% (P<0.001).
Conclusion: The liver cells are the first target of non-synthesized toxins Dust exposure intensified the trophic-circulatory disorders and exacerbated the alterative-dystrophic and inflammatory changes in the organ. The free lipids level increased in the cytoplasm of both liver cells and stellate reticuloendotheliocytes, which indicates increased destructive changes in cytoplasmic membranes and membrane complexes. Simultaneously, glycogen utilization in liver hepatocytes is enhanced, that led to inhibition of enzymes synthesis.

PS-05-002
Potential role of neutrophil extracellular traps in non-alcoholic steatohepatitis
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Background & objectives: Recent experimental evidence suggests that there are elevated levels of neutrophil extracellular traps (NETs) in sera of patients with NASH. We investigated the presence of NETs in liver biopsy specimens with NASH and potential correlations with inflammation and fibrosis.
Methods: This retrospective study included 40 liver biopsy specimens from 21 patients with NASH. Fourteen patients underwent sequential liver biopsies according to clinical indications. We assessed the presence of NETs by double immunofluorescence using the markers neutrophil elastase (NE) and citrullinated histone 3 (citH3). Immunofluorescence signals and colocalization of these markers were visualized with a confocal microscope.
Results: NETs were detected in 60% of the biopsy specimens, as extracellular colocalization of NE with citH3. In 54% of the NET-positive biopsies significant production of NETs was apparent, in an aggregated pattern, within areas of portal and lobular inflammation. In contrast, 46% of the biopsies showed small numbers of NETs, despite the presence of inflammation and/or fibrosis. In most cases of mild inflammation or established cirrhosis NETs were absent.
Conclusion: Our findings suggest that neutrophils are involved in the pathogenesis of NASH through NET release. Further research will be needed to clarify whether production of NETs is involved in the progression of NASH to cirrhosis or the development of hepatocellular carcinoma as suggested by recent experimental studies.
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PS-05-003
Histopathological features of inflammatory pseudotumours of the liver on resection specimens
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Background & objectives: Inflammatory pseudotumours of the liver are nonneoplastic masses that cause clinical confusion due to their capacity to

mimic malignancy. The aim of this study was to identify the histopathological features of these lesions and their clinical correlates.
Methods: We have reviewed the slides of 15 hepatic inflammatory pseudotumours resected between 2013-2018. The localization, presence of a pseudocapsule, the type and distribution of inflammatory cells, the presence of bile ductules/ducts within the lesion and of perilesional occluded large vessels and the degree of fibroblastic proliferation and fibrosis were noted. These were analysed in conjunction with clinical and imaging data.
Results: The mean age was 63 years and there was a slightly male predominance among patients. The relevant clinical associations were chronic cholecystitis, HBV infection, obesity, type 2 diabetes mellitus and malignancy. The masses had an average maximum diameter of 5 cm. The most common histological features were lack of a pseudocapsule, presence of foamy cells, variable inflammatory cells and necrosis, in both perihilar and peripheral localization. Two cases were entirely composed of lobules of foamy cells with no atypia. One case lacked foamy cells and necrosis, but showed no association with IgG4-related disease and no periductal growth. No relapse was noted, although three cases were complicated by postoperative abscesses.
Conclusion: Inflammatory pseudotumours of the liver have similar clinical correlates to other infectious/inflammatory lesions. Their pathological spectrum may be related to various aetiologies or inflammatory responses among individuals. Further studies are needed to clarify the pathogenesis and to classify these lesions.

PS-05-005
Paediatric and adult non-alcoholic fatty liver disease (NAFLD) pathogenia: lymphocyte populations characterisation in the liver microenvironment
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Background & objectives: The immune system is one of the main drivers of NAFLD pathogenesis. The role of each liver lymphocyte population of the infiltrate in the pathogenesis is uncertain. Aim: to characterize liver infiltrate in relation to histological damage in NAFLD patients.
Methods: Twenty-six paediatric [11.5 yrs (4-17)] and 34 adult NAFLD patients [50 yrs (28-72)] were enrolled. On liver biopsies histological changes as well as T helpers Lymphocyte (Th), Cytotoxic T Lymphocytes (CTL), Regulatory T lymphocytes (Treg) and Th17 localization and frequency were evaluated by immunohistochemistry. Statistical analysis were performed to assess the relation between the immune response and the observed damage.
Results: Portal-periportal-CTL and -Th frequencies were similar in paediatric and adult NAFLD cases. Th17 seemed to be nearly exclusive of this location. In children Treg and Th17 counts were comparable, but in adults Tregs were higher than Th17 cells. In intralobular area CTL>Th>Treg predominance was observed both age group. Comparison between them demonstrated higher portal-periportal-Treg ($p<0.006$), intralobullar-CTL, -Th and -Treg counts ($p=0.025$, $p=0.0004$ and $p=0.013$) and lower Th17/Treg ratio ($p=0.041$) in adults.
In children higher intralobular-Treg were associated with inflammation severity ($p=0.026$), while in adults more severe inflammation stages showed lower Treg and higher Th17 counts. Paediatric and adult cases with fibrosis ≥ 2 displayed portal-periportal lower Treg and higher Th17.
Conclusion: The composition of the inflammatory liver infiltrate differ between paediatric and adult NAFLD, but the interplay between Treg and Th17 seems to condition the progression of the damage in both groups.

PS-05-006
Digital histopathological characterisation of b cell subsets in early and advanced biliary atresia
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Background & objectives: Biliary atresia (BA) is a neonatal cholangiopathy of various potential aetiologies. The role of B lymphocytes in the pathogenesis of BA has been hypothesised through murine models. We aimed to characterise B cell subsets in BA using triple immunohistochemistry.
Methods: CD20, CD24 and CD38 immunohistochemistry was carried out on three samples (hilum and peripheral liver (wedge) samples at time of Kasai hepatoportoenterostomy and an explant sample) for each patient (n=28). The slides were scanned to allow digital appraisal. Semi-quantitative analysis of inflammatory cells and fibrosis was performed. Phenotypic groups were formed using inflammatory cell frequencies and correlated with clinical outcome.
Results: Three B cell subsets were identified in the wedge samples at Kasai and the explant samples. CD20+CD24+CD38-cells were present in both sample types in all 28 patients. CD20+CD24-CD38+cells were present in 1 of 28 wedge samples and 3 of 28 explant samples. CD20+CD24+CD38+cells were identified in 4 of 28 explant samples. Patient stratification based on inflammation at the hilum did not predict transplant-free survival. CD20+CD24+CD38-cell frequency correlated with fibrosis scores.
Conclusion: The histopathological analysis of three distinct tissue regions using triple immunohistochemistry in this study is a novel method in studying the evolution of the disease from the extrahepatic (hilum) to intrahepatic biliary system. This work is the first to report distinct B cell subsets in BA and hypothesises the possible role of CD20+CD24+CD38-B cells in biliary damage. This opens the scope for their potential use as therapeutic targets to halt the progression of this highly morbid disease.

PS-05-007
Mesenchymal hamartoma of the liver - diagnostic difficulties
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Background & objectives: Mesenchymal hamartoma of the liver (MHL) is a rare paediatric lesion, usually multicystic, slowly growing, and accompanied by slight elevation of serum alpha-fetoprotein. Diagnosis of MHL depends on its radiological and clinical presentation, while histopathology shows wide spectrum of changes.
Methods: Eight children with mesenchymal hamartoma diagnosed radiologically or histologically, operated in one paediatric surgery centre during last 10 years are presented. The clinical data analysis and detailed pathological examination with wide panel immunophenotyping covering epithelial and stromal components was performed.
Results: There were two girls and six boys in the age ranged 4 – 19 months. All tumours presented with abdominal enlargement, AFP elevation from 80 up to 10000. Radiologically five lesions were problematic, showing some indefinite features of vascular lesion(2), hepatoblastoma(2) or inborn defect(1). Two tumours were mainly solid, while the rest were multicystic. Three cases primarily underwent needle biopsy, with erroneous hepatoblastoma diagnosis in one boy and inconclusive answer in the second child. The final histological diagnosis of MHL was based on morphology and immunophenotyping. Two cases diagnosed radiologically as mixed hamartomatous lesion, were cavernous haemangioma with defect in portal veins and bile duct proliferation.

Conclusion: Mesenchymal hamartoma of the liver can cause diagnostic and therapeutic problems, mainly due to its rarity and different presentation in pathological and clinical aspects. Core needle biopsies in MHL may not be informative to establish the final diagnosis. Some rare vascular hepatic lesions enter the differential diagnostic field of MHL.
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PS-05-008

Primary biliary cholangitis: histological criteria to predict UDCA therapy response - a case series

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Background & objectives: Primary biliary cholangitis (PBC) is a prevalent hepatic chronic cholestatic autoimmune disease characterized by chronic non-suppurative cholangitis affecting small to medium sized interlobular bile ducts. Its progression to cirrhosis and liver failure is associated with the response to UDCA therapy.
Methods: Determine if there is a statistical association between any histological feature included in either the Ludwig stage, the Scheuer stage and the recently proposed FBI score and the response to UDCA treatment in our series of patients with PBC. All the biopsies were obtained before starting UDCA treatment.
Results: 57 patients were studied with 39 cases percutaneous liver biopsies collected retrospectively from the files of our Institution. The histological evaluation according the FBI system showed a bile duct ratio (BDR) index of 0.9 with only one case presenting ductopenia. Respect lobular interphase hepatitis (LIH), five cases showed no LIH, 21 cases showed mild to moderate LIH and three cases showed severe LIH. Regarding fibrosis, 37 patients were in early stages (0-1), and only one biopsy showed histological criteria of cirrhosis. Statistical analysis showed non-statistical association between any histological criteria nor stage and the absence of response to UDCA therapy. However, we detected a trend between UDCA-therapy response and LIH.
Conclusion: The classical scores for staging PBC do not include histological features such as LIH, which might be useful to detect those potential patients whom may benefit from a combined or alternative therapy.

PS-05-009

Identification of differential immune circuits in preneoplastic and neoplastic stages of hepatocellular carcinoma using murine (ABCB4-/-) and human tissues

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Background & objectives: While HCC is a potential candidate for immunotherapy, immune circuits that drive the inflammatory-to-tumour milieu remain to be explored. In this study, we have characterized immune landscape in preneoplastic and neoplastic microenvironment of HCC using murine and human HCC tissues.
Methods: In-vivo murine model of HCC was generated using 3-5 days old Mdr2(Abcb4)-/- mice with intraperitoneal-injection of DEN followed by administration of 0.05%phenobarbital. Moreover, a total of 42 patients diagnosed with HCC and undergoing biopsy/resection were recruited in the study. Mice without carcinogenic-regime and liver from transplant donors were included as controls. Tissues were subsequently analysed using immunohistochemistry, flowcytometry and PCR.
Results: Mdr2-/- mice receiving DEN-and-PB exhibited a significantly different pathology with high proliferative index, increased lymphocyte infiltration, increased neoplastic progression, and increased fibrosis. Microscopically, tumour phenotype ranged from pseudo-tubular to trabecular-type morphology. Importantly, alternatively-activated-macrophages (M2) were heavily infiltrated in in the intra-tumoral compartment as early as 6 weeks. Liver from these mice were heavily infiltrated by the recently identified immune cells ILC1 and ILC2. Moreover, mRNA transcripts of MMP12, MMP13, MMP9, TIMP1, TGF , IL1, IL6, iNOS, CD68 and YM1 were differentially expressed in murine tissues. In human HCC-tissues, there was increased infiltration of macrophages, neutrophils and B-cells, while infiltration of T-cells (CD4+ and CD8+) was not different compared to the controls.
Conclusion: We report detailed analyses of preneoplastic and neoplastic microenvironment of HCC in murine as well as human tissues. These differentially regulated cells may represent novel targets for HCC immunotherapy.

PS-05-010

Differential morphologic characteristics between autoimmune hepatitis (AIH) and drug induced liver diease (DILI)

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Background & objectives: Distinguishing DILI from AIH can be a challenge. There aren´t pathognomonic features of AIH. We reviewed a series of cases to find the more useful morphological features to differentiate DILI and HAI and selected and standardized them in a score.
Methods: We selected a series of 32 patients with clinically well-characterized AIH and DILI (14 DILI and 18 AIH). CIOMS-RUCAM and evolution parameters (including steroids responsiveness) were used to discriminate the patients in the two groups.
Retrospective observational cohorts study was performed assessing 31 histologic variables and comparing them between the two groups. Chi Square and non-parametric tests were applied.
Results: Following histological evaluation of 31 variables, we performed a comparative analysis and only five variables showed statistically significant differences between the DILI and AIH biopsies ($p<0,05$). AIH more frequently presented portal plasma cells and intra-acinar plasma cells inflammation; meanwhile DILI presented more frequently canalicular and/or hepatocellular cholestasis, portal neutrophilic inflammation and intra-acinar neutrophils.
A model combining the five variables with detailed histological evaluation in four grades and a standardized score predicted the diagnosis of most of the cases (AUC 0,913) with high specificity and sensibility
Conclusion: There are some overlap of most histologic findings between AIH and DILI, five variables showed differences: Portal plasma cells, intra-acinar plasma cells, portal neutrophilic inflammation, intra-acinar neutrophilic inflammation and canalicular and hepatocellular cholestasis. We were able to develop a score that could simplify histological evaluation and with clinical data allow the differential diagnosis. To validate our results we are performing a second analysis in a blinded manner by 4 pathologist.

PS-05-011

Role of set protein in hepatocellular carcinoma: an immunohistochemical study

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Background & objectives: HCC targeting therapy still remains unsatisfactory. SET protein is a potent inhibitor of protein phosphatase 2A (PP2A) through its interaction with PP2A-regulated oncogenic pathways. We investigated the oncogenic role of SET in HCC tumorigenesis and clinical aggressiveness in Egyptian patients.
Methods: This study was carried out on 100 HCC Egyptian patients. For each case, paired representative samples were collected from the tumour

tissue and the adjacent non-tumorous liver tissue of the same surgical specimens and analysed for the immunohistochemical expression of SET. Correlation between SET expression levels in HCC and the available clinicopathological parameters and overall survival was done.
Results: SET protein showed significantly higher expression levels in HCC than in the adjacent non- tumorous liver tissue (P<0.0001). 54% of HCC cases exhibited overexpression of SET protein that correlated significantly with large tumour size (P=0.012), lymphovascular invasion (p-value=0.028) and shorter overall survival (P<0.001).
Conclusion: These findings suggested the oncogenic role of SET protein and the adverse prognostic outcome of SET protein overexpression in HCC and the potential to be used as a new prognostic tool and a therapeutic target.

PS-05-012
A clinico-pathological audit of the effect of medical liver biopsies on patient management
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Background & objectives: Medical liver biopsies are used to investigate patients with hepatic dysfunction and diffuse disease on imaging, when non-invasive methods yield insufficient information. We aimed to evaluate our medical liver pathology practice and its influence on patient management, using national standards.
Methods: The UK's Royal College of Pathologists (RCPath) produces "Tissue pathway" guidelines promoting good practice in specimen handling and reporting. We used RCPath audit proformas to collect data on specimen quality/reporting and clinico-pathological effect. The QEUH pathology database was searched for liver specimens in 2019. Reports were retrieved for review (by SS, academic trainee), alongside clinical information from electronic patient records.
Results: After excluding resections, targeted biopsies and referral cases, we identified 135 medical liver biopsies reported in 2019 between three consultant histopathologists (GK,PK,KO). Sixty consecutive cases were included for audit. 51/60 (85%) biopsies met RCPath criteria for adequacy (length>15mm or ≥6 portal tracts); three (5%) samples were inadequate and six reports (10%) lacked enough information to evaluate. Most reports (56/60;93%) were judged to have helped patient management. The clinical diagnosis changed in 23/60 (38%); the different diagnosis was previously unanticipated in nine (39%). Patient management altered in 48/60 (80%); in most of these (33/48; 69%), the decision would not have been possible without the pathology report.
Conclusion: This audit highlights the clinical value of medical liver biopsy in diagnostic work-up and follow-up of patients with liver disease. These results will help optimise the content of our reports and wider clinico-pathological communications.

PS-05-014
Diagnostic utility of von Hippel-Lindau tumour suppressor gene product in intrahepatic/extrahepatic bile duct and gallbladder adenocarcinomas
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Background & objectives: Von Hippel-Lindau tumour suppressor gene protein's (pVHL) loss of expression has been observed in many tumours. Our aim is to assess pVHL expression in intrahepatic cholangiocarcinoma (ICC), pancreatic ductal adenocarcinoma (PDAC), bile duct adenocarcinoma (BDAC) and gallbladder adenocarcinoma (GBAC).
Methods: We examined the immunohistochemical expression of pVHL in ICCs (n=10), PDACs (n=5), GBACs (n=10) and bile duct adenocarcinomas (BDACs) (n=5) in biopsies and surgical resection specimens. A cytoplasmic and membranous staining was treated as positive if at least 5% of the tumour cells exhibited immunoreactivity. Positive staining was further graded as 1+(5%-25% of the tumour cells), 2+(26%-50%), 3+ (51%-75%) or 4+(>75%).
Results: All cases of ICCs were diffusely and strongly positive (membranous and cytoplasmic staining 3+ or 4+). One out of five cases of PDACs was focally positive (1+) whereas the remaining were negative. Two out of five cases of BDACs were negative, one showed 3+ and two 2+ positivity. Four out of ten cases of GBACs were negative, two showed 4+, two 3+ and two 2+ positivity. Non-neoplastic epithelium served as positive internal control. Our results for ICCs and PDACs are in accordance with published data, but positive percentages in BDACs /GBACs are higher than those in the literature. We observed reduced positivity in less differentiated areas especially the tumour front.
Conclusion: pVHL immunohistochemistry can be used as a diagnostic tool in differentiating ICC from PDAC but isn't so helpful in distinguishing ICC from GBAC or extrahepatic bile duct adenocarcinoma. Its prognostic and diagnostic role needs further investigation.

PS-05-015
Liver biopsy in non-neoplastic paediatric liver diseases: 10 year experience at National Liver Institute, Menoufia University, Egypt
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Background & objectives: Liver biopsy despite being invasive technique is considered fundamental in diagnosis and management of paediatric liver diseases. The aim of this study was to assess the role of liver biopsy in diagnosis of non-neoplastic paediatric liver diseases.
Methods: Pathological reports of paediatric patients with non neoplastic liver diseases collected from January 2010 through January 2019 and sorted according to the diagnosis. Pathological diagnoses were sorted into five groups; cholestasis (extrahepatic biliary outflow obstruction and intrahepatic cholestasis), inflammatory (chronic hepatitis and granulomatous inflammation) , metabolic/storage diseases , cirrhotic and finally others that include the remaining entities.
Results: A total 2157 histopathological studies were found; 52.2% were boys, and 47.8% were girls. The major age group was young infants which biopsied mainly for cholestasis (37.5%). Other categories diagnosed included inflammatory group (29%), group with metabolic/ storage diseases (10.6%), group with cirrhosis (5.5%) and the remaining percentages were for other entities (17.4%). Biliary outflow obstruction and intrahepatic cholestasis were the most common diagnoses in young infants while chronic hepatitis was the main diagnosis of elderly children.
Conclusion: Liver biopsy is a main integral component in setting the initial diagnosis of many non-neoplastic paediatric liver diseases. Biliary outflow obstruction, intrahepatic cholestasis, chronic hepatitis and metabolic/ storage diseases are the most common diagnosed diseases.

PS-05-016
The influence of the chronic alcohol intoxication on the morpho-functional status of the liver of rats at the age of 6 months
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Background & objectives: The circadian rhythmicity of biological processes is one of the important properties of the mammalian organism. The

aim of this work was to study the effect of chronic alcohol intoxication on the circadian rhythmicity of some micromorphometric liver parameters.
Methods: The 72 6-month-old male Wistar rats, divided into 2 groups, were kept under fixed light conditions for three weeks, the experimental group received ad libitum a 15% ethanol instead of drinking water. Animals were sacrificed at 9, 15, 21 and 3 hours. Micromorphometric liver parameters were measured. The amplitude-phase characteristics of circadian rhythms were investigated using cosinor-analysis.
Results: In the control, circadian rhythms were found for every parameter. Acrophases for the rhythms of nuclear area, cell area, and nuclear-cytoplasmatic ratio (NCR) were noted at 12.16, 10.22, 13.56 hours, amplitudes were 38.47 μm2, 99.23 μm2 and 0.030, respectively. In the experiment, only the nuclear area rhythm was detected - acrophase at 5.18 hours and an amplitude of 12.72 μm2.
The study testifies that chronic intoxication with ethanol leads to significant violations in the organization and synchronization of CR of the studied morphometric parameters, reflecting the morphological and functional state of the liver of male Wistar rats.
Conclusion: The destruction of the CR of cell area and NCR, as well as change in the amplitude-phase rhythm's characteristics of the nuclear area is evidence of desynchronosis, which is an important link in the pathogenesis of a many of diseases.

PS-05-017
The influence of modification circadian rhythms during the chronic alcohol intoxication
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Background & objectives: The increased consumption of alcohol is a serious problem in modern society. The goal of this study is to find out the effect of circadian rhythms on alcohol intoxication in 72 six-month old male rats.
Methods: The first group was kept at a fixed light mode, light-dark 14:10 and the second in conditions of constant light-light for 3 weeks. The animals were fed with a 15% ethanol solution ad libitum. Animals were removed from the experiment at 9am, 3pm, 9pm and 3am. The material was examined histologically, histochemically and through an electron microscope.
Results: In liver samples, small and large droplet fatty degeneration of hepatocytes, expansion and cellular infiltration of portal tracts, focal necrosis in the liver lobules were seen. The increase in alcohol consumption for the able-bodied population operating in continuous cyclic enterprises is a particular danger, since under these conditions, the rhythmic disturbances in biological processes caused by levelling of the time of day can be aggravated by the use of ethanol.
Conclusion: Changes in the CR, through the introduction of continuous lighting, when modelling chronic alcohol intoxication are accompanied by an increase in the concentration of ethanol in the blood and liver parenchyma and an increase in its toxic effect.

PS-05-018
Lymphocytic apoptosis among the criteria of the histological diagnosis of autoimmune hepatitis in acute-on-chronic patients: the experience of a tertiary referral Italian centre
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Background & objectives: Liver biopsy represents the diagnostic gold standard in autoimmune hepatitis (AIH), but histological diagnostic criteria lack consensus and reproducibility.
Aims: (i) to redefine the histopathological criteria for AIH; (ii) to validate portal apoptosis as a histopathological criteria for AIH diagnosis.
Methods: We retrospectively evaluated 65 biopsies from AIH patients at their first access to our Center. Forty-five (69.2%) had a previous diagnosis of AIH (follow-up patients, FUP), for 20 (30.8%) the AIH diagnosis was made at the moment of the present biopsy (first-diagnosis patients, FDP).
Fourteen histopathological variables were collected, including the count of lymphocytic apoptosis within the portal tracts.
Results: As expected, all variables of active hepatitis were higher in the 20 FDP compared to the 45 FUP ($p<0.05$), while fibrosis Ishak's stage was >2 in 11 (55.0%) FDP and 8 (17.8%) FUP ($p=0.005$).
Mean number of apoptotic bodies in portal tracts was 5.00±4.45 and 9.45 ±6.95 in FUP and FDP respectively ($p=0.002$). Moreover, apoptosis count positively correlated with fibrosis and almost all variable of inflammatory activity.
Conclusion: Most FDP showed an acute-on-chronic histology, highlighting the key role of early diagnosis in AIH patients to prevent fibrosis progression. Moreover, the count of the lymphocytic apoptotic bodies within the portal tracts might reinforce the pathological criteria for AIH diagnosis.

PS-05-019
The role of c-Met signalling pathway in hepatocarcinogenesis and its involvement in Sorafenib resistance
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Background & objectives: Development of resistance to conventional therapies in Hepatocellular carcinoma (HCC) is an important problem. This study aims to explore the role of c-Met signalling in the acquisition of aggressive phenotypes in HCC.
Methods: HCC cell lines and HCC cases were analysed using immunohistochemistry, Western Blot, motility and invasion assays for c-Met expression. In-vitro mechanistic studies using overexpression and silencing vectors for the demonstration of for c-Met activation were made. Specific c-Met inhibitors were used for the reversal of sorafenib resistance in HCC cells.
Results: Immunohistochemical analyses of HCC cell lines and HCC cases, showed that immunoreactivity of phospho-Met and c-Met are increased in HCC compared to normal and cirrhotic tissues. Our Western Blot, motility and invasion assays showed higher c-Met expression in poorly-differentiated, highly motile and invasive HCC cell lines than well-differentiated ones. Our further in-vitro mechanistic studies using overexpression and silencing vectors revealed that c-Met activation was occurred mostly independent of HGF in HCC cells, including receptor cross-talk, non-coding RNAs and environmental factors. We demonstrated that miR-181a-5p regulates c-Met signalling in HCC and played a role in the acquisition of sorafenib resistance. We reversed sorafenib resistance in HCC cells using c-Met specific inhibitors.
Conclusion: Our results provide mechanistic insight into c-Met signalling in HCC and sorafenib resistance. These findings suggest that c-Met might be used as a predictive biomarker to guide patient selection for clinical trials of Met-related therapies.

PS-06 Haematopathology

PS-06-001
Determination of mean HbA2 levels on high performance liquid chromatography (HPLC) in known beta thalassaemia trait individuals
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Background & objectives: Beta thalassaemia is one of the most common inherited haemoglobin disorders. The present study was conducted

to determine mean HbA2 levels of known β thalassaemia trait individuals on HPLC in South East Asian population, taking cellulose acetate electrophoresis as gold standard.
Methods: A descriptive cross sectional study was conducted from Dec 2018 to Dec 2019. A total of 495 patients who were diagnosed as β thalassaemia trait on cellulose acetate haemoglobin electrophoresis were included in the study. The blood samples were run on High Performance Liquid Chromatography (HPLC) and HbA2 levels were recorded on the proforma.
Results: Mean and standard deviation were calculated for HbA2, MCV and MCH. Frequency and percentage were calculated for gender. Effect modifiers like age and gender were controlled by stratification and post stratification independent sample t test was applied. Mean HbA2 levels of β thalassaemia trait individuals on HPLC was 5.63%. This percentage was higher than the mean value of HbA2 on Cellulose Acetate Electrophoresis, which is generally taken as >3.5%. There was no effect of age (p=0.07) and gender (p=0.14) on mean HbA2.
Conclusion: Measurement of HbA2 level on HPLC is a reliable way of detection of β thalassaemia trait individuals. However, a higher threshold of HbA2 is needed to label an individual as Beta Thalassaemia trait in South East Asian population.

PS-06-002
Histopathologic diagnosis of lymph node biopsies in paediatric population: a 5 year descriptive study in a tertiary hospital
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Background & objectives: Lymphadenoapathy is a relevant clinical problem in children and biopsies are usually needed to determine if the cause is neoplastic or non-neoplastic. The aim of this study was to determine the histopathological spectrum of lymphadenectomies undertaken in our hospital.
Methods: An amount of 580 lymph node biopsies of 196 patients were carried out in our hospital from 2015 to 2019 in children from 0 to 18 years old. We reviewed the histological diagnoses in our database for each patient.
Results: Normal lymph node (33%) and reactive lymphoid hyperplasia (29%) were more common. Lymphomas were 14 %, most of them Hodgkin lymphomas. Metastatic lesions make up 8 % which included neuroblastoma, papillary thyroid carcinoma and melanoma metastases. Necrotizing tuberculous granulomatous lymphadenitis was the most common diagnose among infectious pathology (9%). Other diagnoses were post-transplant (6%) or inmunodeficiency related pathology (6%).
Conclusion: Lymph node biopsy plays an important role in establishing the cause of lymphadenopathy. Among the biopsied nodes, one of the most common diagnoses was lymphoid reactive hyperplasia, that shares sometimes common features with neoplastic lesions. It is important to recognise the different patterns of lymph node pathology in children to avoid misdiagnosis.

PS-06-003
Differential expression of BCL-2 and LEF1 in mature T-cell lymphomas and reactive hyperplasia
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Background & objectives: T-cell lymphomas may lack morphologic atypia or T-cell antigen loss, making differentiation from reactive conditions difficult. The goal of our study is to evaluate BCL-2 and LEF-1 expression in reactive lymphoid hyperplasia versus mature T-cell lymphomas.
Methods: BCL-2 and LEF-1 immunohistochemistry was performed on 43 and 42 previously diagnosed cases of T-cell lymphoma and 18 and 17 cases of reactive lymphoid hyperplasia, respectively, confirmed by clinical follow up. Expression was recorded as positive (>90% of cells staining), partial loss (<50%), and negative (<10%).
Results: BCL-2 showed partial loss in 4 cases (9%) and complete loss in 3 cases (7%) of T-cell lymphoma. LEF-1 showed partial loss in 7 cases (17%) and complete loss in 17 cases (40%) of T-cell lymphoma. None of the 18 cases with reactive lymphoid hyperplasia showed complete loss of BCL-2 or LEF-1. Two cases of paracortical hyperplasia showed partial loss of BCL-2, one of which also showed partial loss of LEF-1.
Conclusion: Complete loss of BCL-2 or LEF-1 expression is often seen in T-cell lymphoma but not in reactive lymphoid hyperplasia and may be helpful in the diagnosis of challenging cases of T-cell lymphoma without other T-cell antigen loss.

PS-06-004
Molecular characterisation of acute myeloid leukaemia among Filipino patients using comprehensive next-generation sequencing
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Background & objectives: AML is the most common adult acute leukaemia. New molecular technologies allowed prognostication & targeted therapy. To date, AML molecular characterization in the country is non-existent. The study determined the prevalence of somatic mutations in Filipino AML patients using NGS.
Methods: All 44 bone marrow aspirates or peripheral blood samples of patients diagnosed with AML between January 2018 to August 2019 were subjected for mutational analysis using a NGS platform (Miseq), to screen for mutational hotspots in 40 genes relevant to myeloid neoplasms (Ampliseq Myeloid Panel, Illumina). Clinical characteristics of patients were recorded.
Results: Of the 44 cases in our study, there were 23 males and 21 females with a median age of 41 (9 to 75 years old). At least one non-synonymous gene mutation was detected 42 our AML patients (95%). There was an average of 2.8 mutations (range 1-8) per case. KIT (27%) was the most common mutation, followed by RUNX1 (20%); CEBPA, NPM1, TET2, FLT3 (13%); and NRAS, IDH1, IDH2, ASXL1, WT1 (7%) . The remaining genes showed a frequency of <5%. In our study, the most frequently identified mutations involve signalling and kinase pathways followed by epigenetic modifiers. We detected NPM1 and FLT3-ITD mutations at frequencies similar to previous reports.
Conclusion: Our study underscores the heterogeneity of AML among Filipinos. Although it is challenging to implement molecular testing in resource-limited countries, our study highlights the necessity of implementing NGS testing in AML patients, to aid in risk stratification and treatment planning.

PS-06-005
Epstein Barr virus (EBV) recruits PD-L1 + cells in paediatric Hodgkin lymphoma microenvironment
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Background & objectives: Introduction: In Hodgkin lymphoma (HL), PDL1 are expressed by tumour cells and its expression could be upregulated in the microenvironment as well. Aim: To evaluate PD-1 /PDL1 pathway in children with HL from Argentina, a population with increased EBV-associated lymphomas
Methods: Methods: Formalin-fixed paraffin-embedded biopsy samples (FFPE) of 94 patients with HL (2-18 years, median 9) were collected at

Ricardo Gutiérrez Children's Hospital. PD1 and PDL1 expression was studied by immunohistochemistry (IHC). FISH for 9p24.1PDL1 gene amplification in HRS cells was performed in 38 patients. EBV status was defined by in situ hybridization for EBERs and IHC for LMP1.
Results: Results: 64 % of cases were EBV+. There were no statistical differences for the mean PD1 + cells in EBV + vs EBV- groups($p > 0.05$). A 5% of cases displayed PDL1 amplification, 18% copy gain, 11% copy gain and amplification. There was no significant differences in the means of PDL1+ HRS cells ($p > 0.05$, MW test), or in PDL1 gene alterations among EBV + vs EBV- cases ($p > 0.05$). No differences were found in the PDL1+ cell count with and without 9p24.1 gene alterations ($p > 0.05$). A significant increase in the number of PDL1 + cells in the microenvironment was detected in EBV + cases ($p = 0.042$).
Conclusion: Conclusions: EBV positivity in HRS tumour cells may not influence PDL1 gene amplification or copy gain in paediatric HL. However, EBV presence would favour the recruitment of PDL1+ cells at the microenvironment in paediatric, possibly leading to a tolerogenic milieu.

PS-06-007
Prognostic value of the immunoexpression of H3K4me3 and H2K27me3 epigenetic marks in follicular lymphoma

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Background & objectives: Follicular lymphoma is the second most common subtype of non-Hodgkin lymphoma. Additional prognostic markers are under investigation. Epigenetic changes are now recognized as playing an important and early role in the lymphomagenesis process, contributing to the disease progression.
Methods: A retrospective transversal study was completed using archival biological material from 48 patients with follicular lymphoma, diagnosed between 2007 and 2012 at the Portuguese Oncology Institute Porto. The H3K4me3 and H3K27me3 marks were assessed by immunohistochemistry, using the Hscore. Relevant clinical and pathological data was extracted from the database of the Department of Oncohaematology.
Results: In this series, the median age at diagnosis was 60 years and recurrent/transformed disease was experienced by 34% of the patients. The median follow-up time was 71.5 months. The overall survival was estimated as 74.7% at 5 years. The disease-specific survival was estimated as 77.3% at 5 years. No difference in prognosis was observed concerning gender ($p=0.755$). The FLIPI score ($p<0.001$) and age at the time of diagnosis ($p=0.019$) were confirmed as prognostic factors. There was a statistically significant association between the immunoexpression of H2K27me3 and the FLIPI score ($p = 0.038$). When evaluating the epigenetic marks H3K4me3 and H3K27me3 no significant association with clinical outcome was found.
Conclusion: In this study, the immunoexpression H3K4me3 and H3K27me3 did not disclose prognostic value. A larger study is needed to fully determine the prognostic value of H3K4me3 and H3K27me3.

PS-06-008
Morphology and histotopography of megakaryocytes in Ph-negative JAK2-mutated, CALR-mutated and triple-negative myeloproliferative neoplasms

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Background & objectives: The aim of study was to assess the quantity of megakaryocytes, histotopography (endosteal translocation), clusters formation, nuclear features (bulbous, staghorn-like, naked, dysmorphic, separated nuclei) in bone marrow biopsies (BMB) of patients with JAK2-positive, CALR-positive and triple-negative (TN) myeloproliferative neoplasms (MPN).
Methods: We investigated 62 BMB of patients with Ph-negative MPN. Patients were divided into the groups: JAK2 (N=31), CALR (N=17), triple-negative (N=14). Serial sections from BMB were stained with haematoxylin-eosin. A standard light microscope (x400) was used. The quantity of megakaryocytes, the nuclei and clusters were assessed in 10 HPF. The endosteal translocation were assessed on the full histological section.
Results: The biggest quantity of megakaryocytes was detected in JAK2-group (mean value (MV): JAK2=203,7±79,1; CALR=142,1±52,9; TN=134,4±48). The smallest number of clusters was in TN-group (MV: TN=7,5±4; JAK2=18,8±6; CALR=11,7±5,8). The bulbous nuclei were prevalent in JAK2-group (MV: JAK2=29,8±26,3; CALR=12,6 ±12,5; TN=3,2±2,9), the dysmorphic nuclei were prevalent in CALR-group (MV: CALR=14,5±2,5; JAK2=3,2±3; TN=5,2±6), the separated nuclei were detected only in TN-group (MV: TN=3,2±1). There was no significant difference in counting of other nuclear forms.
Tendency to the endosteal translocation was demonstrated by CALR-group in 82% (14/17) in comparison with JAK2-group - 58% (18/31) and TN-group - 43% (6/14).
Conclusion: Ph-negative MPN with various mutation status have differences in morphology and histotopography of megakaryocytes. According to the results, the MPN can be divided into additional molecular subtypes. It can be useful for supporting the diagnosis and classification.

PS-06-009
Impact of accurate quantification of bone marrow plasma cells in the trephine core biopsy for the diagnosis of multiple myeloma patients

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Background & objectives: The presence of clonal PCin≥10% marrow cellularity is the threshold for diagnosis of PCM. Cellular counts differ between bone marrow aspirate (BMA)and bone marrow biopsy (BMB).We evaluated the concordance in the PC quantification by aspirate cell count and absolute quantification by IHC withMUM1 staining and the clinical correlation in cases with discordant results.
Methods: We analysed BMA and BMB samples at diagnosis from 48patients. Quantification of BM plasma cell infiltrates in the BMB was done by MUM1 immunohistochemistry. 3 representative images at HPF (40X) were acquired, the number of MUM1 positive and negative cells was quantified by visual enumeration. Semiquantitative estimation of the %of plasma cells was done by 2 pathologists in 28 cases with a BMA count below10%. A three-tiered score was used:<10%,10-60% and>60%MUM1+ cells.
Results: 71%of cases showed a concordant result between the BMA and BMB counts [20 cases with≥10%plasma cells(PC) and 14cases with<10%PC in both samples] 29% of cases were discordant with≥10% MUM1+PC in the BMB and<10%in the BMA.5 out of these 14cases fulfilled clinical criteria(CRAB)for MM and 9cases were considered smouldering MM. Cohen´s kappa coefficient for the semiquantitative categorization of cases according to the BMB cell counts was 0,862with only 2out of 28cases with discordant results among the 2 pathologists
Conclusion: Bone marrow trephine biopsy evaluation of plasma cell infiltrates is critical for the early identification of MM patients. The conversion rate of BMA PC<10% patients to ≥10% in BMB after absolute quantification of MUM1+PC was 29%.In 10%of the cases the patients fulfilled clinical criteria for overt MM. In cases with low BMA cell counts, semiquantitative evaluation of BMB plasma cell infiltrates with MUM1 immunohistochemistry is consistent among pathologists and may be used in the diagnostic setting when absolute quantification methods are not available

PS-06-011

BCL2 in follicular lymphomas (FL): the overrated guy?

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Background & objectives: The t(14;18)(q32;q21) is considered the genetic hallmark of FL. However, some authors have observed a high proportion of FL lacking t(14;18), supposing geographic differences.
Our aim was to test the incidence of BCL2- FL and investigate alternative genetic aberrations.
Methods: We collected a series of 76 consecutive FLs from our Pathology Department between 2013 and 2016. All lymphomas underwent histopathological revision and were immunohistochemically characterised. Interphasic fluorescent in situ hybridization (FISH) was performed targeting BCL2, IGH, BCL6 and MYC on paraffin embedded (PE) and fresh frozen (FF) specimens. Conventional cytogenetic was applied to a subset of cases as well.
Results: Overall, BCL2 rearrangements and protein expression were detected in 54% and 87% of cases, respectively, with statistical correlation between the two dramatically increasing with increasing intensity of immunostaining ($p<0.0001$). BCL2 expression was related to a lower proliferative index, as assessed by Ki-67 ($p=0.02$).
Among cases lacking t(14;18), 6 showed IGH rearrangement, and were further tested: 1 was characterized indeed by a variant BCL2 translocation, 1 had a IGH/BCL6 rearrangement, whereas the other 4 were negative for both BCL6 and MYC. FISH performed on FF specimens detected small BCL2-rearranged clones in three BCL2-negative PE cases. Finally, karyotype reconstruction documented 3q27 and 1p abnormalities in 3 cases, respectively.
Conclusion: Our study suggests that t(14;18) is not a constant finding in FL, its incidence being probably affected by geographical factors. Alternative genetic aberrations exist in negative cases, and conventional cytogenetic may still represent a useful tool to investigate their role in lymphomagenesis.

PS-06-012

Haematological indicators of Dengue illness and recovery: emphasis on white blood cells

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Background & objectives: In Dengue, as a norm platelet count guides the treatment and prognosis. This study assesses if WBC (white blood cell) count can be used as an equally sensitive parameter and it also analyses other haematological parameters in dengue.
Methods: This is a retrospective observational hospital-based study conducted over 6 months. 140 cases of dengue fever were included by complete enumeration method. Consecutive WBC count, Platelet count, WBC differentials and haematocrit were obtained from day of admission till discharge as part of treatment. Analysis was done using Spearman's rank correlation method and descriptive statistics to find for associations and patterns.
Results: Majority (67%) were males with mean age 30 years. On day of admission, 51% patients had leukopenia while 89% showed thrombocytopenia. By third day, leukopenia was seen in 33% patients while thrombocytopenia noted in 94%. On discharge, 12% patients showed leukopenia while 70% had thrombocytopenia. On day of admission, third day and day of discharge, mean WBC count obtained were 4568, 5547 and 6989 respectively and mean platelet count were 88217, 78479 and 131850 respectively. Mean WBC count and platelet count showed moderately positive correlation ($R=0.6, p<0.05$). Neutrophils showed decreasing trend while lymphocytes, monocytes, eosinophils and haematocrit showed an increasing trend post admission. Reactive lymphocytes were noted in conjunction with lymphocytosis.
Conclusion: In dengue patients, WBC count normalized with clinical improvement earlier than platelet count for majority making it an equally important parameter and a good indicator of recovery. The other studied haematological parameters also contributed in understanding the disease progress.

PS-06-013

The study of the toxic effect of the heavy metals salts on the erythropoiesis in the rats

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Background & objectives: Heavy metals salts (HMS) are the most common pollutants that are proved to have the negative effect.
The objective is to determine the morphological features of the marrow in rats, caused by the combined effect of the heavy metals salts.
Methods: The study was carried out on the laboratory male rats (n=24), which were divided into 2 groups (control and experimental – the rats received HMS (zinc, copper, iron, manganese, lead, chromium). The animals were taken out from the experiment on the 30th and 90th day.
Results: The HMS intake leads to the significant changes among the precursors of the erythropoiesis. The islet location of its predictors has been disturbed, they were found as the indistinct assembles of the cells and separately in the areas of myxomatosis and oedema. The size of the survived islets and the number of the cells in their structure gradually reduce, the single precursors of the erythropoiesis with the features of dyserythropoiesis: the signs of karyorhexis, irregular shape of the nuclei, internuclear bridges, are observed among them. The morphological changes in the marrow increase with the extension of the experiment and reach the maximum on the 90th day.
Conclusion: The excessive entry of the HMS to the animals' body leads to the qualitative (dyserytropoiesis) and quantitative (reduced number and size of the erythroid islets) changes in the erythropoietic tissue, which depend on the term.

PS-06-014

Multiparametric flowcytometry in the diagnosis of plasma cell disorders

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Background & objectives: Plasma cell disorders present a spectrum from benign to aggressive course. The diagnosis involves clinical, laboratory, and imaging data. Multiparametric flowcytometry (MFC) is used to determine clonality and aberrant immunophenotypes.
Evaluate the contribution of MFC to the diagnostic work-up.
Methods: All patients with plasma cell disorders (n=203) diagnosed between 2008 and 2014 and followed up for a median of 46 months. A comprehensive flow cytometry panel was applied to bone marrow aspirates, supplemented by biopsies with immunohistochemistry. Antigen aberrations and clonality differentiated between normal and abnormal cells. Expression patterns and quantitative characteristics were further correlated with clinical and lab tests.
Results: MFC-confirmed clonality and abnormal antigen expression supported diagnosis. Antigens were frequently co-expressed (CD20, 29%, and CD28 43%, $p<0,001$ CD200, 90% and CD27, 41%, $p=0,008$), or appeared mutually exclusive (CD20, 29% and CD56, 72%, $p=0.023$). Phenotypically abnormal plasma cells showed correlation with tumour volume - ISS stage ($p=0.002$), haemoglobin ($p=0.001$) and platelet counts ($p=0.01$) and, expectedly, morphological bone marrow infiltration ($p<0.001$). Moreover, myeloma patients with abnormal/total plasma cell ratio of <95% at diagnosis had significantly lower tumour volume and

excellent overall survival compared to other similarly treated patients. This correlation was maintained in patients receiving stem cell transplant (not reached vs. 51 months) or non-intensive therapy (73 vs. 16 months, p=0.003).
Conclusion: MFC supports the diagnosis of plasma cell disorders and contributes valuable prognostic data.

PS-06-015
Primary cerebral lymphoma: clinicopathological analysis of 9 cases
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Background & objectives: Primary cerebral lymphomas are relatively rare neoplasms (represent < 4 % of all brain tumours) and in this context diagnostics and treatment are accordingly challenging.
Methods: We enrolled newly diagnosed cases between 2015-2019. Patients who were diagnosed with secondary CNS lymphoma (n = 4) or acquired immune deficiency syndrome (n = 4) were excluded. Remaining cases were retrospectively analysed considering localization, tumour morphology and immunophenotype, prognosis and overall survival.
Results: Nine cases diagnosed as primary diffuse large B-cell lymphoma (DLBCL) were analysed. The patient's age ranged between 33-74 years, predominantly females (F/M-7:2). On stereotactic biopsy samples, all of them were diagnosed as DLBCL. In four cases the histological differentiation was limited by the reduced tissue sampling, rich in necrosis, without distinct tumour mass. Microscopic examination mostly highlighted an angiocentric growth pattern of tumour cells. Applying the Hans algorithm, using CD10, BCL-6 and MUM-1, 6 cases belonged to non-germinal centre subtype, associated with high Ki67 (>70%). In the subgroup of elderly patients (over 65 years), a high Ki67 index and non-germinal centre subtype has been associated with short survival (three months).
Conclusion: Stereotaxic biopsy and histology of the affected area in most cases will provide a reliable diagnosis. The diagnosis of primary cerebral lymphomas is complex, the histological subtypes are difficult to evaluate due to reduced tissue sampling and requires the application of a large immunohistochemistry arsenal. Non-germinal centre subtype with a high Ki67 index in our patients has been associated with worse survival.

PS-06-016
Molecular signatures of anaplastic large cell lymphoma, ALK-negative – pilot study with 125 genes panel and recurrent MSCE116K mutation testing
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Background & objectives: Anaplastic large cell lymphoma, ALK-negative [ALCL-ALK(-)] is CD30-positive T-cell neoplasm which should be distinguished from primary cutaneous ALCL, other B-cell/T-cell lymphomas with anaplastic features and CD30(+) and classic Hodgkin lymphoma. Lately, a novel molecular signature [*MSCE116K* mutation] has been described.
Methods: We selected 4 cases with clinically and histopathologically confirmed ALCL-ALK(-). The immunohistochemical assessment included: pan-B/pan-T panel, ALK-1, the axis: CD30-IRF4/MUM1-MYC. All cases were tested with FusionPlex Lymphoma 125 genes panel. The *MSCE116K* mutation was evaluated in the Sanger technique.
Results: The patients were 2 males: 2 females with a median age of 68 years and generalized lymphadenopathy and advanced clinical stage of the disease. None of the patients had skin involvement. The histopathological characteristics and immunophenotype were concurrent: pan-T(+), ALK1(-), CD30(+), IRF4/MUM1(+), MYC(+) in >40% of cells. None of the cases were *DUSP22* rearranged nor had *ALK* alteration; all lymphomas had splicing mutation of *KMT2A*[c.11321+2delC] gene and one case presented *p63* fusion. Additionally, none of the cases harboured the *MSCE116K* mutation.
Conclusion: Molecular profiling of ALCL-ALK(-) started to be a key point in prognostication. The presented series of ALCL-ALK(-) could be categorized molecularly as 3 cases triple-negative, and 1 case *p63* rearranged (poor prognostic factor). According to the literature, the *MSCE116K* mutation has been found among *DUSP22* rearranged lymphomas only (none of our cases). The quality and validation of molecular testing from FFPE is relevant.
Funding: This work has been implemented using the Project infrastructure POIG.02.03.00-14-111/13.

PS-07 Infectious Diseases Pathology

PS-07-001
Diagnosing congenital malaria in the eastern province of Rwanda - a comparison of infant peripheral blood smear, cord blood smear and placental histopathologic examinations
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Background & objectives: Congenital malaria is detected within a neonate's first week of life and the diagnosis is made by detecting Plasmodium parasites in peripheral blood smear (PBS). We compared the results of placenta histology to blood smears for diagnosis of congenital malaria.
Methods: Peripheral and cord blood smears (CBS) were sampled, from neonates whose mothers were diagnosed with positive (+) malaria within the last 2 weeks of pregnancy, for light microscopic exam as well as placenta histology (PH) for detection of malaria parasites after consenting the mother. Regression analysis were done and results were considered significant if p-value <0.05, 95%CI.
Results: 111 neonates were recruited for 5 months. 86(77%) had at least one of the 3 tests positive. 58% had CBS+, 56% had PH+ and 44% had PBS+. Of those with PBS+, 61.6% had CBS+, while 50% had PH+. Neither the PH nor CBS alone was significant predictor of a positive PBS. However, when both were positive, there was a 95.5% chance that the PBS will be positive (p-value: 0.000, RR: 18.8).
Conclusion: There is high prevalence of congenital malaria in new-borns from mothers presenting malaria during the last two weeks of pregnancy. Combined PH and CBS can be more reliable in early detection of parasites and allow treatment without sample from neonate.

PS-07-002
Strongyloides stercoralis: hyperinfection syndrome with periumbilical purpura
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Background & objectives: Strongyloides Stercoralis is a pathogenic filariform nematode which causes mostly an asymptomatic chronic disease. Under immunosuppression conditions its life circle is exacerbated. Massive

multiplication of larvae develops clinical manifestations within the usual pattern of migration, which is known as hyperinfection syndrome.
Methods: We report two cases of strongyloides stercoralis hyperinfection syndrome with periumbilical purpurae.
Results: 25-year-old female, HTLV1 positive, presented with abdominal pain, loose stools, severe malnutrition and non-confluent petechial and purpura lesions in abdominal region, flanks and proximal limbs. Tomography evidenced alterations in the gastrointestinal tract. Esophagogastroduodenoscopy showed petechial involvement of the duodenum and jejunum.
Biopsies of skin and colon evidenced mature filariform larvae.
40-year-old male with history of smoking and cocaine addiction consulted for abdominal pain, diarrhoea, unquantified weight loss and non-confluent petechiae in the periumbilical abdominal region. Tomography evidenced a heterogeneous consolidation in right lung and parietal thickening of jejunum and ileum. We received a bronchoalveolar lavage cytology, where mature filariform larvae were encountered.
Stool culture revealed Strongyloides Stercoralis in both cases.
Conclusion: Petechial and purpuric lesions in abdomen, flanks and limbs have been documented in the literature as a rare form of cutaneous presentation of hyperinfection syndrome but they may be a valuable diagnostic sign. Skin biopsy is essential for accurate diagnosis.

PS-07-003
Histoplasmosis presenting as a cecal mass: report of two cases
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Background & objectives: Histoplasma Capsulatum is a dimorphic fungus, worldwide disseminated. It presents as a self-limited respiratory infection or is asymptomatic. Disseminated disease occurs in immunocompromised individuals. Gastrointestinal involvement is rare. Ileum is the most common site and clinical manifestations are exceptional and unspecified.
Methods: We report two cases of disseminated Histoplasmosis syndrome initially presented as a cecal mass, one in a non immunocompromised patient.
Results: 67-year-old woman, treated with oral medication for type 2 diabetes mellitus presented with anorexia and weight loss (10kg). Videocolonoscopy showed a sessile lesion, with central ulceration in the cecum. Biopsy specimens were obtained.
26-year-old male, HIV positive, presented with abdominal pain, liquid bowel movements, chills and unintentional weight loss in the last two months. Videocolonoscopy showed deformed, ulcerated and indurated cecum.
Diagnosis of histoplasmosis was done in both cases by histological examination of cecum biopsies, which revealed multiple intracellular small organisms suggestive of Histoplasma capsulatum.
First patient was HIV negative with positive serology for Histoplasma Capsulatum and PCR negative bronchoalveolar lavage. Second patient PCR in bronchoalveolar lavage was positive.
Conclusion: Histoplasmosis with gastrointestinal presentation and without respiratory symptoms is rare, as well as disseminated disease in patients without immunosuppression. Symptomatology can mimic tuberculosis infection, malignant lesions and others. Biopsy during endoscopic evaluation should be obtained to achieve the correct diagnosis.

PS-07-004
Abdominal actinomycosis simulating a colorectal neoplasia – 2 cases
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Background & objectives: Intra-abdominal actinomycosis (AIA) is a progressive, granulomatous and suppurative disease that can simulate a neoplastic process and consequent inadequate treatment. It is most commonly ileocecal, mimicking colorectal neoplasia, often requiring surgery.
Methods: We present two cases in women with 60 and 84 years, with abdominal pain and a palpable mass with 1.8 and 3.2 months of evolution, one located in the right iliac fossa and the other in the right hypochondrium. Imaging examination did not exclude neoplasia. Endoscopy revealed congestive mucosa and biopsies showed ischemic colitis.
Results: After an antibiotic cycle without improvement, both underwent segmental colectomy resection. The macroscopic evaluation did not exclude a neoplastic process, and histological study showed pseudotumoral lesions consisting of fibrous tissue with abscesses and colonies of actinomyces (Grocott), without evidence of malignancy.
Until the moment of submission, patients were well, without any complications or reinfection.
Conclusion: AIA diagnosis is difficult due to non-specific features. It is often clinically confused with neoplasia or other inflammatory diseases. AIA is rare and a diagnosis of exclusion, usually made after surgery and histological analysis. It should be considered in immunocompromised patients.

PS-07-005
Histopathological and MPT64 immunohistochemical diagnosis of extrapulmonary tuberculosis at the Muhimbili National Hospital
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Background & objectives: Extra-pulmonary Tuberculosis (EPTB) has diagnostic challenges in resource limited setting. Confirmation depends on histology and Ziehl Nielsen stain (ZNS). Immunohistochemistry using anti-MPT64 can detect mycobacterium TB complex proteins. We describe the histomorphology and anti-MPT64 immunoreactivity on Formalin fixed paraffin embedded (FFPE) biopsies.
Methods: FFPE tissue blocks and haematoxylin-eosin stained slides of biopsies which were signed out as EPTB (July 2015 - June 2017) were retrieved from the archive. Slides of included cases were reviewed to confirm the diagnosis prior to resectioning for ZN staining and IHC. Demographic, clinical and histopathologic data were analysed. Proportions of AFB positivity for ZNS and anti-MPT64 immunoreactivity were calculated.
Results: 110 biopsies signed out as EPTB were analysed and biopsies were from patients aged between 2-76 years with mean of 36.3 years. Female represented 60% (n=66), lymph node was more frequent (41.8%, n=46) site and necrotizing granuloma was the most (69%, n=76) frequent lesion. IHC and ZNS positivity were found in 71% and 8% of the biopsies respectively. All ZN positive biopsies were also positive to MPT64 by IHC.
Conclusion: EPTB is encountered frequently among biopsies submitted at our hospital. Despite the challenges faced in establishing EPTB diagnosis, the histomorphology of necrotizing granulomas should be regarded as a strong indicator of EPTB, particularly in TB endemic areas. Furthermore, IHC by anti-MPT64 appears to be useful particularly in controversial cases where ZN staining is negative. EPTB affects mostly young adults in reproductive age group and the female gender and TB lymphadenitis is the most common type of EPTB presentation at MNH.

PS-07-006
Laboratory and anatomopathological aspects in the diagnosis of Dengue in Ceara in 2011 and 2012: the role of the Death Verification Service
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Background & objectives: In Brazil, has expressive epidemic outbreaks of dengue and not all the cases with fatal evolution are diagnosed by the public health service. Evaluate the impact of Death Verification Service (DVS) for detecting non-suspected dengue deaths in Ceara.
Methods: Post-mortem examinations were performed in the period from 2011 to 2012 in cases suspect of dengue and cases non-suspected by the clinician but that were suspected by pathologist. The test to IgM, NS1, viral isolation and PCR and immunohistochemical test were performed. Deaths due to dengue were confirmed only if they fulfilled the WHO criteria.
Results: Were performed 214 post-mortem examinations in which 121 (56.5%) were confirmed as dengue, however 90 of these were asymptomatic for dengue. Co-infections were detected in 46 cases in which bacterial organisms were the most prevalent (93.5%). Oedema and haemorrhage occurred in all exams and organs with more pronounced oedema in the lungs (79%) and central nervous system (71%). Haemorrhage was predominant in the adrenals (31%) and lungs (24%). Acute respiratory failure (47.1%) and shock (33.8%) were the most frequently reported causes of death.
Conclusion: The DVS ,Center for Epidemiological Surveillance and Central Public Health Laboratory helped to increase by 5.1 times the number of dengue's related deaths. This is the largest historic series of autopsied deaths due to dengue in the world.

PS-07-008
Diagnosis of tuberculous lymphadenitis: from morphology to molecular analysis
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Background & objectives: Culture is still the gold standard for diagnosis of tuberculosis (TB), however, molecular methods have also been shown to be effective diagnostic tools. We aimed to investigate the association between histopathological features and molecular TB positivity in this retrospective study.
Methods: Slides of 36 consecutive patients who had undergone lymph node resection with clinical suspicion of TB lymphadenitis (TBLA) were re-evaluated. Molecular TB testing was performed on formalin fixed-paraffin embedded (FFPE) tissues using a real-time polymerase chain reaction (Anyplex™ MTB/NTM, Seegene, Inc). The findings were statistically analysed.
Results: The majority (n=26) were female and median age was 44.50±14.42 (range 17-69 y.o.). All but 2 patients had granulomatous inflammation, however, TBLA was confirmed by molecular analysis in only 8 patients, 5 of which had pure caseous granulomas. 2 patients with confirmed TBLA had mixed caseous and sarcoid-like granulomas, and 1 had suppurative necrotizing granulomas. The bacilli could be demonstrated by acid-fast staining in only 1 TBLA patient. TB-DNA was negative in 14 patients with mixed caseous-sarcoid granulomatous inflammation, 4 with suppurative necrotizing granulomatous lymphadenitis and 8 with sarcoid-like granulomas. Molecular TB positivity was significantly associated with the presence of caseation (p=0.018). No other significant association was found.
Conclusion: Molecular testing seems to be more sensitive for diagnosis of TB in FFPE tissues compared to acid-fast staining. Morphological overlaps of different granulomatous patterns can be seen in TB, and although widely considered to be characteristic for TB, caseation is not always a sign of TB positivity.

PS-07-010
Tissue reactions in cases of progression of tuberculosis in patients with HIV/AIDS
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Background & objectives: Development of the inflammatory response in pulmonary tuberculosis in patients with HIV/AIDS are of interest from the point of view of establishing mechanisms of resistance to infection, and, accordingly, finding ways to increase resistance to tuberculosis
Methods: We conducted a retrospective morphological analysis of 15 autopsies of patients with HIV/AIDS with progressing tuberculosis (2016-2018). All patients (3 women and 12 men) had a diagnosis of pulmonary TB, MBT (+), TBMLU. The duration of inpatient treatment varied from 7 to 100 days. The average age of patients was 37 years.
Results: The progression of TB varied: in 6 cases we observed the development of a tissue reaction in organs with the formation of giant cell granulomas with central caseous necrosis and limited foci of tuberculous inflammation from the surrounding tissue. In 9 cases, there was a predominance of the exudative type of tissue reaction with the formation of large fields of caseous necrosis, surrounded by perifocal oedema. In the latter case, the inflammatory process was widespread with the involvement of both lungs, parietal pleura, and peritoneum. The cause of death was pulmonary haemorrhage (14 cases), diffuse purulent peritonitis (1 case). In all cases, cachexia was established.
Conclusion: Tuberculous inflammation in patients with HIV/AIDS is characterized by a variety of morphological manifestations, including a predominance of productive tissue reactions and the development of exudative reactions with massive zones of caseous necrosis. Differences in tissue reaction can be considered as one of the cytological mechanisms of sensitivity and resistance of tissues to tuberculosis infection.

PS-07-011
Immediate death causes in HIV infection
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Background & objectives: HIV remains important infection frequently revealed in the deceased. In spite of numerous clinical investigations, many questions can be discussed only basing upon the results of post-mortem autopsy findings.
Methods: Detailed analyses of pathology records since the first lethal cases occurring in S.P. Botkin infectious hospital and Cities' centre for Diagnostics and treatment of AIDS. Minor discrepancies between clinical and pathological diagnosis are revealed in majority of cases. Practically in all observations several secondary diseases (till10) are diagnosed, in many cases they disappear from the statistical analysis.
Results: Analysing the spectrum of secondary infections and immediate death causes we noted not significant changes since 1996. Thus, recently we observed increase of PML (25 in 2018) and different neoplasms (35 in the same year). Among The number of cases with pneumocystosis (51) , cytomegaly (2), cryptococcosis (17) and toxoplasmosis (38) formed sinusoid like variations. In HIV encephalitis we started to see giant-cell reactions never noted before.
In rare lethal cases of the treated patients we considered the cases not directly associated with HIV (in 2016 - 348). In certain cases we still can't exclude the indirect role of the virus.
Conclusion: Thus, the exact data concerning HIV lethality and better understanding of the disease mechanisms can be obtained only in complex studies including post-mortem morphological.

PS-08 Nephropathology

PS-08-001
Morphological findings in frozen non-neoplastic kidney tissues of patients with kidney cancer from large-scale multicentric studies on genomics of renal cancer
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Background & objectives: Analysis of non-neoplastic tissues helps to better understand the process of carcinogenesis. We performed microscopic examination of non-neoplastic kidney tissues from kidney cancer patients who were recruited to large-scale multi-centric kidney cancer genomic studies from countries with variable incidence rates.
Methods: By applying digital pathology, we performed microscopic examination of 1012 frozen non-neoplastic kidney tissues from kidney cancer patients from Czech Republic, Romania, Serbia, United Kingdom, and Russia, with variable incidence rates of kidney cancer. Renal parenchyma was evaluated and scored for the interstitial inflammation and fibrosis, tubular atrophy, glomerulosclerosis, and arterial wall thickening, globally called chronic renal parenchymal changes.
Results: Moderate or severe chronic renal parenchymal changes was observed in 54 (5.3%) with predominance of occurrence among patients from Romania (OR=2.67, CI 1.07-6.67) and Serbia (OR= 4.37, CI 1.20-15.96) in reference to Russia. To assess the potential confounders, we adjusted for age, sex, history of hypertension and diabetes mellitus, percentage of medulla, stage of tumour, tumour size, and type of nephrectomy, which rendered no significant effect on the risk estimates.
Conclusion: Frequency of chronic renal parenchymal changes in kidney cancer patients varies by country, significantly more frequent in countries located in central and southeastern Europe where the incidence of kidney cancer has been reported to be high. This is unlikely to be due to sampling method or known confounding factors. We suggest that these parenchymal changes, possibly linked to environmental exposures, may be relevant to renal carcinogenesis in these countries.
Funding: Part of the samples are from CAGEKID study that is funded by European Union FP7 241669.

PS-08-003
Lymphocyte populations in lupus nephritis
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Background & objectives: Studies targeting the profile and role of lymphocyte populations in lupus nephritis (LN) are limited, most of them being from experimental research. Within this context, our study aims to analyse the T lymphocytes (Ly) populations in different classes of LN.
Methods: 53 LN renal biopsies (2 cases class II, 4 cases class III, 19 cases class IV, 22 cases class V, 6 cases class VI) were immunohistochemically investigated by using anti-CD4 and anti-CD8 antibodies. CD4 and CD8 T Ly were quantified in three distinct territories: periglomerular, intraglomerular and interstitial, at 400X. The results were expressed as the number of positive cells/mm2.
Results: We registered significant differences ($p<0.05$) for: periglomerular CD4 T Ly, class II versus class III; interstitial CD4 T Ly, class IV versus class V and class V versus class VI; periglomerular and intraglomerular CD8 T Ly, class III versus class IV; periglomerular and interstitial CD8 T Ly, class IV versus class V. Significant differences between CD4 Ly and CD8 Ly were recorded in all three territories, in all LN classes.
Conclusion: Quantification of T Ly offers the possibility to analyse their involvement in the immune pathogenic mechanism. LN lymphocytic infiltrate is predominantly composed of CD8 T Ly. This finding is in agreement with the immunological theory that supports the effector role of CD8 T Ly and that of initiator and target for CD4 T Ly. Our data complement the limited number of published studies on this topic and support the different behaviour of the two T Ly populations in LN pathogenesis.

PS-08-004
Expression of indoleamine 2,3-dioxygenase 1 in tubular epithelial cells in renal grafts as a key feature of maintaining the local immunosuppression
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Background & objectives: Indoleamine 2,3-dioxygenase 1 (IDO1) is an enzyme that contributes to inducing local immunosuppression. The aim of our study was to evaluate the expression of IDO1 in renal transplant biopsies and to analyse the correlations between IDO1 expression and clinical parameters.
Methods: Immunohistochemical expression of IDO1 was analysed in 121 renal transplant biopsies in three tissue compartments: tubular epithelium (TE), glomeruli (G), and in foci of interstitial immune infiltrates (III). The scores for TE and G were dichotomized into two categories: no or any expression. IDO1-positive cells in foci of immune infiltrates were dichotomized into negative or positive group (any IDO1-positive cells).
Results: Rejection was observed in 32% (25/76) of patients with IDO1 expression in tubules (TE 1 or 2), and in 62% (28/45) of patients without IDO1 expression in tubules (TE 0) ($p=0.0017$). Increased number of IDO1-positive interstitial immune infiltrate cells was correlated with the presence of histopathologic features of any type of rejection. Rejection was observed in 56% (45/80) of patients from IDO1-positive group vs 19.5% (8/41) in IDO1-negative group ($p=0.0001$).
Conclusion: The expression of IDO1 in tubules had a potential protective role but enhanced number of IDO1-positive interstitial immune cells was associated with the presence of rejection. The analysis of IDO1 expression in renal transplant biopsies might be considered for better transplant immunological risk assessment. Our preliminary results should be validated in a larger group of patients.

PS-08-005
Dent's disease: clinicopathologic and genetic findings of two patients with novel variants/mutations in the CLCN5 and OCRL genes
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Background & objectives: Dent's disease is a rare X–linked-disorder characterized by low-molecular-weight proteinuria and often considered a renal tubular disease. It is frequently underdiagnosed or diagnosed after patients have failed an immune suppression regimen. We present two well documented cases of Dent's disease.
Methods: A Caucasian boy aged 9,5years and a young Caucasian man aged 30years, underwent a renal biopsy due to low molecular weight proteinuria (1.3-1.9gr/24h), without haematuria, with normal renal function.
Light microscope, immunofluorescence, electron microscope (EM) and genetic testing [Kidney Seq TM v3.0. and Whole Exome Sequencing (WES)] were performed.
Results: The main histologic finding in both biopsies was the presence of intratubular calcium salts (Von Kossa+).
Immunofluorescence and EM were negative or nonspecific.
Genetic testing revealed that the boy was hemizygous for a pathogenic variant in CLCN5, NM_000084:c1934-2A>G. Variants in this gene are responsible for X-linked Dent's disease. This variant alters a canonical acceptor splice site and has not been reported by the Genome Aggregation Database. The young man had a new mutation in the OCRL gene (p.Asp631Glu) which was verified by Sanger sequencing.

Further analysis showed that the patient was homozygous for the c.2986G>T polymorphism in the CASR gene and heterozygous for the c.2878C>T polymorphism in the same gene.
Conclusion: Two cases of Dent's disease with novel variants/mutations in the CLCN5 and OCRL genes - corresponding to Dent's disease 1 and Dent's disease 2, respectively- are presented. Dent's disease must be kept in mind in the differential diagnosis of nephrocalcinosis and genetic testing should be performed.

PS-08-006
Factors affecting outcome in pauci-immune crescentic glomerulonephritis: a single centre study
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Background & objectives: Pauci-immune crescentic glomerulonephritis (PICN) presents as rapidly progressive renal failure. Present study was undertaken to determine factors influencing renal survival based on Berden's classification, renal risk score (Brix et al.) and individual risk factors.
Methods: Retrospective study done from January 2013 to December 2018. Cases were grouped into focal, crescentic, mixed and sclerotic categories based on histology. Serum creatinine, eGFR at biopsy and follow-up, were recorded. Renal biopsies were scored based on renal risk score [% of normal glomeruli (>25%,10-25% and <10%), percentage of tubular atrophy and interstitial fibrosis(≤25%,>25%) and eGFR(>15ml/min,≤15ml/min)] into 3 risk categories.
Results: 51 adult patients were included. Mean serum creatinine at biopsy was 7.05±4.57 mg/dl and eGFR was 13.6±12.16 ml/min/1.73m2. 33 cases were ANCA positive and 18 were negative. Based on Berden's classification, cases were grouped as focal(4), crescentic(29), mixed(12) and sclerotic(6). Based on renal risk score cases were grouped as low(8),medium(23) and high(20). Univariate Cox regression analysis showed eGFR at biopsy (p 0.024), % IFTA (p 0.001) and % normal glomeruli(p 0.023) are predictors of ESRD. Multivariate Cox regression analysis confirmed IFTA (p<0.001) and % normal glomeruli (p 0.018) as significant predictors of ESRD. Kaplan-Meier survival analysis for histological categories (Log-Rank p=0.046) and the renal risk categories was done (Log-Rank p=0.002).
Conclusion: Percentage of normal glomeruli, IFTA and eGFR at time of biopsy were important risk factors influencing renal survival. Our study validate that renal risk score is a better predictor of survival as compared to histological classification proposed by Berden.

PS-08-008
C4d deposition in lupus nephritis; clinicopathological correlation
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Background & objectives: C4d deposition in native kidney has been investigated increasingly in recent years. For lupus nephritis, there are few studies reported and the results are conflicting. We aimed to investigate the association of C4d deposition with histopathological and clinical parameters.
Methods: Renal biopsies of 51 biopsy-proven lupus nephritis patients were evaluated for C4d immunohistochemistry. Clinical information at the time of biopsy and follow up data were collected from hospital database. Glomerular C4d staining scores, separately for mesangial and capillary wall, were obtained considering the pattern, extent and intensity of C4d deposition. Spearman's correlation analysis was used for nonparametric correlations.
Results: According to 2003 ISN/RPS classification system for lupus nephritis; 5 biopsies were classified as class II (9.8%), 16 as class III (31.4%), 16 as class IV (31.4%) and 12 as class V (23.5%) in the cohort. All biopsies except one showed glomerular C4d staining in mesangium and/or capillary wall. Glomerular staining scores were significantly higher in class V compared to class III (p=0.016), whereas it was not significant between class III and class IV. Glomerular capillary wall staining was positively correlated with levels of 24-h proteinuria (p:0,020), and the staining scores were significantly lower in patients in remission compared to patients with active lupus nephritis (p:0.006).
Conclusion: C4d immunohistochemistry is useful to show both the presence and the localization of immune deposits in lupus nephritis. Besides, glomerular C4d load is correlated with clinical disease activity in terms of proteinuria.

PS-08-009
The value of DARC expression as diagnostic marker in renal transplant biopsies
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Background & objectives: Duffy antigen receptor for chemokines (DARC) is one of the genes most upregulated in antibody mediated rejection (ABMR) and is associated with endothelial injury. We investigated whether immunohistochemistry (IHC) for DARC might serve as a diagnostic marker for active ABMR.
Methods: 82 renal allograft biopsies performed during a prospective clinical trial (BORTEJECT Study) with detailed patient and biopsy characteristics available were included. IHC for DARC was performed on 2μm paraffin sections using a mouse monoclonal anti-human DARC-Fy6 antibody. DARC-IHC positive peritubular capillaries (PTC) were quantified and the distribution of the cortical stained PTC were further described
Results: DARC that was mainly observed in peritubular capillaries (PTC) and in small venules and arterioles. 61 biopsies showed positive DARC staining in ≥5% of PTC, mainly located in areas of interstitial fibrosis or inflammation. Most of the ABMR cases were DARC positive (n=40 vs. n=7, p=0.01), but a substantial amount of biopsies without signs of rejection still showed DARC positive PTC. C4d positivity was not associated with DARC positivity (p=0.365). On a molecular level, we see a significant difference of DARC gene expression in DARC positive vs. negative biopsies with higher DARC gene expression linked to more DARC positive PTC in biopsies (log scale: 8.68(7.91-9.32) vs. 7.52(6.99-8.14), p<0.001; rs=0,546, p<0,001)).
Conclusion: DARC expression on endothelial cells generally matches DARC gene expression and is associated with ABMR. However, DARC expression could also be observed in biopsies without signs of rejection which limits its value as diagnostic marker for ABMR.

PS-08-010
Co-occurrence of spherocytosis and UMOD disease causing variant in a three-generation family presenting with kidney failure in adulthood
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Background & objectives: Hereditary spherocytosis is clinically and genetically heterogeneous disorder, but patients rarely present with kidney diseases. Seven patients from the same family with spherocytosis were evaluated to assess the kidney failure presented in all affected adult patients.
Methods: Clinical, radiological and laboratory investigations were assessed to evaluate the spherocytosis and kidney disease. We performed genetics testing with next generation sequencing of genes related to hereditary spherocytosis, inherited glomerular disorders and tubulointerstitial kidney disease.

Results: Two adults had end-stage kidney disease and one chronic kidney disease stage 4 with histopathological findings of interstitial fibrosis/tubular atrophy and glomerulosclerosis. There were no signs of kidney disease in four paediatric patients. Novel nonsense variant in SPTB gene (NM 001024858; c.4796G>A; p.Trp1599Ter) was detected in all family members with spherocytosis. Furthermore, all adult patients with kidney failure and two paediatric cousins of the index patients were heterozygous for the UMOD gene variant (NM 003361.3:c.552G>C, NP 003352.2:p.Trp184Cys) previously reported in patients with autosomal tubulo-interstitial kidney disease. UMOD variant was not present in the index patients. Renal biopsy in two adult patients revealed diffuse interstitial fibrosis, tubular atrophy and glomerulosclerosis.
Conclusion: Kidney failure in all adult patients was probably related to disease causing UMOD variant characterized by deficient production of functional uromodulin. It is not possibly to evaluate whether the haemolytic crises due to spherocytosis were influencing the progression of the UMOD related renal disease. The kidney disease in the family is warranting the regular monitoring in UMOD positive paediatric patients in order to recognize early signs of tubular injury.
The study was supported by the financial support from the Slovenian Research Agency (research core funding P3-0343 and P1-0170).

PS-08-011
A histopathological study of childhood clinically complicated acute diffuse proliferative glomerulonephritis and correlation with serum creatinine and serum albumin. A study at a tertiary care hospital in Sri Lanka
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Background & objectives: Acute diffuse proliferative glomerulonephritis (ADPGN) is usually self-limiting. This study was conducted to document reversible and irreversible pathologies seen in complicated ADPGN in a paediatric population and to ascertain whether biochemical parameters would give a clue to the changes observed.
Methods: Forty-eight ADPGN proven renal biopsies were assessed. Severity of the glomerular injury and tubular injury were scored as GI 1+ and 2+ (reversible lesions), 3+ and 4+ (irreversible lesions), TI 0(no lesions), 1+ and 2+ (reversible lesions), 3+ (irreversible lesions) . Serum creatinine (SC) and serum albumin (SA) were correlated with above lesions using the "Spearman's rank-order correlation".
Results: All cases showed glomerular injury. 69% had reversible glomerular lesions while 31% were irreversible. Irreversible lesions included crescents and necrotizing lesions. Tubular injury was present in 46% and 92% were reversible and 8% were irreversible. Irreversible tubular injuries included tubulorrhexis. The group that showed reversible glomerular injury did not have crescents or necrotizing lesions at all. However, 42% had tubular injuries. A significant statistical correlation was not seen between the glomerular/tubular injuries and serum creatinine and serum albumin (P value was > 0.05).
Conclusion: Approximately 2/3 of the lesions in complicated ADPGN are reversible where the kidney is salvageable. More than a third have non-reversible lesions possibly culminating later on sclerosis of glomeruli. Determining the renal pathologies on the biochemical parameters is not possible.

PS-08-013
Fibrillary glomerulonephritis concurrent with IgA nephropathy: a case series of 14 patients
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Background & objectives: Fibrillary glomerulonephritis (FGN) is a rare glomerular disease characterized by glomerular deposition of randomly oriented fibrils that stain with IgG and DNAJB9. In contrast, IgA nephropathy (IgAN) is characterized by IgA-dominant glomerular deposits which appear granular by electron microscopy (EM).
Methods: The characteristics of 14 cases of FGN (defined by smudgy glomerular staining for IgG with corresponding randomly-oriented fibrils on EM, mean thickness 16 nm) concurrent with IgAN (defined by granular mesangial IgA by immunofluorescence with corresponding granular electron dense deposits by EM) are provided. This represents the first study on the clinicopathologic and outcome characteristics of this dual glomerulopathy.
Results: The cohort included 11 males & 3 females, mostly White, with median age of 56, who presented with haematuria (86%), proteinuria (100%), and renal insufficiency (71%). 1 patient had carcinoma, 1 hepatitis C, and 1 lupus. None had hypocomplementemia or monoclonal gammopathy. On follow up (median 27 months), 8 progressed to ESRD. Histologically,12 cases showed mesangioproliferative GN, 1 crescentic GN and 1 mesangial sclerosis. DNAJB9 IHC was positive in all.
Conclusion: Most cases of FGN concurrent with IgAN are idiopathic, and not associated with liver disease, hepatitis C, malignancy, autoimmune disease, or monoclonal gammopathy. The pathologic diagnosis can be established by correlating the findings on immunofluorescence and electron microscopy. DNAJB9 IHC is useful to establish the diagnosis of FGN in these cases, particularly in centres that do not perform electron microscopy. The prognosis of this dual glomerulopathy is guarded with >50% of patients progress to ESRD within 2 years.

PS-08-014
Immunological prospective of glomerulonephritis
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Background & objectives: Glomerulonephritis (GN) is a manifestation of various immune mediated and inflammatory mechanisms. Autoantibodies play a significant role in the diagnosis and pathogenesis. Antinuclear antibodies (ANA) were reported in 33% patients. This research aims to determine various autoantibodies in glomerulonephritis patients.
Methods: Two hundred clinically diagnosed patients of glomerulonephritis were included who had ANA. These patients were further evaluated for presence of anti-dsDNA and anti-extractable nuclear antibodies (ENA). ANA (pattern and titer) and Anti-dsDNA were evaluated via Indirect immunoflourecence assay. Anti-ENA were determined by Immunoblot assay which included anti-Sm, -anti-SSA, anti-SSB, anti-Scl-70, anti-jo-1, anti-PCNA, anti-Histones, anti-nucleosomes, anti-CENP B, anti-PM-Scl and anti-Rib.P-protein antibodies.
Results: Main causes of glomerulonephritis were Lupus nephritis 126(63%), idiopathic membranous GN 10(5%), post infectious GN 7(3.5%), FSGS 6(3%), Overlap syndrome 8(4%), RPGN 5(2.5%), Systemic sclerosis 3(1.5%) in 35(17.5%) no underline cause was identified. Autoantibodies were detected in 111(56%) patients. Anti-dsDNA was found in 56(50.4%) whereas anti-ENA were detected in 94(84.7%) patients. Single antigen specificity was found in 55(27.5%) individuals. Frequencies of various anti-ENAs were anti-SSA 58(61.7%),-Sm 18(19.1%), - histones 18(19.1%),-Rib. P-protein 15(16%)-RNPs 13(13.8%),-SS-B 8(8.5%), -Scl-70 7(7.4%),PCNA 3(3.2%),-Jo-1 3(3.2%) -CENP B 2(2.1%) and-PM-Scl 2(2.1%). Single ANA patterns was observed in 181(91%),among them speckled pattern was most common 72(36%).Frequencies of ANA titer were 1:40 ;30(15%), 1:80 ; 28(14%), 1:160; 62(31%), and ≥1:320; 80(40%)
Conclusion: ANA are hallmark of autoimmune connective tissue disorders however they are also found in normal individuals (5%-10%) and in other diseases and infections. ANA profile (anti-dsDNA and anti-ENA) helps in identifying underlying diseases, hence improves management in patients primarily presenting with glomerulonephritis. In this study

patients were identified having high ANA titer with no underline autoimmune disorder. This group needs close monitoring as autoantibodies develop earlier before clinical manifestation of disease

PS-08-015

BK-virus associated nephropathy in native kidneys and BK-virus in urothelial carcinoma

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Background & objectives: Patients with non-renal organ or stem cell transplantation (Tx) may suffer from BK-viral nephropathy (BKVN) of their orthotopic kidneys by reactivating their own viral population living in latency of urothelial cells. BK-virus might be underdiagnosed in such uncommon patients.
Methods: We identified yet unknown cases and aimed to know how patients with BKVN after non-renal organ transplantation and patients with urothelial tumours differ from renal transplant patients with BKVN. We screened the past 20 years of the pathology archives of Hannover Medical School for suspective cases (lung-, heart-, liver-, stem cell- tx, patients after solid organ tx with urothelial carcinoma).
Results: We evaluated SV40 immunohistochemical stains in >100 identified cases and followed retrospectively the clinical course of patients with BKVN. Six lung-Tx, two lung-Tx/HSCT, one heart-Tx, one leukaemia and two stem cell-Tx patients showed positivity for SV40 in their renal biopsies. Three other patients after heart respective combined heart/kidney respective kidney-tx developed urothelial carcinoma with SV40 positive tumour cells six respective five respective nine years after high BK-viruria. Currently, BKV genotypes are being identified by PCR from the formalin-fixed paraffin-embedded tissues.
Conclusion: BKVN in orthotopic kidneys is seen preferentially after lung transplantation. In patients with BKVN after non-renal organ transplantation diagnosis is often established late and with high viral load of long persistence. Patients develop severe renal insufficiency and often end-stage renal disease. The course of BKVN of orthotopic kidneys after non-renal transplantation might be more detrimental than BKVN in renal transplants. BKVN might be a risk for urothelial cancer in Tx-patients.

PS-08-016

Computer-assisted measurement of glomerular size in IgA nephropathy: practical issues and correlation with the Oxford Classification

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Background & objectives: Glomerular size has been demonstrated as an independent prognostic marker in IgA nephropathy. Using digital pathology, this study aims to determine reproducibility of GD measurement, defining minimum number of glomeruli required for accurate measurement, and correlating GD with MEST-C scores.
Methods: The diameter of all non-sclerosed glomeruli from renal biopsies of 420 patients with IgA nephropathy was measured independently by 3 pathologists, using the ruler device on Aperio ImageScope software. Inter-observer and intra-observer variability was then assessed using interclass correlation coefficient (ICC). Mean and maximum GD were correlated with Oxford Classification MEST- C scores, using the independent samples T test.
Results: There was excellent interobserver (between 3 pathologists) and intra-observer (one pathologist measuring 2 levels from the same biopsy) correlation with ICC of >0.9. Accuracy of measurement of maximum and mean GD increased with number of glomeruli measured, levelling off between 12-15 non-sclerosed glomeruli. T score was the only MEST-C variable to significantly correlate with glomerular diameter.
Conclusion: Use of the ruler device on digital slide viewing software provides a rapid and reproducible estimate of glomerular diameter. Greater than 12 non-sclerosed glomeruli are required to provide an accurate measurement of the glomerular diameter. Glomerulomegaly results from adaptive changes associated with hyperfiltration that is in part determined by the severity of chronic renal injury, reflected by correlation of GD with Oxford Classification T score.

PS-08-018

A clinicopathological study to determine the different morphological patterns of renal biopsy in adult patients of nephrotic syndrome

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Background & objectives: Nephrotic syndrome is pathognomonic of glomerular diseases. Examination of renal biopsies only by light microscopy is not sufficient. Immunofluorescence studies can modify the final diagnosis. Hence this study was undertaken to know the spectrum of histopathological changes and immunofluorescence pattern.
Methods: A prospective observational study over a period of one year. Ultrasound guided renal biopsies of newly diagnosed patients of nephrotic syndrome were included. 10% Neutral buffered formalin fixed biopsies were processed and stained with H and E, PAS, Jones Silver, Masson Trichrome and congo red. Direct immunofluorescence studies done on saline samples with IgG, IgM, IgA, C3 and C1q.
Results: Present study evaluated 87 cases. Membranous nephropathy was the commonest type. FSGS was more common in elderly age group. In Membranous Nephropathy IgG positivity was seen in 97% of the cases whereas IgM positivity was seen in 26.4% cases. Linear pattern was the commonest pattern for both IgG (44.8%) and IgM (24.1%) followed by the granular pattern. Final diagnosis was modified in 8.05 % of cases after immunofluorescence studies.
Conclusion: Immunofluorescence studies are necessary for the evaluation of renal biopsies as they can modify the final diagnosis in a significant number of cases. Many cases of nephrotic syndrome can be diagnosed without the aid of electron microscopy. This study may help to understand the regional geographical variations in various aetiologies of nephrotic syndrome.

PS-09 Neuropathology

PS-09-001

PlexinA1 receptor and its ligand, axon guidance molecule semaphorin 6D are implicated in medulloblastoma progression

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Background & objectives: Medulloblastomas (MBs) are the most common malignant childhood brain tumours. Axonal guidance molecules specifically activated during brain development such as Semaphorin pathways also participate to the molecular signature of SHH and subgroup 4 of medulloblastoma which act with plexins.
Methods: - Cohort study of patients for QRT-PCR mRNA and protein analysis of PlexinA1 / Sema6D expression(13 MBs biopsies).
- Animals and cerebellar granule precursor cells purification
- Immunoblotting PlexinA1 and Semaphorin 6D antibodies. (Abcam (ab 32960) and R&D systems MAB 2095)
- Apoptosis and Proliferation assay (BrdU immunofluorescence staining and caspase 3 activity).
- Transwell migration assay and Immunofluorescence.

Results: - Sema6D mean values tended to be higher in demsoplastic MBs.
- PlexinA1 transcript expression was increased in all classic MBs compared to desmoplastic MBs.
- mRNA & protein PlexinA1 expressions are restricted to DEV cell line.
- High expression of PlexinA1 found in classic MB which enhance migration process.
- Higher expression of PlexinA1 was found in group 4 MBs and in metastatic MBs (6D).
Conclusion: We underscored a new role for Sema6D/PlexinA1, promoting MB cell migration and further correlated PlexinA1 expression to metastatic status. Altogether these data showed that Sema6D/Plexin-A1 may provide new insights into MB metastatic potential. The striking in vitro blockade of cell migration resulting from PlexinA1 ectodomain deletion let envision new fields of research to target this receptor in MBs. PS: Immuno-histochemistry study of plexinA1 in MBs in progress.

PS-09-002
Clinical management and genomic profiling of paediatric low-grade gliomas in Saudi Arabia
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Background & objectives: Paediatric Low Grade Gliomas (PLGGs) display heterogeneity regarding morphology, genomic
drivers and clinical outcomes. The treatment modality dictates the outcome and optimising
patient management can be challenging.
Methods: In this study, we profiled a targeted panel of cancer-related genes in 37 Saudi Arabian patients with pLGGs to identify genetic abnormalities that can inform prognostic and therapeutic decision-making.
Results: We detected genetic alterations (GAs) in 97% (36/37) of cases, averaging 2.51 single-nucleotide-variations (SNVs) and 0.91 gene fusions per patient. The KIAA1549-BRAF fusion was the most common alteration (21/37 patients) followed by AFAP1-NTRK2 (2/37) and TBLXR-PI3KCA (2/37) fusions that were observed at much lower frequencies. The most frequently mutated-genes were NOTCH1-3 (7/37), ATM (4/37), RAD51C (3/37), RNF43 (3/37), SLX4 (3/37) and NF1(3/37).
Conclusion: To our knowledge this is the first report of GOPC-ROS1 fusion in PLGG. Taken together, we reveal the genetic characteristics of pLGG patients can enhance diagnostics and therapeutic decisions. In addition, we identified a GOPC-ROS1 fusion that may be a biomarker for pLGG.

PS-09-003
Review of atypical teratoid/rhabdoid tumours in a tertiary hospital
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Background & objectives: Atypical teratoid/rhabdoid tumour (AT/RT) is a rare entity accounting for 1-2% of all paediatric brain tumours. It is characterized by inactivation of SMARCB1 (INI1) or SMARCA4 (BRG1) genes. Our aim is to review the AT/RTs diagnosed in our hospital.
Methods: We searched our database for every AT/RT diagnosed since the introduction of immunohistochemical staining for INI1 in our hospital (2013). For each case we studied age, sex, location and tumour extent, tumour size measured by magnetic resonance, histopathological patterns (including rhabdoid, small-cell, gland-like and spindle cell patterns), immunophenotype, follow-up time, treatment and outcome.
Results: We gathered 5 AT/RTs. Four of them were children (median age of 4,5 years; range 1-11 years) and one was an adult (46 years). Male-to-female ratio was 1:1,5. Median tumour size was 6,4 cm and cerebrospinal fluid dissemination was found in one case. Histopathological analysis always revealed a combination of patterns. Rhabdoid features were present in 4/5 cases, being the predominant pattern in one of them. Every case showed negative INI1 expression by immunohistochemistry. Three patients died (mean survival 43 weeks), one was lost to follow-up, and one of the paediatric patients (11 years) is still on follow-up after 72 weeks.
Conclusion: AT/RTs have a wide differential diagnosis. We emphasize the importance of considering AT/RT in heterogeneous tumours in paediatric population, especially in infants. Due to its low prevalence in adults, other INI1-negative tumours should be ruled out prior to diagnosing AT/RT and the performance of additional studies should be suggested. We present our experience willing to provide data for a better understanding of this uncommon entity generally associated with poor prognosis.

PS-09-004
Diffuse gliomas with non-canonical IDH mutations
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Background & objectives: The majority (90%) of IDH mutated diffuse gliomas carry IDH1 R132H mutation, while other (non-canonical) IDH1 or IDH2 mutations are rare. In this study, we aimed to analyse the histopathological features of diffuse gliomas with non-canonical IDH mutations.
Methods: We sequenced by Sanger IDH1/IDH2 genes in 89 IDH1 R132H immuno-negative diffuse gliomas and validated our findings using data in TGCA database.
Results: Diffuse gliomas with non-canonical IDH mutations were rare (3.3%). Non-canonical mutations in IDH1 were exclusive to astrocytic tumours, while IDH2 mutations were significantly more frequent, though not exclusive to, oligodendrogliomas ($P = 0.0019$). In oligodendrogliomas, IDH2 mutation was significantly associated with frontal lobe localization ($P=0.005$). Similarly to diffuse gliomas with IDH1 R132H mutation, those with non canonical IDH mutations were significantly more frequent in patients < 55 years ($P< 0.0001$) and had significantly better prognosis than IDH wt gliomas ($P< 0.0001$).
Conclusion: Non-canonical IDH mutations are mainly found in diffuse gliomas of younger patients and have prognostic significance similar to that of IDH1-R312H mutation. Non-canonical IDH1 mutations are exclusive to astrocytic tumours, IDH2 mutations associate with oligodendroglial histotype and frontal lobe localization.

PS-09-005
Clinicopathological characterisation of tumours of the pineal region (tpr): a case series
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Background & objectives: TPR are rare and present most frequently in children. Variable biological behaviour and histological features makes tumour grading a challenge. This case series aims to study the clinicopathological features of these tumours diagnosed at a Portuguese tertiary centre.
Methods: All cases of TPR diagnosed in our institution from 1999 to 2019 were retrieved from our files. Their clinicopathological features, including imaging, histology and imunophenotype, treatment and follow up (six years on average) were reviewed.

Results: We identified 24 TPR (16 males, 8 females; 19.8 years on average at diagnosis): eleven tumours of pineal parenchyma (six pineoblastomas, five parenchymal tumours of intermediate differentiation); four papillary TPR; four germ cell tumours; two embryonal tumours; one rosette-forming glioneuronal tumour and a pilocytic astrocytoma. Nineteen patients received radiotherapy, fourteen of whom had additional chemotherapy. Three patients had disseminated disease at diagnosis; four had craniospinal spreading on follow up (after 21 months on average). One patient died 23 months after the initial diagnosis. In our case series, recurrence and mortality were associated with disseminated disease at the time of diagnosis and high grade histology irrespective of tumour type.
Conclusion: The prognosis of TPR depends on the clinical factors and response to therapy, but also on the pathological features. However, further molecular characterization is essential to make an accurate diagnosis, establish prognosis, define therapeutic targets and predict therapy response.

PS-09-006

Embryonal tumour with multilayered rosettes; unusual stromal desmoplasia and extracranial extension; a case report and review of literature

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Background & objectives: Embryonal tumour with multilayered rosettes (ETMR), is a recently described very rare tumour entity included in the latest update of the WHO classification of tumours of the central nervous system.
Methods: A case of ETMR in the left frontal lobe in a 3-year-old girl with extensive extracranial extension and associated desmoplastic stroma. The child complained of seizure, vomiting and headache. MRI showed a huge heterogenous left frontal mass infiltrating the skull with extracranial soft tissue extension. The diagnosis of ETMR was established based on histopathologic, immunohistochemical and molecular features.
Results: Histopathologic examination showed a neoplasm composed of primitive small cells arranged in sheets with scattered multilayered rosettes with extensive foci of desmoplastic stroma. Immunohistochemistry was performed using panel of antibodies and revealed positive expression for synaptophysin, glial fibrillary acidic protein, Olig2, smooth muscle actin, and LIN28A. Molecular testing revealed focal amplification of the chromosome 19q13.42 microRNA cluster (C19MC) with breakpoints of the amplification immediately preceding the C19MC locus at the 5' boundary and within the TTYH1 gene at the 3' boundary, thus confirming the integrated diagnosis of ETMR, WHO grade IV. The other chromosomal copy number changes in the tumour were losses of interstitial 5q and portions of 10q.
Conclusion: Desmoplastic stroma can occur as a very rare and unusual histologic finding in ETMR due to tumour invasiveness with extracranial extension.

PS-09-007

Bifocal, anaplastic cerebellar liponeurocytoma with ABL1-L292M mutation

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Background & objectives: Cerebellar liponeurocytoma (cLNC) is a rare tumour of adults with no sex predilection. MRI/CT scan, with fat-suppressed views can support preoperative diagnosis. It is a WHO grade II, neurocytic tumour with lipomatous component, minimal atypia and low proliferative index.
Methods: The specimen was routinely processed, H&E-stained, then immunohistochemicaly stained for glial fibrillary acid protein (GFAP), neuron-specific enolase (NSE), synaptophysin, neuronal nuclear antigen (NeuN), S-100, neurofilament (NF), and Ki-67. Furthermore, the specimen was submitted for Next generation sequencing (NGS) analysis using TruSight solid tumour panel.The generated reads were aligned against the hg19/Genome Reference Consortium Human Build GRCh37.
Results: Here is a 41-year-old lady presented with headache and fever. MRI highlighted two contrast enhancing masses in both cerebellar hemispheres (3.2 x 2.6 x 2.3 cm and 1.9 x 1.6 x 1.2 cm). Gross total resections were performed, two months apart. Histologicaly, both tumours were similar. They showed sheets of monotonous neurocytic cells, admixed with fatty component. The tumour cells are positive for GFAP, Vimetin, Synaptophysin and Chromogranin, with weak focal expression of Neu-N, Desmin, and negative for EMA, ATRX, CD34, NFP and P53 immunostains. Anaplastic features and high Ki-67 (10%) were seen. NGS revealed ABL1-L292M mutation with alternate variant frequency of 5%. TP53, PTCH, CTNNB1 abnormalities were not detected.
Conclusion: We are reporting the fifth case of a multifocal cLNC in English literatures. Only a few other reports are describing cLNC with anaplasia, either as a tumour recurrence or with history of chemotherapy exposure due to other cancers. Limited data is available on the molecular genetic background of cLNC. There was no enough evidence in the literature to support the pathogenicity of the ABL1-L292M mutation detected in our case.

PS-09-008

Comparison of clinicoradiological and histological findings in 8 patients with radionecrosis following treatment of cerebral avms with stereotactic radiosurgery: a single institution case series

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Background & objectives: "Radionecrosis" is a poorly defined entity, occurring in 7.1% patients following stereotactic radiosurgery (SRS) for arteriovenous malformation (AVM).
We report an unmatched case series of 8 patients who underwent surgery for suspected Radionecrosis at our institution over a 15-year period.
Methods: Retrospective interrogation of prospectively captured records of eight patients that underwent symptomatic lesion resection following SRS treatment for AVM was carried out. Patient Demographics, AVM clinical/angiographic features and treatment modality prior to SRS were reviewed and compared with histopathological findings, paying note to presence of AVM, fibrotic response, necrosis and evidence of neoplasia.
Results: 75% of patients underwent embolisation prior to SRS, median time from embolisation to SRS was 18.5 months (1-45m). Median latency from SRS to Radionecrosis was 91.5 months (12-209m) Shorter latency in patients who underwent prior embolization. 100% had MRIT1 post-gadolinium enhancement. FLAIR-signal change was average 2.3 times the size of the enhancing lesion
All patients had angiographic confirmation of obliteration of AVM post SRS. 5 patients had evidence of AVM on histology. 2 patients were reported to have changes in keeping with suspicion of Radionecrosis, supported by presence of fibrinoid degeneration and gliosis. Gliosis was present in 5 patients, haemorrhage in 3. No patients had evidence of neoplasia.
Conclusion: The latency and histopathological classification of Radionecrosis following SRS for Cerebral AVM requires definition. Our case series demonstrates a latency of 7.5 years. The heterogenous nature of the histology and presence of active AVM despite radiological obliteration requires further interrogation.

PS-09-009

Glioblastoma with extracranial metastasis – case report and genetic analysis

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Background & objectives: Glioblastoma (GBM) is aggressive brain tumour with low rates of extracranial metastases, affecting only 0.4 – 0.5% of patients. Molecular alterations in GBM are well described but there is only limited understanding of alterations associated with metastatic potential of GBM.
Methods: A case report of 44-year-old woman with left frontal GBM (IDH wildtype), surgically resected followed by standard chemoradiation. Five month after surgery, the patient was diagnosed with extracranial intraspinal metastasis, with no signs of intracranial tumour recurrence. Next generation sequencing analysis of both primary and metastatic GBM tissues was perfomed using Illumina TruSight Tumour 170 assay and NextSeq 500 sequencer.
Results: The number of the single nucleotide variants (SNVs) observed in the metastatic sample was more than 2-times higher compared to the primary GBM. Mutations in TP53, PTEN and RB1 observed in the both samples are indicative for mesenchymal subtype of GBM. Among others, there were two inactivating mutations (Arg1026Ile, Trp1831Ter) in the NF1 gene and two novel NOTCH3 variants of unknown significance predicted to be damaging (Pro1505Thr, Cys1099Tyr) detected only in the metastatic sample.
Conclusion: Based on the literature evidence, inactivation of NF1 and NOTCH3 could explain, at least in part, acquired invasiveness and metastatic potential in this particular GBM case. Further data are warranted to confirm these findings.
This work was supported by Grant Agency of Masaryk University (MUNI/A/1429/2019) and the Czech Health Research Council project NV18-03-00398.

PS-09-010

Apoptosis of neurons in the hippocampus in rats during septoplasty modelling

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Background & objectives: Damage to the nasal septum when modelling septoplasty in rats blocks the peripheral link of the olfactory analyser is also damaged. Objective:to study the effect of modelling septoplasty in rats on the activation of apoptosis of neurons in the hippocampus.
Methods: The mucous membrane of the nasal septum in rats was scarified over its entire length in 20rats under anesthesia. Brain sections were stained 2&4days after surgery with mouse anti-p53 antibodies. Apoptotic neurons in each hippocampal subfield (CA1,CA2,CA3&DG)in the pyramid layer was calculated over a length of 574.3±13.5μm and a width of121.94±31.5μm. The results obtained were compared with a control group(CG,10rats).
Results: On the 2nd day, more apoptotic neurons were detected in the hippocampal subfields CA1, CA2, CA3 (35.54±2.31, 38.91±3.05, 24.09 ±3.65), respectively, compared with CG (10.77±1.68, 11.54±2.04, 9.66 ±2.12, respectively) ($p < 0.001$). On the 4th day, p53-positive neurons decreased compared to the 2nd day (26.13±2.78, 31.27±2.43, 18.85 ±2.99) ($p < 0.01$), but there were more of them than in the CG ($p < 0.001$).
Conclusion: The septoplasty modelling in rats provokes an acceleration of triggering of apoptosis mechanisms of hippocampal neurons in the CA1, CA2, CA3 subfields.
This work was supported by a grant from the Medical Institute of RUDN University No. 031823-0-000.

PS-09-012

Inflammation and macrophage imbalance as risk factors for rupture in saccular intracranial aneurysms

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Background & objectives: Mechanisms leading to rupture of saccular intracranial aneurysms (IA) are still insufficiently described. Based on our findings from preliminary study, we compared structural and inflammatory changes in the aneurysmal walls between unruptured and ruptured IAs from updated set of patients.
Methods: Samples of 41 aneurysms resected after clipping (ruptured n = 14; unruptured n = 27), and 11 control samples of analogous regions of the circle of Willis were included to this study. For each sample we evaluated structural changes, and quantified lymphocytes, as well as M1 and M2 subtypes of macrophages using immunohistochemistry (anti-LCA, anti-HLA-DR, and anti-CD163, respectively).
Results: The absence of the internal elastic membrane was observed in both, ruptured and unruptured aneurysms. The presence of organized thrombus and severer fibrosis of vessel wall was more frequent in ruptured IAs. The inflammatory infiltrate was significantly smaller and the M1 subset prevailed among the macrophages in unruptured IAs. In the ruptured IAs, there was significantly more intense lymphocytic infiltration, and ratio of M1/M2 was almost balanced. Neither structural nor inflammatory changes were observed in controls.
Conclusion: Our findings suggest that chronic inflammation along with decreasing of the M1/M2 macrophages ratio may play a role in the progression of cerebral aneurysms to rupture.
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PS-09-013

Clinical relevance of BRAF V600E mutation status in brain tumours: a review of evidence and directions for the management

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Background & objectives: Despite limitations imposed by the blood-brain barrier, heterogeneity and adaptive tumour resistance, the possible application of BRAF-targeted therapy in brain tumours grows continuously. In this study, we explore the relationship between BRAF mutations and prognosis following the accesible treatment options.
Methods: We analysed clinical strategies that address BRAF activation in primary brain tumours. Next, we verified current recommendations regarding screening for BRAF mutations and discussed issues that need to be solved before implementation of the treatment.
Results: There is preliminary evidence for a range of positive responses in certain brain tumour types harboring BRAF V600E mutation. We selected groups of patients, in which the immunohistochemical screening should be considered. Finally, we portrayed how these patients might benefit from targeted therapy.
Conclusion: BRAF V600E mutation emerges as a promising molecular target. Herein, we propose workup and treatment algorithm for primary brain tumours with the particular emphasis on BRAF V600E mutation.

PS-09-014

An embryonal tumour with NUT expression and CIC-NUTM1 rearrangement mimicking desmoplastic infantile astrocytoma (DIA) – unsolved diagnostic boundaries

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Background & objectives: DIA is a rare grade I central nervous system (CNS) tumour usually following a favourable course regardless of a possible poorly differentiated component. Conversely, grade IV poorly differentiated/embryonal tumours (ET) include the NOS category (ET,NOS) sometimes exhibiting limited glial differentiation.
Methods: We describe a case highlighting challenging differential diagnostic problems between DIA and ET,NOS. The tumour pertains to an 1 year-old child that presented with apathy and de novo strabismus associated with a large frontoparietal mass whose imagiologic features were consistent with DIA. Total gross ressection was performed.
Results: Histologic exam showed a tumour comprising: a) desmoplastic areas with mature spindle astrocytes (GFAP positive) surrounded by a dense reticulin network and pericellular collagen IV (DIA-pattern); b) a poorly differentiated component (GFAP negative) of small round blue cells. Mitotic figures were restricted to poorly differentiated areas; microvascular proliferation and necrosis were absent. A diagnosis of DIA was made. Recurrence with aggressive progression within few weeks led to comprehensive genomic profiling that revealed a CIC-NUTM1 rearrangement. Additional immunohistochemical study showed strong NUT expression within both DIA-patterned and poorly differentiated components. The tumour was reclassified as ET,NOS with extensive mature astrocytic differentiation in a DIA-like pattern, a feature not previously described.
Conclusion: ET,NOS harbouring CIC-NUTM1 rearrangements may exhibit extensive astrocytic DIA-like differentiation, blurring diagnostic boundaries with "true" DIA, a differential diagnostic problem not previously addressed. NUT immuno-expression may be diagnostically useful in identifying these cases. DIA-patterned tumours may need molecular workup for appropriate classification/management.

PS-09-015
Retrospective observational study of gliosarcomas
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Background & objectives: Gliosarcoma (GSM) is a variant of glioblastoma IDH-wiltype, characterized by a biphasic pattern, with areas of glial and mesenchymal differentiation. Our objective is to describe the population and results obtained in a cohort of patients with GSM.
Methods: We conducted a retrospective observational study from 2010 to 2019, of patients with GSM over the total glioblastomas (GBM) in that period, reviewing the clinical histories and histopathological characteristics. In one of them a molecular genetic analysis (NGS) is carried out.
Results: We reviewed 8 GSM out of a total of 238 GBM (3.3%). 5 women and 3 men with a mean age at diagnosis of 57 years. At debut, the most frequent symptoms were behavioural disturbance, motor and sensory deficit. The temporal localization was the most frequent (87%) and all tumours were more than 3 cm in size, necrosis and oedema in MRI. Complete resection in one of them. 100% IDH-wildtype and 75% EGFR-negative tumours. One patient completes the entire treatment and 63% have progression. The molecular genetic analysis is performed in one of the cases, in which the result was an imbalance in NTRX1.
Conclusion: There is a great shortage of studies on GSM due to its low incidence, hence the importance of molecular study to identify target alterations that help improve the prognosis and quality of life of these patients.

PS-09-016
Globular glial tauopathy type I presenting as atypical progressive aphasia, with comorbid limbic-predominant age-related TDP-43 encephalopathy
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Background & objectives: Globular glial tauopathies (GGT) have heterogeneous presentations with little available information regarding typical clinical manifestations. We report on a case of atypical primary progressive aphasia due to comorbid GGT and limbic TDP-43 proteinopathy.
Methods: The initial clinical phenotype of a 69-year-old, right-handed man was compatible with the nonfluent-agrammatical variant of primary progressive aphasia and early hippocampal amnesia. Progressively, parkinsonism and supranuclear oculomotor impairment occurred, and finally, late mutism with frontal type dementia, impaired comprehension, and behavioural manifestations developed.
Results: The neuropathology was characteristic of globular glial tauopathy type I with vascular changes and comorbid limbic-predominant age-related TDP-43 encephalopathy (LATE).
Conclusion: Our findings expand the clinical spectrum of globular glial tauopathies to include a complex progressive aphasia syndrome. The extraordinary feature, in this case, was the combination of two progressive aphasia subtypes, i.e., the early nonfluent-agrammatical variant and the late semantic variant. Our findings also expand the spectrum of neuropathological comorbidities in GGT.
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PS-09-017
Carbonic anhydrase IX expression in high grade astrocytomas
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Background & objectives: Carbonic Anhydrase IX (CAIX) expression has been associated with a negative overall survival (OS) in Grade III-IV astrocytomas (AA+GBM). The effect of IDH status on CAIX status with regards to OS in AA+GBM is relatively unexplored.
Methods: 748 AA+GBM were examined prospectively over 7 years by IHC for CAIX Labeling Index (LI%), Ki-67 LI%, MGMT promoter methylation (PM), EGFR LI%, EGFRvIII LI%, VEGF LI% and VEGF-R2 LI%; 602 Grade IV (GBMs) and 146 Grade III (AA) were studied.
Results: Mean age was 55 years. 502 AA+GBM were newly diagnosed (ND) and 246 were recurrent (RD). CAIX expression (defined as CAIX LI>5%) was identified in 456 GBM (76%) and 32 (22%) AA. IDH status performed on 222 AA+GBM (30%) revealed 197 wild type (AA+GBM IDH1 mutated n=25). IDH WT AA+GBM exhibited a higher median CAIX LI%. Only in GBMs was Ki-67 LI correlated with CAIX expression.
Conclusion: In AA+GBM, VEGF LI%, VEGFR2 LI%, and EGFRvIII LI% correlated with CAIX expression. The correlation between CAIX and VEGFR2 LI% was independent of grade. Among GBM, factors associated with an adverse OS were MGMT PM and age. Among AA, factors associated with an adverse OS were CAIX, Ki67 LI% and age. CAIX negative AA have a prolonged survival not seen with CAIX positive AA and all GBM. CAIX expression is useful in characterizing prognosis in AA+GBM.

PS-09-018

Histomorphological spectrum and trend of neoplastic spinal lesions: a 40-year review

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Background & objectives: Neoplastic spinal lesions cause significant morbidity with poor neurological outcome in many patients. Studies describing their spectrum are generally few. Our objective was to determine the histomorphological spectrum of neoplastic spinal lesions and the trend in occurrence over four decades.
Methods: We reviewed Patients' age, gender and histomorphological data of all the neoplastic spinal lesions from the patients' hospital records over a 40-year period (January 1st, 1980 to December 31st, 2019). All the cases seen were classified as either benign or malignant neoplasms with their spectrum, frequencies and trends in decades determined using Statistical Package for Social Sciences (SPSS), version 20.
Results: Ninety-four cases of neoplastic spinal lesions were seen over the four decades of study with the highest number of cases observed in the last decade. The male to female ratio was 1.2:1. The mean age was 34.8 years with a peak incidence in the 5th decade. Benign and malignant spinal neoplasms comprised 55.3% and 44.7% respectively. Meningiomas and peripheral nerve sheath tumours had the highest occurrences (16% each), while germ cell tumours had the least occurrence (2.1%). Other spectrum of spinal tumours seen include metastatic tumours (14.9%), soft tissue tumours (14.9%), haemato-lymphoid tumours (9.5%), glial tumours (8.5%), bone tumours (7.5%), Vascular tumours (5.3%) and neuronal tumours (5.3%).
Conclusion: This study showed that benign spinal tumours are more common than malignant spinal tumours, with a slight male predominance and most of the spinal tumours occurring below 50 years. The increased number of spinal tumours observed in the last decade of study may be due to an increase in skilled personnel and improved diagnostic facilities in our health institution in addition to rising awareness of disease among the populace.

PS-09-019

Two rare cases of IDH1-mutated gliosarcomas arising in IDH1-mutated, 1p/19q non-codeleted diffuse gliomas with prominent oligodendroglial morphology

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Background & objectives: Gliosarcomas may arise de novo or represent tumour progression in previously diagnosed diffuse glioma. Majority of gliosarcomas are IDH1/2 wildtype and mutated tumours are rare. Here we present two such cases.
Methods: Two males (case 1 - age 49, case 2 -age 39) were diagnosed with IDH1-mutated diffuse gliomas in left temporal (case 1) and left frontal (case 2) area. They recurred as gliosarcoma after 6 and 5 years respectively. Gliosarcomas and concurrent/precursor gliomas were studied using immunohistochemistry (IDH1 R132H, ATRX, GFAP, Olig2, SOX10, p53) and FISH (1p/19q probes).
Results: Both tumours showed conspicuous oligodendroglial morphology in glioma component. In both primary gliomas, immunohistochemistry showed expression of IDH1 R132H and ATRX and these were also expressed in sarcoma components. In case 1, repeated FISH showed no 1p/19q codeletion. In case 2, partial deletion of 1p (in 40% of cells) without loss of 19q was detected. Sarcoma components showed positive reticulin stain, loss of Olig2 expression and loss of GFAP expression in majority of tumour cells. Mutant-type (strong and diffuse) p53 expression was observed in both gliosarcomas, but not in the glial component of case 2. In case 1, 50% of cells of original glioma showed p53 expression.
Conclusion: We report two IDH1-mutated gliosarcomas, arising in IDH1-mutated/ATRX-positive gliomas with oligodendroglial morphology and lack of 1p/19q codeletion. In one case, mutant-type p53 expression was acquired in sarcomatous component during progression of the tumour.
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PS-09-020

The role of skeletal muscle biopsy in the diagnostic algorithm of anti-signal recognition particle myopathy

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Background & objectives: Myopathies with serum antibodies to the signal recognition particle (anti-SRP) represent a rare category of refractory immune-mediated necrotizing myopathies. Muscle biopsy, along with immunological and clinical data may provide key information in understanding the pathological mechanisms of these controversial diseases.
Methods: Open muscle biopsy was performed on 42 patients with suspected inflammatory myopathy during the year 2019 in our hospital. We evaluated the main pathological features using histological, immunohistochemical, enzyme histochemical techniques, routine and special stains on cryosections and paraffin-embedded tissue. Among them, we identified 3 patients (7%) with myopathology suggestive for anti-SRP myopathy. Anti-SRP antibodies were further tested positive.
Results: Muscle biopsies showed the picture of a severe active necrotizing myopathy with marked variability in size of the fibres, numerous necrotic and regenerating fibres and rare scattered mononuclear cells in all three cases. ATPase staining showed type 1 fiber predominance myopathic pattern with a reduced size of type 2 fibres. Immunomarking with MHC Class I antibody showed a rather unexpected prominent expression in non-necrotic fibres in two cases and normal expression in the third one. Differential diagnosis with other types of inflammatory myopathies, especially dermatomyositis, polymyositis, and anti-HMGCR myopathy, even with muscle dystrophies proved sometimes to be challenging because of the similarity of both clinical and morphological aspects.
Conclusion: Anti-SRP myopathy is a distinct entity in terms of clinical traits, biopsy changes and response to conventional combined immunosuppressive therapy. Histopathology of muscle, along with complementary investigation, may provide useful clues regarding the correct diagnosis, in deciphering the mechanisms of this disease with a major impact on clinical management of this potentially life-threatening disease.

PS-10 Paediatric and Perinatal Pathology

PS-10-001

Composite hemangioendothelioma - a clinicopathological study of site, composition and immunohistochemistry of an additional series

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Background & objectives: Composite Hemangioendothelioma (CHE) is a recently described new entity classified under the Hemangioendothelioma group of vascular tumours, it was first described in 2000 by Nayler et al, and it is a rare vascular neoplasm of low malignancy that exhibits a composite of hemangioendothelioma variants. It usually presents on the skin and soft tissue of upper and lower extremities,

especially the lower leg and foot. We describe additional series of CHE in paediatric age group.
Methods: Three cases of CHE were retrieved from our archives. Blocks were cut and stained with H&E. Immunohistochemical stains were done using DB Biotech protocol. Antibodies used include CD34, EMA and vimentin
Results: All cases of CHE encountered in this study were in the paediatric age group that is 8, 10 and 14 years respectively. The sites of presentation of CHE were head and neck, upper and lower extremities. Histology showed composite of hemangioendothelioma variants that is, Dabska, retiform, epitheloid and spindle cell haemangioma in varying proportions with brisk mitosis seen. All were positive for CD34 and vimentin but negative for EMA.
Conclusion: CHE can present with composite of hemangioendothelioma variants. In our environment this vascular lesion of low malignant potential is mostly seen in the paediatric age group. No recurrence was seen after one year of follow up.

PS-10-002
Correlation between histology and genetic testing in surfactant dysfunction disorders
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Background & objectives: Genetic surfactant dysfunction disorders are rare paediatric conditions. Three major genes are involved in their pathogenesis (ie *STFPB*, *STFPC*, *ABCA3*). Histologically, several patterns may be observed, and although suggestive for one of these disorders, they are not specific.
Methods: 10 patients with a positive genetic testing were identified. We blindly reviewed their biopsies (H&E, trichrome, PAS, SMA, CK7 and CD68 stains), recording the main histological findings according to a previous set list of items. Electron microscopy (EM) findings were also assessed, when available. The collected information was correlated with the corresponding mutation. Finally, we revised the clinical outcomes.
Results: 6 patients were female and 4 male, aged 0 to 11 (mean 1.6 years). The most common mutation was *SFTPC*(50%), followed by *ABCA3*(40%) and *SFTPB*(10%). All the biopsies presented features of chronic pneumonitis of infancy (CPI), with alveolar simplification, thickened septa and type II pneumocyte hyperplasia. All the cases with *ABCA3*mutation showed the most prominent fibrosis and muscularization of the septa. The histology in *SFTPC*mutated cases was more variable. The only patient with a *SFTPB*mutation died shortly after birth (3 weeks), presenting an unspecific histology. Electron microscopy was available in 3 cases, yielding a definite diagnosis in 2 of them.
Conclusion: Surfactant dysfunction disorders present histologically as CPI, but the accompanying morphological findings are variable. The most relevant finding is the marked fibrosis and muscularization of the alveolar septa in *ABCA3*mutated cases. *SFTPB*is reportedly the most severe of the mutations, as seen in our series. EM is helpful in achieving a definite diagnosis.

PS-10-003
The role of placental examination in evaluating perinatal death: a retrospective analysis of 192 cases
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Background & objectives: Most common causes that lead to intrauterine foetal death are the placental abnormalities. The aim is to analyse how many of the intrauterine/ perinatal deaths present morphological changes in the placenta and which are the associated clinical-pathological factors.
Methods: We have retrospectively analysed all placentas sent to the Pathology Laboratory from the Maternity of Oradea (Romania) during December 2018 - June 2019 from a clinical, macroscopic and microscopic point of view. We reassessed and compared the "sick" placentas (those with worse foetal outcome) with the "healthy" ones.
Results: 197 placentas were sent for histopathological examination. Of the autopsies performed during the same period, 22 had the placenta examined. The analysis of the association between the sick and the healthy placentas reveals statistically significant differences regarding education ($p = 0.01$), the type of birth ($p = 0.0002$), the gestational age ($P < 0.0001$), the aspect of amniotic membranes ($p = 0.011$) and placental anomalies ($p = 0.0012$).
Conclusion: The low socio-economic status and prematurity are the risk factors associated statistically with a higher rate of adverse foetal outcome. Placental abnormalities, infections, and placental abruption are most commonly noted. A systematic histopathological analysis of the placenta is imperative in order to more accurately assess the causes of death and to reduce the rate of unexplained deaths.

PS-10-004
Identification of SRF-STAT6 fusion transcript in a cellular myofibroma of the forearm in a 15 years old boy: expanding the molecular spectrum of the recently described entity
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Background & objectives: The spectrum of mesenchymal tumours keeps increasing with the input of NGS. Recently myofibroblastic tumours arising within deep soft tissue with high cellularity and a more differentiated immunophenotype towards myoid lineage have been described harbouring a recurrent SRF-RELA fusion.
Methods: We report the case of a 15 years-old patient who presented with a calcified soft tissue mass of the left forearm. Histological features and unpreviously reported genetic data are described.
Results: Microscopic examination showed a fascicular proliferation mainly composed of spindle cells with variable eosinophilic cytoplasm. Areas with higher cellularity with basophilic cells were also found giving a biphasic appearance. Tumour stroma contained calcifications. There were no necrosis and mitotic index was 1 mitosis/50HPF. Cells stained for alpha smooth actin, H-caldesmon and desmin. Whole RNA-sequencing identified SRF-STAT6 fusion that joined SRF exon 5 to STAT6 exon 17. STAT6 immunohistochemistry was positive.
Conclusion: We have described a new variant of SRF-rearranged neoplasm. This case shared histological features with the recently described group of SRF-rearranged myofibroblastic neoplasms but involved STAT6 as a 3' partner, which resulted in a strong nuclear expression of STAT6, a potential diagnosis pitfall with solitary fibrous tumours. The clinical relevance of this novel fusion requires further investigations.

PS-10-005
Histological chorioamnionitis in placentas of extremely premature neonates: the impact of maternal and foetal inflammatory responses on clinical findings and neonatal outcome
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Background & objectives: The aim of this study was to explore if placental histological chorioamnionitis (HCA) with or without a foetal inflammatory response (FIR) differ in clinical findings and neonatal outcomes in a group of extremely premature (EP) neonates.

Methods: Singleton neonates with gestational age (GA) < 28 weeks and HCA at placental examination were included in the study. Data on maternal history, delivery, neonatal course, and placental findings were recorded prospectively. Staging of the inflammatory responses was performed in accordance with the Amsterdam Placental Workshop Group Consensus. A multivariate logistic regression model was used for prediction of neonatal outcomes.
Results: Of 84 included cases, 59 (70%) had FIR. FIR was associated with preterm prelabour rupture of membranes (PPROM) (p=0.002), clinical chorioamnionitis (CCA) (p=0.003), use of antibiotics before/during birth (p<0.001), antenatal steroids (0.008), higher neonatal leucocyte levels (p<0.001), and bronchopulmonary dysplasia (BPD) (p=0.007). No significant association was found for other common neonatal complications of extreme prematurity. After adjusting for GA and birth weight (Z-score), babies of mothers with clinical chorioamnionitis (CCA) had increased odds of neonatal death (OR=10.75, p=0.007). Surprisingly, FIR seemed to have a protective effect (OR=0.15, p=0.036) on mortality.
Conclusion: In a group of EP neonates with HCA, FIR was significantly associated with PPROM, CCA and BPD. CCA increased the odds of infant death during the first year, but a foetal inflammatory response seemed to have a protective effect.
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PS-10-006
A histopathological study of paediatric teratomas in Khartoum state 2010-2018
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Background & objectives: To study the histological spectrum of teratomas and clinical presentation in paediatric patients presenting in Khartoum State hospitals.
Methods: Paediatric teratoma cases that underwent surgery at the main state hospitals in Khartoum State during the period from 2010 to 2018 were enrolled in a retrospective analytical study. The case slides were reviewed and correlated with the clinical data submitted.
Results: A total of 60 cases were included of which 82% were females and 26.7% were less than one year of age and 56.6% were 6-16 years of age. The main presentation was a mass. The site of origin was the ovaries in 57% (49), sacrococyx in 25%, abdomen in 8.3%, pelvis in 8.3%, head and neck in 6.7%, chest in 3.3% and testis 0.9% (1). Mature teratomas accounted for 81.7%, mixed teratomas for 13.3% and 5% were immature. Altman class I was the main classification in 53.3% of sacrococcygeal teratoma cases. Immature grade 3 was the predominant (62.5%) with neural component the commonest (71.4%).
Conclusion: Presentations were diverse regarding age, location, gross features and degree of differentiation. Mature teratomas predominate and the majority of the sacrococcygeal teratomas were mature in females less than one year of age.

PS-10-007
Epidemiology of children and adolescents served in burning ambulatory in Brazilian public hospital
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Background & objectives: Among domestic injuries in children and adolescents, skin burns deserve special attention because they can lead to serious residual injuries.In adolescence, alcohol burns are the most common. Describe the epidemiological profile of hospitalizations of children and adolescents who suffered burns.
Methods: A cross-sectional descriptive study analysed hospitalizations between 2013 and 2019, regarding gender, age, severity of injury and causative agent. The data on the care provided at the Burn Clinic in a reference hospital in the Northeast of Brazil.
Results: During the study period, 2.564 patients were admitted, of which 1.433 were children between 4 and 12 years of age and 1.131 adolescents between 12 and 19 years of age. The odds ratio among children and adolescents was (OR = 1.5; CI 1.3-1.7) and boys are (OR = 1.3; CI 1.2-1.4) times more likely to suffer burns than girls. Among adolescents, the prevalence of burns is higher among girls (59.6%) (OR = 1.2 CI 1.1 - 1.4). Liquids were responsible for most accidents and adolescent girls are more likely to suffer burns with liquids when compared to boys in the same age group (OR = 1.6; CI 1.32-2.0).
Conclusion: The epidemiological surveys provide objective information on dangerous agents and on the profile of the populations where burns are most likely to occur. They are essential for the development of appropriate prevention strategies.

PS-10-008
Value of autopsy examination in early neonatal death: report of 4 unusual cases
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Background & objectives: Early neonatal death (ENND) is defined as newborn´s death in the first week of life. We present the unexpected autopsy findings in four cases of ENND that can change the clinical tenders and the Genetic counselling.
Methods: Gross and histopathological findings of four ENND post-mortem examinations.
Results: The four cases included 3 newborn males and 1 newborn female, aged between 25' and 3 days old. The causes of death were clinically unexpected and clearly assessed by the post-mortem examination: extralobar pulmonary sequestration, cardiac malformation, iatrogenic pericardial effusion and thymus hypertrophy with heart compression. None of them were previously diagnosed.
Conclusion: Although the main causes of ENND are perinatal asphyxia, low birth weight/prematurity, and infections, a few unexpected congenital malformations or other causes are detected when a systematic autopsy examination is performed. These unusual cases highlight the importance of a minicious post-mortem examination in ENND, its important role in the knowledge of neonatal pathology and its contribution for Genetic counselling.

PS-10-009
Foetal autopsies, a retrospective study in a tertiary institution
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Background & objectives: Foetal neoplasias are rare and have a poor prognosis. They can be associated with death and are an indication for termination of pregnancy. A diverse range of tumours affecting foetuses have been described.
Methods: We conducted a retrospective study at a tertiary hospital in Portugal – Centro Hospitalar e Universitário de Coimbra, and reviewed 1482 cases of autopsied foetuses.
A description of each case correlating with the gestational age, placenta histology, karyotype and ecographic findings was made.
Results: We have identified 10 foetal autopsies with neoplasias out of 1482 autopsies (0.67%). 60% were benign and the remaining malignant. The following tumours were found: cervical lymphangioma (n=4),

choroidal plexus papilloma (n=2), neuroblastoma (n=1), embryonal tumour with abundant neuropil and true rosettes (n=1), immature sacrococcygeal teratoma (n=1) and diffuse astrocytoma (n=1). 60% of the autopsies were result of termination of pregnancy and 40% resulted from intrauterine death.
Conclusion: In this study, we concluded that histologically benign tumours can also result in intrauterine death as the location, size and other factors influence the clinical outcome. Foetal tumours are different from childhood' tumours in their distribution, incidence and clinical outcome.

PS-10-010
Morphological defects in distal 18q deletion syndrome: a case report
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Background & objectives: There are two groups of 18q deletions: within the bottom half of the centromere (distal deletions) and closer to the centromere (proximal deletions). Distal 18q deletion syndrome can lead to a wide variety of signs and symptoms among affected individuals.
Methods: We report the case of a 35-year-old female admitted to the Department of Obstetrics-Gynaecology with a 21-weeks pregnancy featuring multiple cerebral and cardiologic malformations detected on foetal MRI. The multidisciplinary commission recommended therapeutic abortion with subsequent genetic analysis and the patient agreed. The product of conception, placenta and umbilical cord were sent to the Department of Pathology for histopathological evaluation.
Results: The most striking morphological defects were the presence of right cleft lip, bilateral anophthalmia with wide nasal base and low implantation of the ears. The eyelids appeared normal, but the lachrymal puncta were absent. Palpebral apertures were sealed and no vestigial ocular globe was identified. Orbital cavities were smaller than normal. A perimembranous ventricular septal defect measuring 0.3 x 0.2 cm with overriding aorta was also present. A modified female profile with a loss of genetic material was identified on chromosome region 18q21.1-18q23 with the size of 30.5 Mb. According to the databases, this region is responsible for deletion syndrome 18q, which presents with a clinically variable picture.
Conclusion: The most common phenotypic aspects of distal 18q deletion syndrome are small stature, intellectual disabilities, learning difficulties, hypotonia, hearing problems, microcephaly, cleft lip and cleft palate, foot abnormalities and heart malformations.

PS-10-011
Childhood and adolescent malignant solid tumours in Rwanda: distribution of tumour types and challenges to diagnosis
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Background & objectives: Data on paediatric tumours are very scarce in Rwanda. The goal of this study is to determine the distribution of childhood and adolescent malignant solid tumours in Rwanda and to shed light on the pathology-specific limitations to their diagnosis.
Methods: In this retrospective, descriptive multicenter analysis, we collected cases of solid malignant tumours diagnosed in patients aged 0-18 years from four regional hospitals over a 3-year period (2016 to 2018). Tumours were classified using the International Classification of Childhood Cancers (ICCC). All cases were then analysed in terms of age, age group, gender, residence, morphological features and immunophenotype, where possible.
Results: This study revealed that the most common solid tumours in children and adolescents diagnosed in Rwanda were retinoblastoma, followed by nephroblastoma, rhabdomyosarcoma, and osteosarcoma. The most common tumours by category were retinoblastoma (25%), soft tissue sarcomas (20%), renal tumours (18.5%) and bone tumours (14%). These tumours were more frequently seen in children between 1 and 4 years of age and were less frequent in infants. There was a slight male predilection (M/F ratio = 1.18). Among the cases where staging information was available, most patients presented at early stages; however, staging was not applicable or not provided for most cases (83.5%). Diagnostic immunohistochemistry was not performed in 46.1% of cases.
Conclusion: In slight contrast to other studies of paediatric malignant solid tumours in the region, our study showed the most common paediatric tumour was retinoblastoma. Specialty-trained pathologists and diagnostic tools such as immunohistochemistry are paramount for accurate diagnosis of paediatric tumours.

PS-10-012
Peripheral medulloepithelioma: two cases report
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Background & objectives: Medulloepithelioma is an extremely rare, of high malignancy embryonic tumour, generally located in the eye or in the central nervous system; a peripheral location is even rarer and will be the subject of our report.
Methods: We report two cases of female children; 30 months and 8 years old with a pelvic mass. Imagery found a secondary hepatic nodules in one of the two cases.
Histologically, it showed a proliferation of embryonic appearance of papillary, tubular and rosette architecture expressing CKAE1/AE3; CD56; WT1 and synaptophysin, without expression of CD99, AFP, CD30, Oct3 / 4 and BHCG.
Results: Medulloepithelioma is an embryonic tumour classified in the subgroup of primitive neuro-ectodermal tumours. It is a rare and highly malignant tumours made up of undifferentiated cells resembling germ or matrix cells of the embryonic neural tube.
These tumours most often survive during the first decade of life and have specific radiological, histological features.
It is most often found in the nervous system and in the eye.
Peripheral locations are extremely rarely known.
Treatment is based on chemotherapy, surgery and radiotherapy, targeted anti-PDGFR therapies are being evaluated.
Conclusion: We report two paediatric cases of peripheral medulloepithelioma.
Since this entity is rare with an unusual location, peripheral medulloepithelioma requires a correct diagnosis and proper classification to predict the clinical behaviour and for optimal management.

PS-10-013
Cardiomyopathy in paediatric autopsy: the importance in the diagnosis after death
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Background & objectives: Cardiomyopathy is defined as a myocardial disorder in which the heart muscle is structurally and functionally abnormal, without a cardiac malformation.

Our objective was evaluate cardiomyopathies in paediatric autopsies (PA) and correlate with genetic studies performed for further counselling.
Methods: We retrospectively reviewed the PA performed in a third care centre in Portugal between 2007 and 2019, contemplating those with heart disease (excluding heart malformations) and correlate with ultrasonography results and with the genetics reports when possible.
Results: From 2007-2019, were performed 1482PA. Four have a cardiomyopathy (0,23%), including one female and three male; one was a stillbirth death (29weeks, with normal ultrasonographic evaluation at 21weeks), two neonatal deaths (one peri-partum, other at 7hours of life) and one with 5months old.
The autopsy findings describe two dilated cardiomyopathy (one endocardial fibroelastoses) and two hypertrophic, without any evidence that could point a diagnosis, principally storage diseases.
One case had performed echocardiographic study (consistent with the autopsy findings).
There was family history of heart related disease in two and only in one of them was found a deletion (c.94316_94317del (p.Val31439Alafs*), classified as probably pathogenic in TTN gene, in heterozygosity.
Conclusion: Cardiomyopathy in children can be a diagnostic challenge, even after the autopsy. But due to the possibility of genetic cause, it is important to put our efforts in the correct diagnosis to provide guidance for the family and future generations.

PS-10-014
Expression of VEGF and its receptors in placental villi in early and late preeclampsia
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Background & objectives: Preeclampsia is formidable complications of pregnancy. An important role in the development of preeclampsia is assigned to violations of the expression of angiogenic factors. A comparative analysis of VEGF expression and its receptors in early (EPe) and late (LPe) preeclampsia.
Methods: We performed complex morphological and immunohistochemical study of 9 placentas from EPe cases, 14 placentas from LPe cases and 10 term placentas from uncomplicated pregnancies (control group). VEGF expression and its receptors (VEGFRs -1 and -2) in syncytiotrophoblast and endothelium of capillaries of terminal villi were detected by immunohistochemical methods.
Results: As a result of an immunohistochemical study, we identified changes in the expression levels of VEGF and its receptors in the structures of terminal villi in EPe and LPe.In the EPe observations, expression levels of VEGF and VEGFR-2 in syncytiotrophoblast and capillary endothelium were lower than in the control group.VEGFR-1 expression levels were slightly lower than control values.Similar changes were detected in the LPe, but the degree of deviation from the control levels were less.
Conclusion: The detected changes of VEGF and its receptors expressions indicate violations of angiogenesis in the placental villi. More pronounced changes in EPe reflect the features of the damage pathogenesis and compensatory processes in the placenta with various forms of preeclampsia.

PS-10-015
Unsuspected myocarditis presenting as sudden death in infants and children
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Background & objectives: Acute myocarditis is an inflammatory disease of the heart mostly diagnosed in young people which can present as sudden death. The aetiology includes infectious agents, systemic diseases, drugs and toxins. We aim to characterise myocarditis in infants and children.
Methods: Retrospective evaluation of 813 paediatric post-mortems conducted at Sheffield Children's Hospital between 2009-2019. Data retrieved included histological features, virology, microbiology and clinical history.
Results: 23c of 813c corresponded to acute myocarditis (2.7% incidence) and 1c to a dilated cardiomyopathy related to undiagnosed remote Parvovirus infection. Most cases were below 2 years age. Histological features showed diffuse myocardial inflammation in 15c, focal in 8c and none in dilated cardiomyopathy. PCR identified Enterovirus (7c), Parvovirus (7c, 2 also with HHV6 and 1c with EVB), Influenza A (1c), Parainfluenza type 3 (1c). 2c were hypersensitivity myocarditis, 1c was Group A Streptococcus related and 5 idiopathic myocarditis.
Enterovirus was frequent in infants (7/10), and in new-borns was associated to meningoencephalitis or congenital myocarditis.
Presenting symptoms included vomiting, abdominal pain (2-3 days) and breathing difficulties (up to 10 days).
Conclusion: Myocarditis represents almost 3% of all sudden deaths in infants and children. Enterovirus and Parvovirus represented the most common aetiologies. Although patients experienced preceding viral symptoms, all remained clinically unsuspected, highlighting the need for clinical awareness of this condition.

PS-10-016
Malignant childhood solid tumours in Ile-Ife, Nigeria: a 10-year retrospective review
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Background & objectives: Childhood cancer is fast becoming a global challenge especially in developing countries where morbidity and mortality is still very high. The review is to determine the pattern of malignant solid tumours and to compare this with previous studies.
Methods: A 10-year retrospective review in which all histologically diagnosed childhood malignant solid tumours between ages 0-15 years were analysed.
The surgical daybook and the histopathology request card were retrieved and the patient's biodata, nature of specimen and site were extracted. The histopathology reports were also retrieved and the size of the tumour, diagnosis, grade and stage (where applicable) were retrieved.
Results: A total of 120 cases of malignant childhood solid tumours were analysed in the study period with an average of 12 cases per year. 75 (62.5 %) cases were male, while 45 (37.5%) cases were female, hence a male to female ratio of 1.7:1. The peak age group was 5-9 years accounting for 37.5 %, while 0-4 years and 10-15 years accounted for 33.3% and 29.2% respectively. The fIve commonest tumours were lymphoma (27; 22.5%), nephroblastoma (25; 20.8%), soft tissue sarcoma (20; 16.7%), central nervous system tumours (13; 10.8%) and retinoblastoma (10; 8.3%).
Conclusion: Lymphomas as a group is the still the commonest childhood solid tumour in our centre as previously reported. However, nephroblastoma is the commonest single entity. There seems to be a decline in the diagnosis of Burkitt lymphoma in our centre over the last 10 years, whether this translate to reduction in incidence of Burkitt lymphoma needs further clarification.

PS-10-017
Placenta referrals in a teaching hospital
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Background & objectives:
- To document and quantify reasons for referral of placenta specimens for histological analysis.
- To establish whether referrals are often received in line with RCPath guidelines (October 2019) (Appendix A).

- To investigate reasons behind inappropriate or ambiguous referrals, and to consider steps to minimise these in the future.

Methods:

- 215 sequential referrals were prospectively collected, in which placenta specimens were referred for histopathological analysis.
- Referrals were categorised according to which part of the Appendix A, RCPath (October 2019) guidelines they pertained to (some fell into more than one category).
- Inappropriate and ambiguous referrals were investigated further using WinPath but not rejected.

Results: The majority (97%) of referrals for placenta pathology are in line with RCPath guidelines. Common reasons for referral are; severe foetal distress, requiring neonatal unit admission (23%), prematurity of less than 32+0 weeks gestation (20%) and prematurity between 32+0 and 36+6 weeks (17%). No referrals were made for foetal hydrops, maternal coagulopathy and maternal substance abuse.

No referral information received in 1.9% specimens. Chorioamnionitis was sole indicator in 7 cases.

Conclusion: The overwhelming majority of referrals are appropriate.

No clinical information was offered in a small percentage

Chorioamnionitis and sepsis are not in the RCPath criteria, however maternal pyrexia is

Referral practice in Low Apgar Scores requires further study

PS-10-018

Violation of immunological tolerance as a predictor of the development of complications of allogeneic pregnancy

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Background & objectives: The high frequency of complications in allogeneic pregnancy is presumably associated with a violation of the immunological privilege of uteroplacental region. It is necessary to study the expression of markers reflecting the formation of immunological tolerance in placenta and placental bed.

Methods: the study was performed on placenta material and placental bed biopsies from 89 women; a histological and immunohistochemical examination was performed using antibodies to CD8, CD138, CD56, CD4, CD 25. xpression was evaluated by a quantitative method for calculating the number of stained cells in 10 fields of view at SW 400.

Results: Placentas taken from women after allogeneic pregnancy had pronounced signs of immune alteration, such as chronic histiocytic intervillositis, lymphoplasmacytic deciduitis, chronic chorioamnionitis, chronic villitis, perivillous fibrinoid with lymphocytes (p (F) <0.05). Immunohistochemical study of the placentas showed accumulation of CD138 + plasma cells, CD8 + T-lymphocytes and uNK cells, and a decrease in the number of CD25 \ CD4 + Treg cells in the structures of the uteroplacental region (Kruskal-Wallis test, p <0.05)Placentas after IVF with donor oocytes are characterized by similar changes associated with the development of chronic inflammation in the structures of the placenta and immunohistochemical signs of impaired immunological tolerance at the maternal-foetal interface.

Conclusion: The obtained data allow us to classify pregnancies under the surrogate motherhood programs and oocyte donation as a risk factor for the development of pregnancy complications with immune pathogenesis.

PS-10-019

Correlations between mismatches in HLA II in mother-recipient – child couples and immunomorphological characteristics of placentas in allogeneic pregnancy

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Background & objectives: The number of mismatches in the HLA II gene system during allogeneic pregnancy can affect the development of complications and be a selective factor in the selection of a donor blastocyst.

Methods: Allelic polymorphisms of class HLA II genes (DQA1, DQB1, DRB1) were studied in pairs of 89 mother-child pairs by PCR. In accordance with the results, all pairs were divided into 4 groups according to number of mismatches (from 0 to 3). Morphological and IHC studies using antibodies to HLA-DR, HLA-C were performed on the material of placentas and placental sites.

Results: It was shown that with an increase in the number of mismatches, the incidence of foci of chronic inflammation in the tissues of the placenta and placental bed increases: perivascular infiltrates of the radial arteries, chronic chorioamnionitis, basal deciditis (p (F) <0.05). In the absence of discrepancies and with their maximum number, a change in the optimal level of HLA-C expression by villi syncytiotropholastome occurs, as well as an increase in HLA-DR expression in deciduas basalis and the stroma of the placental bed (Kruskal-Wallis test, p <0.05)

Conclusion: Both a high degree of antigenic spillage and significant coincidence in the HLA gene system result in structural changes and an imbalance in the immunological balance in the structures of the placenta and placental bed, which can be a selective factor in the selection of donor oocytes and the recipient mother.

PS-10-020

Assessment of umbilical cord tissue morphology with α-SMA and desmin expressions under circulatory hypoxia

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Background & objectives: The umbilical cord(UC) insertion site, anatomical abnormalities are associated with foetal growth potential and clinical outcomes for the newborn. The aim of present study is to elucidate UC structural features in gestations under conditions of congenital heart disease(CHD) in pregnant women.

Methods: 35 full term placentas were divided into group I(20 cases of maternal CHD) and 15 cases of physiological pregnancy(control group-CG).The length and diameter of the UC were measured. Histological sections stained with H&E were studied microscopically, then by computer morphometry. The immunohistochemical(IHC) staining with monoclonal murine antibodies to α-SMA and Desmin conducted. The differences between groups were elucidated by the non-parametric Mann-Whitney U-test,p<0.05.

Results: Results of the study showed a decrease in the length (31.37±1.43 cm) and the diameter (1.01±0.11 cm) of the UC during pregnancy with CHD compared to the control group (respectively: 34.40 ±1.76 and 1.55 ±0.22 cm, p<0.05). Microscopic examination revealed an enhanced fibrosis and lack of Warton's jelly in the fiber- free stromal clefts. α-SMA and desmin expressions were higher and more diffuse in the group I than in the CG.

Conclusion: The decreased area of the jelly-filled UC stomal clefts, reduced hydrophilicity of the tissues is accompanied by enhanced sclerosis a reduction of its turgidity. This results in the advancement of the sensitivity of the vessel walls to damaging mechanical influences. The umbilical cord structure remodeling is considered in the aspect of placental adaptation to circulatory hypoxia due to hemodynamic impairments in women with CHD.

PS-10-021

Structural profile of the placental terminal villi stroma remodelling with emphasis on oxidative stress during pregnancy

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Background & objectives: Morphological alterations of placental terminal villi can cause organ's dysfunction, leading to deficiency of a foetal oxygen and nutrients supply.
The aim of this study was to investigate the remodelling of the placental terminal villi stroma under oxidative stress conditions.
Methods: Morphological study was carried out in following groups: I- 20 placentas from mothers with non-operated congenital heart defects (CHD);II- 19 cases of operated CHD and 15 cases of physiological pregnancy-control group(CG).The immunohistochemical(IHC) staining protocol with monoclonal mouse antibodies to collagen IV and collagen III for placental tissue has been developed. The differences between groups were identified by Mann-Whitney U-test at $p<0.05$.
Results: Histological study revealed violations of the placental chorionic villi maturation in CHD groups, especially in the I group. Morphometry showed a decreased volume fraction (VF) of the terminal villi stroma in CHD cases(I– 20.0(11),II- 20,0(4),CG- 24.0(12)%,$p<0.05$). IHC analysis discovered the expression of the atypical collagen III type in the group I. The VF of the type IV collagen decoration area consistently decreased from I to the II group and to the CG(respectively:19,0(6)-16,0(5,75)-11,5(7,75)%,$p<0.05$).
Conclusion: Hypoxia during gestation impacts both maternal health and foetal development. Placental villi maturation disorder with enhanced villi immaturity may cause the disruption of foeto-maternal metabolism and gas exchange via placental membrane(PM). The decreased VF of the villi stroma contributes the thinning of PM, thus promoting to the enhancement of transplacental exchange. Placental villi stroma remodelling, the role of collagen types III and IV discussed in the aspect of placental adaptations to oxidative stress due to hemodynamic disorders in CHD cases.

PS-10-023

Basal plate myometrial fibres: a lesion of shallow placental implantation

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Background & objectives: Basal plate myometrial fibres (bpmf) with or without intervening decidua is the earliest and clinically asymptomatic lesion of abnormal placentation. This retrospective analysis is an expansion of our clinicoplacental studies combining bpmf and occult placenta accreta.
Methods: 169 most recent consecutive cases with placental bpmf with or without intervening decidua (Group 1) were compared to 1661 cases without bpmf (Group 2). Frequencies of 25 independent clinical and 40 placental phenotypes were statistically compared between the groups.
Results: Of 1830 placentas examined since 2009, 169 showed bpmf (11.2%). Placentas with bpmf as compared with placentas without bpmf were statistically significantly ($p<0.05$) more common in association with cesarean sections (11.2% vs 7.5%), antepartum haemorrhage (17.7% vs 11.6.%), gestational hypertension or preeclampsia (23.1% vs 6.0%), complicated 3rd stage of labor (18.9% vs 6.4%), villous infarction (14.2% vs 8.9%), uterine pattern (14.8%, vs 9.6%), massive perivillous fibrin deposition (9.5% vs 5.3%), chorionic disc chorionic microcysts (21.8% vs 15.9%), clusters of maternal floor multinucleate trophoblasts (27.8% vs 21.2%), excessive trophoblasts of chorionic disc (24.3% vs 17.3%), segmental villous avascularity (27.8% vs 19.9%), and foetal vascular ectasia (26.2% vs 15.2%).
Conclusion: Because of the association of bpmf with increased extravillous trophoblasts in the chorionic discand maternal floor trophoblastic giant cells, they should be included into the spectrum of placental lesions of shallow placental implantation rather than linked to decidual deficiency only.

PS-11 Pulmonary Pathology

PS-11-001

Polytropic effect of polymetallic dust on the experimental rats lungs

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Background & objectives: Polytropic effect of dust depends on a complex chemical composition, which impact with possible effects of summation or potentiation on the organism. To study the polymetallic dust effect on the lung tissue of experimental animals at intratracheally exposure.
Methods: The experiment included 30 outbred white male rats weighing 180-220g. for 30 days. Lung pieces were fixed in neutral formalin 10%, morphological studies were carried out according to standard methods. The object of the study was the lung tissue of experimental animals. The experiment was realized according to «Rules for biomedical experiments conducting» of MH RK (November 12, 2009 №697).
Results: The initial stages of desquamative bronchitis and a pathological tumour in the middle lobes of the lungs with compaction of the lungs stroma of oncological nature were revealed after intratracheal dusting. An accumulation of dust as rounded formations surrounded by fibroblasts, fibrocytes and macrophages was noted in the adventitial bronchi membrane.
The number of destroyed alveoli increased, the formation of pronounced emphysematous zones occurred subpleural in the lungs of rats.
Conclusion: It can be assumed that dust causes a polytropic effect on lung tissue, provokes the formation of a tumour of a malignant nature and degeneration of fibrous tissue, since it is associated with a violation of the parenchyma of the lungs and blood vessels with the subsequent formation of cell-dust foci and expressed subpleural emphysematous zones.
The preserved alveoli were different shape, the blood vessels were characterized by plethora and severe perivascular oedema.

PS-11-002

Pathomorphological changes in the lung parenchyma at the exposure of multicomponent polymetallic dust

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Background & objectives: The clinical picture of dusty diseases indicates damage of the lung tissue and respiratory tract with the development of pneumosclerosis, chronic bronchitis and bronchial asthma.
To study the pathomorphology of the lung parenchyma after exposure of dust in various doses.
Methods: Experimental study was carried out on outbred white rats weighing 180-220 g for 30 days. Effective doses of the toxicant 10 mg/m3 and 25 mg/m3 were used. The experiment was carried out by «Rules for biomedical experiments conducting» of MH RK (November 12, 2009 №697).
Results: The initial stage of desquamative bronchitis was revealed in the bronchi; in the bronchi adventitia, cell-dust foci of polymetallic dust accumulation surrounded by fibroblasts, fibrocytes and macrophages were observed. The number of destroyed alveoli increased with dose increasing, and the formation of expressed emphysematous zones of pneumosclerosis increased.

The behavioural activity of rats was studied after dust inhalation. The motor activity decreased after dusting dose increase.
Conclusion: The metals of the dust cause a polytropic effect with an increase of the toxicant dose, have high bioactivity and accumulate in the stroma of the bronchi and alveolar tissue. A significant decrease in the weight and muscle strength was observed at the exposure of dust maximum dose, which was clearly expressed by the experiment end.
The behavioural activity of rats at a dose of 10 mg/m3 was moderate, at 25 mg/m3 – expressed behavioural reactions were reduced.

PS-11-003
Congenital pulmonary airway malformation diagnosed at elderly age – experience from a tertiary hospital
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Background & objectives: Congenital pulmonary airway malformation (CPAM) is a nonhereditary lung anomaly mainly detected prenatally or during early life, but some remain asymptomatic during adulthood.
This study summarizes the clinicopathological features of CPAM diagnosed in elderly patients over a 10-year period.
Methods: We retrospectively identified all CPAM diagnosis between 2009-2019 and selected all the cases in which patient age was equal or superior to 70-years-old. These cases were reviewed and classified according to the Stocker system. Clinical and radiological data were obtained from Hospital registries.
Results: Five CPAMs were diagnosed on patients older than 70-years; two were men. Three patients had registries of previous pneumonia and two were former smokers.
Presentation symptoms were haemoptysis, cough and/or fever. TC scan showed nodular formations or caveated masses. All patients were submitted to lobectomy: four were diagnosed with Stocker type I CPAM, one with Stocker type II CPAM. Two patients were concurrently diagnosed with mucinous adenocarcinoma.
Conclusion: CPAM can be asymptomatic or course with nonspecific lung infections, so it must be considered at any age.
Two patients presented with mucinous adenocarcinoma, supporting the need to treat every CPAM as it can potentially evolve to carcinoma.

PS-11-004
Results of intraoperative consultation in lung and mediastinal lesions
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Background & objectives: The determination of histopathological diagnosis during mediastinal surgery is important for proper surgical staging. The aim of our study is to determine the accuracy rate of our intraoperative consultation results and to review the diagnostic problems that may cause errors.
Methods: In this study, frozen results of 563 lung, pleural, mediastinal masses and lymph nodes diagnosed by intraoperative consultation between December 2013 and July 2018 at Çukurova University Faculty of Medicine Pathology Department were retrospectively evaluated. Frozen sections were compared with paraffin sections.
Results: One hundred fifty six (27.6%) cases were female and 407 (74.4%) were male. The mean age was 57.6 years (3-90). The diagnostic accuracy rate was 95.9% in the frozen section results. Of the 16 patients who were misdiagnosed, 6 (1.06%) had false positives and 10 (1.77%) had false negative results. In 7 (1,24%) cases, the diagnosis was left to permanent sections. In the re-evaluation of 16 cases with incorrect results in our series, we found that the causes of misdiagnosis were caused by macroscopic sampling error, technical reasons and interpretation error.
Conclusion: Intraoperative consultation is a procedure that effects to surgery in mediastinal and lung parenchymal lesions. In order to minimize misdiagnosis rates, it is important to have sufficient number of samples and to eliminate technical problems.

PS-11-005
An AI-based tool to identify cancer areas in lung biopsies
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Background & objectives: Histopathology of lung-cancer forms the backbone of diagnostics but is dependent on the experience of the pathologist. Even skilled pathologist, has a challenge to evaluate biopsies. To better the process, we trained a deep-segmentation neural-network to identify cancer in lung-biopsies.
Methods: We retrieved 90 retrospective cases of lung cancer, containing 200 WSIs of H&E-stained biopsies including clinical metadata form Uppsala University Hospital. The slides were scanned and two pathologists made pixel-level multiclass annotations, one reviewing the other, using Contextvision´s INIFY viewer and annotation tool. A U-Net was trained on 160 of the WSIs and was evaluated on the remaining 40 WSI's
Results: Visual comparisons using probability heat maps revealed striking agreements between manual annotations and the predicted cancer areas selected by the model. In addition, the model correctly assigned areas to the Benign, Necrosis, or Cancer histological subgroup.
The table shows the median pixel-level performance statistics on the evaluation images:

	Benign	Necrosis	Cancer
Precision	0.95	0.97	0.81
Recall	0.93	0.73	0.72

Conclusion: We present a deep learning network that could identify and outline cancer in lung biopsies with good accuracy. This network could be further developed into a decision support tool for pathologists in their routine diagnostic process.
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PS-11-006
Her family genes, DDR2 and PI3KCA mutations may be early events in pre-neoplastic lesions and in atypical bronchial type epithelium
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Background & objectives: Early diagnosis will decrease lung cancer incidence through molecular changes identification in pre-neoplastic and in pre-invasive lesions.
NGS was applied to either adenocarcinoma and atypical bronchial type epithelium and to cases of AIS and MIA.
Methods: Three pulmonary adenocarcinomas and concomitant atypical bronchial type epithelium were manually/independently microdissected from FFPE blocks; adenocarcinoma in situ (1 case) and minimally invasive adenocarcinoma (2 cases) were also selected.

Routine immunohistochemical panel was applied for precise diagnosis. NGS (colon/lung panel) was performed in a PGM platform and ALK, ROS1 and MET FISH analysis was also performed on 4-μm-thick.
Results: Adenocarcinomas expressed CK7 /TTF1; two also expressed Vim and p63 to a lesser extent. AIS and MIA cells expressed CK7 and TTF1.
Identified somatic mutations concerned KRAS, FGFR2 and DDR2 in two adenocarcinomas and respective ABTE; PI3KCA, EGFR and MET represented another duet while ERBB2 raised up also.
ALK and ROS1 rearrangements or MET amplifications were not found by FISH.
The AIS case exhibited ERBB2/4, EGFR and SMAD4 somatic mutations while the two MIA cases were sequencing apparently wild-type for the applied panel.
Conclusion: Mutational status in ABTE identical to concomitant adenocarcinomas provides concern about early genetic events present in lung adenocarcinoma carcinogenesis deserving further studies to be emphasized as pre-neoplastic lesion to lead early clinical guidance for high-risk patients identification in bronchial – pulmonary carcinoma in screening.

PS-11-007
Nucleolin expression in pleural mesothelioma – a potential therapeutic target
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Background & objectives: Treatment of pleural mesothelioma includes surgery/chemotherapy often palliative. Cisplatin/pemetrexed constitute current standard but curative therapy remains unclear. Nucleolin involvement in tumorigenesis/angiogenesis might be related to metastisation raising nucleolin expression determination in pleural mesothelioma necessary.
Methods: Biopsies/lobectomy samples of 21 mesotheliomas without any preoperative chemotherapy or radiotherapy treatment and classified after calretinin/CK5.6/WT1/vimentin/podoplanin/Ber-Ep4/TTF1 had nucleolin expression validated through positive cells percentage/field: 0% = 0 (negative); 1-10% = +1 (low positive); 11-49% = +2 (positive) and ³50% = +3 (highly positive).
Results: Histopathological characteristics and nucleolin scoring correlated biphasic mesothelioma +3 – eight cases; epithelioid mesothelioma +2-five cases and +3-four cases and sarcomatoid mesothelioma +1 – +3 – three cases, all with consistent fusiform cellular stroma. Positive and strong staining of the nucleus was observed in all the cases, albeit it was also possible to see some cells that did not express the protein. Cytoplasmic staining accompanied by membrane staining was observed in 3 of the 20 mesothelioma samples analysed.
Conclusion: Nucleolin value as both prognostic factor and possible therapeutic target in several types of cancer has been extensively studied. Also subject of interest for targeted delivery systems in the context of oncological diseases reveals to be a promising mesothelioma therapeutic target.

PS-11-008
NUT carcinoma: a tertiary single institute experience with a case of EWSR1 rearrangement
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Background & objectives: NUT carcinoma is a rare and aggressive tumour, defined by chromosomal rearrangement of NUT (nuclear protein in testis, i.e. NUTM1) gene. Herein we describe clinical and histological characteristics of seven cases in a single institute experience.
Methods: Seven cases of NUT carcinomas were identified from June 2014 to February 2020. All cases were confirmed by diffuse nuclear NUT immunoreactivity and/or NUT rearrangement by FISH. Clinicopathologic parameters were reviewed. Next-generation sequencing (NGS) was performed in three cases.
Results: Primary sites included lung, frontal and ethmoid sinuses, larynx, and axillary area. Five patients had multiple metastases at the time of diagnosis. The tumours showed small round cell morphology with/without abrupt keratinization. The tumour were immuno-positive for cytokeratin (ck, 6/6, 100 %) and p40 (4/5, 80%). One showed EWSR1 rearrangement by FISH which initially diagnosed as Ewing sarcoma. Another one showed mutations of NF1 and APC genes by NGS.
Conclusion: NUT carcinoma is a diagnostic challenging disease and has been misdiagnosed as poorly differentiated carcinoma, squamous cell carcinoma, Ewing sarcoma, and desmoplastic small round cell tumour. The recognition of this entity is important to prevent misdiagnosis and to suggest the proper treatment. In addition, the name of NUT rearranged tumour is more favourable due to CK -negative NUT positive tumour.

PS-11-011
A unique case of extrasomatic angiomatoid fibrous histiocytoma arising from the pulmonary hilum
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Background & objectives: Angiomatoid fibrous histiocytoma (AFH) is an uncommon soft tissue tumour that typically occurs in the extremities. Fewer than 10 cases having been reported in the pulmonary region. Herein we report the first case of AFH arising from the pulmonary hilum.
Methods: A 32-year-old male presenting with recurrent haemoptysis was found to have a hypervascular mass (53mm) in the right pulmonary hilum, involving the pulmonary vein, the interlobar artery and the middle lobe bronchi on CT scan. The routine staging including PET scanning, disclosed no evidence of disease elsewhere. After several inconclusive biopsies, a right pneumonectomy was performed due to massive haemoptysis.
Results: The tumour comprised a multinodular proliferation of bland spindle to histiocytoid cells with dense lymphoplasmacytic infiltrate and angiomatoid features, which had invaded into bronchial and vessel walls (exhibiting an impressive endovascular growth) and two hilar lymph nodes. There was no significant atypia, mitosis or necrosis. Immunohistochemical profile (CD99, CD68, EMA diffusely positive; desmin focally positive with dendritic-like pattern) and detection of EWSR1(22q12) gene rearrangements confirmed the diagnosis of AFH.
Conclusion: AFH can occur at unusual sites, including the pulmonary hilum. Diagnosis can be extremely difficult, especially in limited biopsies or when involving lymph nodes. Once completely resected, pulmonary AFP discloses a benign clinical behaviour, even if nodal metastases occur.

PS-11-012
Pitfalls in ROS1 immunohistochemistry in non-small cell lung carcinoma: equivocal ROS1 immunostaining can be associated with alternative mutation status
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Background & objectives: ROS-1 gene rearrangement is an important predictive biomarker for targeted tyrosine kinase inhibition. The College of American Pathologists supports the use of ROS-1

immunohistochemistry as a screening tool followed by confirmation of rearrangement by sequencing in all positive cases.
Methods: We retrospectively examined the correlation between immunohistochemistry (IHC) using the Ventana SP384 ROS-1 antibody, on routine diagnostic tissue sections, and rearrangement status by next generation sequencing (Lung panel Oncomine Focus Assay, Ion Torrent). Clinicopathological details including age at diagnosis, tumour morphology and rearrangement /molecular status were collated.
Results: The cohort included 39females and 25males, age range 36-88 (average 66). 64 were tested: 2 lung resections, 52 biopsies(40 lung/pleura, 5 bone/soft tissue, 5 lymph node, 2 liver) and 10 cytology specimens. 55/64(86%) were adenocarcinomas. ROS-1 expression was detected in 33%(21/64). 3/21 showed strong positive staining with 1 confirmed CD74-ROS1 fusion, 1 KRAS codon 12 mutation and 1 negative for fusions/mutations. Equivocal expression was present in 28%(n=18) without subsequent ROS-1 rearrangement, but with KRAS(39%, n=7), EGFR(17%, n=3), and HER2(6%, n=1) mutations, giving a false positive rate of 17%. 3 showed no fusions/mutations and 4 were insufficient/not sequenced. ROS-1 expression was also noted in reactive type II pneumocytes and mesothelial cells.
Conclusion: ROS-1 immunoreactivity should be interpreted with caution as tumours lacking ROS-1 rearrangement may still express ROS-1 by IHC and harbour alternative mutations (i.e. KRAS in 39%). Reporting of IHC staining should be done in conjunction with mutational status if possible.

PS-11-013
Bronchiolar adenoma: a report of four cases with morphological, immunophaenotypic and genomic analysis
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Background & objectives: To improve the capacity of differential diagnosis and avoid confusion of recognition caused by various morphological changes of bronchiolar adenoma(BA).
Methods: Various patterns and trilineage cell of four cases were reviewed morphologically and immunohistochemically (IHC), and meantime, performed genomic analysis by Next-generation sequencing (NGS, Illumina Hiseq).
Results: Different intensity/pattern of immunophenotype was demonstrated at trilineage cell, including basel cells(BCs), ciliated cells(CCs), mucous cells(MCs). #1 was composed of bilayers of BCs with both MCs and CCs, the MCs was predominant. IHC expressed strong for TTF-1, NapsinA, p40, and Braf-specific antibodies with Braf mutation(p.V600E). #2 was similar to #1. However, luminal cells consisted of MCs, negative for NapsinA without Braf mutation. #3, "distal-type BA" contained predominant CCs and cuboidal cells without MCs, papillary/glandular architecture. Bilayered architecture were equivocal, and possible to overlie BCs layer by luminal cells. IHC showed strong for TTF-1, NapsinA, EGFR; weak p40; with EGFR mutation (L858R, E709K). #4 appeared to BA mixed with malignant component.
Conclusion: Variour morphology, immunophenotype and gene mutation appeared in our four cases. This suggests that BA may arise from different stem cells or differentiate for different lineage cells. It is possible that BA occured at respiratory bronchiole lacks completely bi-layered architecture.

PS-11-014
Alveolar proteinosis: The Cruces University Hospital experience in the last 20 years
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Background & objectives: To describe the clinic-pathological features of patients with alveolar proteinosis (AP) diagnosed in our Institution during the last 20 years.
Methods: Archive retrieval and retrospective study of the histological sections of cases diagnosed of alveolar proteinosis and review of clinical records (including follow-up) of patients in the period 1998-2019.
Results: Four cases with the diagnosis of alveolar proteinosis (3 adults - 2 males, 1 female) were found in the retrospective review. The average age was 37 (range 27-44). A fourth case was diagnosed in a 2-year-old girl and was confirmed as hereditary. Diagnostic biopsies were obtained by thoracotomy. The 3 adult cases were smokers, one of them having had professional contact with aluminium, and another being cocaine user. Crazy paving pattern was detected in the two patients in whose CT scan was performed. Histological sections showed in all cases the typical pasty eosinophilic material fulfilling the alveolar spaces. Three cases were treated with whole-lung lavage with good initial response.
Conclusion: Alveolar proteinosis consists in the accumulation of surfactant in alveolar macrophages and alveoli and results in severe gas exchange impairment. It is considered a rare disease. 90-95% of adult cases have an autoimmune origin and the rest are secondary. Less than 1% of the cases are congenital. The diagnosis requires lung biopsy which shows the typical histology of diffuse alveolar fulfilment of proteinaceous eosinophilic material.

PS-11-015
Driver mutations and PD-L1 expression frequency in Galician non-small cell lung cancer patients
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Background & objectives: Driver mutations and PD-L1 expression in lung cancer are potential therapeutic targets. We investigate the prevalence of these molecular alterations in a group of Galician non-small cell lung cancer (NSCLC) patients and compare it with reported in the literature.
Methods: Paraffin-embedded tissue samples from 103 NSCLC patients from our files were reviewed. Immunohistochemical study for PD-L1 expression, mutational screening for EGFR, KRAS, NRAS and BRAF by PCR and analyses for ALK and ROS1 rearrangements by fluorescence in situ hybridization were performed.
Results: PD-L1 expression levels were as follows: ≥50% in 14.5% cases; 1%-49% in 27.2% and <1% in 58.3%. The overall frequency of mutations were: EGFR 10.7%; ALK 2.9%; ROS1 0.97%; KRAS 22.3% and BRAF 1.94%. There were no tumours with NRAS mutations.
Conclusion: Compared to the literature, frequencies of driver mutations and PD-L1 expression level ≥50% are consistent, but frequencies of 1-49% levels are lower and those of <1% higher than expected, probably due to interobserver variability and tumour heterogeneity.

PS-11-016
Matrix metalloproteinases and their inhibitors in foci of pulmonary fibrosis in workers of a plutonium production facility
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Background & objectives: Morphogenesis of radiation-related pulmonary fibrosis (PF) has not been sufficiently investigated. Current studies are focused mainly on matrix metalloproteinases (MMP) and their inhibitors (TIMP). The present study was aimed to investigate the role of MMP-TIMP in pathogenesis of radiation-related PF.

Methods: We investigated immunomorphological characteristics of PF based on autopsy material taken from 101 Mayak nuclear workers. 32 samples of plutonium-induced PF (PuPF); 34 samples of non-plutonium PF (non-PuPF) collected from workers with a clinical diagnosis of chronic obstructive pulmonary disease; 35 samples of normal tissue free from pulmonary pathology. The sections were incubated with antibodies against MMP-2, MMP-9, TIMP-1, TIMP-2.
Results: MMP and TIMP expression was examined in macrophages and stromal fibroblastic components. MMP-2 density was markedly lower in PuPF specimens (0.37:0.15;1.14) compared to non-PuPF specimens (1.41:0.53;3.40) and normal lung tissues (0.84:0.48;1.76), p=0.0012. On the contrary, MMP-9 was hyper-expressed in PuPF and non-PuPF (5.02:4.08;7.75 and 4.17:3.30;6.55, respectively) compared to normal lung tissues (0.87:0.53;1.47), p<0.0001. TIMP-1 was downregulated in PuPF specimens, while TIMP-2 was markedly upregulated (p=0.0365 and p=0.0021, respectively).
MMP hyper-expression and proteinase-anti-proteinase disbalance in PF foci in individuals who had been occupationally internally exposed to alpha radiation over prolonged periods might promote disruption of the extracellular matrix and basal membranes and the lung connective tissue remodelling.
Conclusion: The MMP disbalance is likely to contribute to the pulmonary neoplastic process. This study provides findings on expression of components of metalloproteinase-anti-proteinase system of the pulmonary tissue and its role as a potential histological marker for diagnostics and prognosis purposes.

PS-11-017
A potential panel of four-long non-coding RNA signature to improve survival prediction of small cell lung cancer
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Background & objectives: The prognostic significance of long non-coding RNAs (lncRNAs) in small cell lung cancer (SCLC) remains unclear and needs to be investigated.
Methods: We obtained and analysed lncRNA expression profiles in two cohorts of 69 SCLC patients by repurposing the publicly available RNA sequencing and microarray datasets from the Gene Expression Omnibus (GEO) database. Functional enrichment analysis of lncRNAs-related protein-coding genes (PCGs) includes DAVID bioinformatic tool, GSEA, and cytoscape enrichement map.
Results: In the discovery series of 48 patients, we identified a set of four lncRNAs that was significantly associated with patients' overall survival (OS) using univariate Cox regression analysis. The four-lncRNA signature classified patients of the discovery series into the high-risk group and low-risk group with significantly different survival outcome ($p < 0.0002$). The four-lncRNA signature was further tested in the independent dataset. Moreover, the prognostic value of the four-lncRNA signature is independent of conventional clinical factors. Functional analysis suggested that four-lncRNA signature may be involved with SCLC through exerting their regulatory roles in known cancer-related pathways, DNA repair, glycosylation and metabolism.
Conclusion: Our study not only highlighted the potential role for lncRNAs to improve clinical prognosis prediction in patients with SCLC but also provided alternative biomarkers and therapeutic targets for SCLC patients.

PS-11-019
A lipofuscin-detecting immunohistochemical marker of senescence relates with low proliferation and poor prognosis in non-small-cell-lung cancer
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Background & objectives: Cancer cell senescence is associated with a permanent cell cycle arrest. Senescent cells exert potent bystander effects that may regulate clinical tumour behaviour. Senescence role in defining local and metastatic aggressiveness at a clinical level remains obscure.
Methods: A sensitive histochemical/immunohistochemical method (SenTraGor™/STG) has been developed to detect senescent cells, based on the synthesis of a hapten-linked Sudan Black B analogue that selectively binds to lipofuscins and labels accumulating dysfunctional lysosomes. In our study, we validated the STG method in 98 paraffin embedded surgically resected non-small-cell-lung carcinomas. Proliferation index MIB1 (PI), p16 and p21 was in parallel assessed.
Results: Strong expression of SGR in 10-100% in 36/98 cases (36.7%), but no association with stage, histology or differentiation was noted. Linear regression analysis showed a significant inverse association between SGR and PI (p=0.007, r=0.28). SGR was related with p21, but not with p16 expression. Kaplan-Meier survival curves showed a direct association of high STG expression with poor postoperative prognosis and independent of stage. MIB1 was not related with prognosis.
Conclusion: STG provides a reliable methodology to detect lipofuscin accumulation in cancer cells, in paraffin-embedded tissues, opening a new field for translational studies focusing on senescence. High presence of SGR+ senescent cells relates with poor prognosis in NSCLC.

PS-11-021
PD-L1 assays and their performance in Nordic immunohistochemical quality control (NordiQC)
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Background & objectives: Immunohistochemistry for PD-L1 expression is applied in different cancer types to identify patients eligible for treatment with immune checkpoint inhibitors. NordiQC provides proficiency testing for immunohistochemical (IHC) demonstration of PD-L1 expression with primary focus on non-small cell lung carcinomas (NSCLC).
Methods: NSCLC samples characterized for PD-L1 with critical and relevant expression levels, using the companion diagnostic (CDx) assay 22C3, Agilent, as reference standard method, were used for the assessments. In each assessment, tissue micro arrays comprising 6–12 NSCLCs, were constructed. Sections were circulated to the participants performing IHC for PD-L1 by their routine method. Results were evaluated by experienced assessors.
Results: Between 2017-19, six PD-L1 assessments were performed. The number of participants have increased from 68 in C1 to 182 in C6 with a total number of 881 submitted protocols in the first six runs. The pass-rate varied from 50% in C1 to 91% in C3, with an average of 81%. 37% of the participants used CDx assays performed accordingly to vendor guidelines provided an average pass-rate of 92%, compared to 67% for laboratory developed (LD) assays, used by 44%. 19% modified the protocol settings for CDx assays, providing a pass-rate of 88%. 75% of insufficient results were characterized by false negative staining reactions changing PD-L1 status of the included carcinomas.
Conclusion: Results obtained in all six assessments showed performance differences between LD and CDx assays. Within LD assays, meticulous calibration and validation is required. Participation in proficiency testing has improved the overall pass-rate for PD-L1 in NSCLC in NordiQC.

PS-11-023
BAP1 loss in malignant mesothelioma: distribution according the histological subtype
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Background & objectives: Malignant mesothelioma (MM) constitutes a diagnostic challenge overall in small biopsies and cytology. Recently, BAP1 Loss, MTAP and EZH2 IHC and NF2 and CDKN2A/p16 FISH has immerged as useful tools and could help in problematic cases of mesothelial proliferations.
Methods: We evaluate the distribution of histological subtype of MM and the immunohistochemical expression of BAP1 in complete sections of 42 cases diagnosed between 2005 and 2018 in our institution (Hospital Universitario Puerta de Hierro).
Results: A cohort of 42 patients was recruited, 31 males (73,8%) and 11 females (26,2%) from 35 to 79 age. The specimens were small biopsies in 4 cases (9,6%), surgical biopsies in 30 cases (71,4%), surgical resection in 6 cases (14,2%) and metastatic tissue in 2 cases (4,8%). All cases were initially evaluated with at least two mesothelial and two carcinoma markers. Regarding to the histologic subtype were 30 cases of epithelioid mesothelioma (71,4%), 3 sarcomatoid (7,1%) and 9 biphasic (21,5%). Loss of BAP1 protein expression was observed in 21 of 42 MM cases (50%). According the histologic type, 66.6% of biphasic, 46.6% of epithelioid, and 33.3% of sarcomatoid MM were BAP1-deficient.
Conclusion: In our series we usually obtained the diagnosis of MM in surgical biopsies. BAP1 immunohistochemistry could help in mesothelial proliferations. According our data we observed BAP1 loss more frequently in biphasic and epithelioid subtypes.

PS-11-024
Retrospective analysis of lung transplant explants: incidence of incidental malignancies in our institution
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Background & objectives: The incidental discovered of unexpected neoplasms in lung explants has importance due to the immunosuppressive therapy that patients received and, in some cases determine the overall survival. Few series evaluate this incidence, and usually describe it as 0,7% and 2%.
Methods: We evaluated the rate of incidental malignancies detected in explanted lungs at our institution in a period of 24 years. A literature review was performed to evaluate the prevalence and the risk factors mainly involved.
Results: 6 of 639 consecutive explanted lungs have unexpected cancer (0,9%). All male smokers. There were 4 cases of adenocarcinoma (66,6%), 1 squamous cell carcinoma (16,6%) and 1 case of metastatic papillary thyroid cancer (16,6%). Of them, 3 cases were in the setting of idiopathic pulmonary fibrosis (IPF) (50%), 2 cases in the setting of chronic obstructive pulmonary disease (COPD) (33,3%) and one case due to bronchiectasis (16,6%). 1 of 6 neoplasms was detected at an advanced stage in the setting of IPF and recurrence occurred 5 months after transplantation.
Conclusion: Incidence of unexpected cancer in our lung explants was 0,9 % and more frequently due to adenocarcinoma in the setting of IPF similar with the data published in the literature.
IPF is an indepent risk factor associated with lung cancer and regarding to the literature, IPF seem to be risk factor for undetected neoplasms in lung explants. Efforts to improve screening in these populations could be considered.

PS-11-025
Peribronchiola metaplasia (lambertosis) what is the pathological significance?
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Background & objectives: Peribronchiolar metaplasia (PBM) is a non-specific reaction to injury, resulting in the extension of bronchiolar epithelium through the canals of Lambert into alveoli. The genesis remains unknown. We aim to investigate the character of this lesion.
Methods: We reviewed the resected operation materials of 70 patients with the primary lung cancer and 13 patients of metastatic lung cancer (MLC). Comprehensive histological review and immunihistochemical staining for TTF-1, p40, ALK and Ki-67. We checked the lesions of PBM, atypical adenomatous hyperplasia (AAH), lung fibrosis, tumourlet and smoker's bronchiolitis.
Results: We observed PBM was in 20(28.6%) in 70 cases; 14(28%) in adenocarcinoma (AC), 2(15.4%) in 13 squamous cell carcinomas. (SCC), in 3(60%) in 5 large cell neuroendocrine carcinoma (LCNEC), and in one (7.7%) in MLC 13 cases. AAH wass in 12(17.1%) in 70 cases; 11(22%) in AC, 0 in SCC, one (20%) in LCNEC and in one (7.7%) in MLC cases. Lung fibrosis was in 9(12.9%) in 70 cases; in 5(10%) in AC, 4(30.7%) in SCC, in 0 in LCNEC and in one (7.7%) in MLC cases. Tumourlet was in (11.4%) in 70 cases; in 7(14%) in AC, in 0 in SCC, in one (20%) in LCNEC.
Conclusion: PBM is a very common finding in the lungs of the primary lung cancer (28.6%) vs. in the lung of MLC (7.7%). Our results suggest also PBM may be related to the pathology of AAH and tumourlet in lung adenocarcinoma.

PS-11-026
ROS1 (SP384) screening in non-small cell lung cancer: experience in real conditions
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Background & objectives: ROS1 is a mandatory biomarker in metastatic lung adenocarcinoma. Immunohistochemistry (IHC) is accepted as a screening method. Our study aims to show our experience with Ventana ROS1 clone antibody SP384 and to propose a diagnostic algorithm based on ROS1 H-score.
Methods: We have reviewed all the ROS1 tested in our centre since the introduction of anti-ROS1 antibody (SP384 clone) and re-evaluated 2 old positive cases. We have calculated an H-score 0-300 using chocolate as a visual aid for ensuring internal reproducibility. We have calculated the best cut-off value with a ROC curve test using STATA software.
Results: We have performed 170 ROS1 IHC and found some expression in 41. We could perform in situ hybridization in a total of 33 cases, identifying positivity by FISH in 7 cases (21,2%). The H-score range was 10-300 (mean 117 and median 95). The best cutoff to identify ROS1 rearrangements was ≥ 200 with a sensitivity of 100% and a specificity of 100%. The total percentage of ROS1 positive rearrangements in the new set of samples was 2,9%.
Conclusion: In our experience ROS1 SP384 clone is a useful screening tool and performing FISH/NGS only in those cases with an H-score ≥200 would be a cost-effective approach. We plan to enlarge the sample and test the reproducibility of the H-score method in a multicenter study.

PS-11-027
PD-L1 expression in non-small cell lung cancers, data of the molecular pathology lab of National Institute of Oncology in Hungary between May 2018 and February 2020
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Background & objectives: Immune checkpoint inhibitor therapy have improved the survival of non-small cell lung cancer (NSCLC) patients. Programmed death ligand-1 (PD-L1) tumour proportion score is

correlating with response and survival. Our goal was to examine the PD-L1 expression rates of NSCLC cases.
Methods: PD-L1 immunohistochemistry (IHC) was carried out on 1687 NSCLC patients' formalin fixed paraffin embedded material. In vitro diagnostic DAKO PD-L1 IHC 22C3 pharmDx assay performed on DAKO Autostainer Link 48. The evaluation of the PD-L1 immunhistochemistry was done according to the guidelines. PD-L1 tumour proportion score (TPS), the histologic subtype and the mutational status of the tumours were compared.
Results: From the 1275 adenocarcinoma, 496 (38,9%) was negative, 368 (28,9%) showed 1-49% TPS and 411 (32,2%) were more or equal to 50%. Of the 412 squamous cell carcinomas TPS distribution was equal in each group, 34,7%, 34% and 31,3% respectively.
42,1 % of the adenocarcinomas were KRAS mutant, 12,5 % were EGFR mutant. KRAS mutant tumours showed higher fraction of TPS>50%, than KRAS wild type tumours. EGFR mutant tumours generally showed low PD-L1 expression.
Conclusion: Our results show strong correlation with the literature datas. Mutation types has effect on PD-L1 expression.

PS-11-028
Mortality for lung cancer among women in the state of Ceara, Brazil
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Background & objectives: Lung cancer in women has shown an increase in its incidence and mortality worldwide. The objective of this study was describe the epidemiological profile and the temporal and spatial trend of lung cancer mortality of the female population.
Methods: This is an ecologic study. Data was collected from the Mortality Information System - Brazilian Ministry of Health. Cases of lung cancer were selected in women recorded in Ceará, Brazilian state, between 2000 and 2015.
Results: A predominantly upward growth pattern was observed in the analysed period. Of a total of 4883 deaths for lung cancer in women ,2729 (55,9%) were in the age groups of 60-69 and 70-79 years of age; mainly among brown and white women, with little or no education. The eastern region of the state had a higher relative risk of lung cancer mortality. Results consistent with the global trend, showing an increase in rates, especially in advanced age groups.
Conclusion: The survey sought to contribute to a better understanding of the mortality of lung cancer; targeted preventive interventions are needed to combat smoking and occupational risk factors associated with the incidence of lung cancer.

PS-11-029
Histological pattern and trend of malignant pleuropulmonary tumours: a ten-year experience review
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Background & objectives: In both sexes combined, lung cancer is the most commonly diagnosed cancer and the leading cause of cancer death globally. Diagnosis is increasingly being made on small tissue samples and cytological specimens. We present here our institutional experience regarding this.
Methods: We reviewed histo- and cytomorphological data of lung and pleural tumour specimens received over a 10-year period (2010-2019). Data was sourced from the surgical pathology records and population-based cancer registry. Diagnostic materials were mainly trucut biopsies of the pleura and lung. Appropriate statistics was applied to evaluate tumour subtype proportions and associate clinicopathological factors.
Results: There were 230 cases consisting of 166 (73%) biopsies and 64 (27%) cytology specimens from 103 (44.8%) males and 127 (55.2%) females giving a female-to-male ratio of 1.2:1. The mean age was 58 ±16 years. Primary tumours constituted 167 (72.6%) of the cases whilst 63 (27.4%) were metastatic tumours. Of the primary tumours, adenocarcinoma was the predominant histologic subtype (52.7%), with small cell carcinoma and mesotheliomas occurring in 3.6%% and 2.4% of patients, respectively. The number of cases diagnosed rose by 37% in the past 5 years (2014-218). Diagnosis of primary versus metastatic tumours was significantly associated with gender (p=0.003), females having more metastatic tumours, likely a reflection of gender incidence.
Conclusion: Our finding suggests a rising incidence of diagnosed pleuropulmonary tumours in this population. This reflects both the increased effort by surgeons to obtain tissue for diagnosis as well as a real projected increase in cancer burden being witnessed in developing countries including lung cancers. As in previous studies, adenocarcinomas predominate in the histomorphology. There is now a need to interrogate adenocarcinomas for smoking association using available genetic markers.

PS-11-030
Synchronous squamous cell carcinoma and malignant pleural mesothelioma: a rare case report
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Background & objectives: The co-existence of malignant pleural mesothelioma (MPM) and lung carcinoma is extremely rare. Herein, we report an uncommon case of co-presence of squamous cell carcinoma (SHC) and MPM.
Methods: A 75-year-old man presented with hemoptizia and dyspnea. He had a history of smoking but no exposure to asbestos. Chest computed tomography (CT) revealed the presence of a right lung mass combined with right pleural effusion and multiple pleural nodules. Positron emission tomography/CT showed increased uptake in the right upper lung mass (maximum standard uptake value:21.16). Then a right thoracentesis was performed.
Results: The smear of the pleural fluid revealed atypical cells with anisokaryosis and hyperchromasia forming papillary arrangements. The tumour cells were immunoreactive to mesothelial markers (calretinin, HBME-1, WT-1, CK5/6 were positive; BAP1 and desmin were negative) and the patient was diagnosed with MPM. The patient underwent bronchoscopy and there was no endobronchial lesion. Bronchial washing and brushing were diagnosed as benign cytology. The lung mass,24x20 mm in dimension, was evaluated on frozen section during surgery. Histologically, islands of large polygonal malignant cells containing keratin and intercellular bridges were seen and it was diagnosed SHC. Formalin-fixed paraffin-embedded sections of the same specimens showed immunoreactivity for p40 and CK5/6. At the same surgery, pleura biopsy was performed and epithelioid type MPM was confirmed.
Conclusion: We presented an extremely rare case of collision of MPM and pulmonary SHC. Possible coexistence of MPM and lung carcinoma should be considered in patients with pleural nodules and effusion.

PS-11-031
Primary pulmonary classical Hodgkin lymphoma with underlying interstitial lung disease: a case report and review of the literature
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Background & objectives: A primary pulmonary lymphoma consists of clonal lymphoid proliferation in the lung parenchyma or bronchus,

without extrapulmonary disease in the next 3 months. Classical Hodgkin Lymphoma (CHL) is an indolent clonal lymphoproliferative neoplasia originated in germinative follicular centre.
Methods: We present a case of an 81 years old man, with hypertension, chronic obstructive pulmonary disease, revealed left lower lung lobe nodule in a Chest X-ray. CT scan demonstrated multiple mediastinal lymph nodes, a spiculated solid lesion, with 3x2cm, hypercaptant on PET scan and diffuse thickening of pleural leaflets on the same lobe. Pleural thickening was considered as inflammatory changes.
Results: It was performed an wedge resection of a semilunar pulmonary fragment weighing 17.6g and measuring 5x3,5x2,5cm. Grossly it was observed an area of 3,2x2,1x1,5cm, heterogeneous, where whitish areas were mixed by black reticulation. Remaining scarce whitish and spongy lung tissue with subpleural cavitation. Histologically revealing a Classic Hodgkin's Lymphoma - nodular sclerosis variant. It was composed by several distinct populations, with predominance of two: Reed-Stenberg neoplastic cells and bulky Hodgkin cells. Both populations expressed CD20, PAX5, CD30, CD15, MUM1 and EBER test was positive. Involving the neoplasia, BALT hyperplasia with lymphoid follicles and activated germinative centres, were present. This case also presented an Usual interstitial pneumonia and an Epstein-Barr virus infection.
Conclusion: The misunderstood spectrum of interstitial preceding tissue where pulmonary Classical Hodgkin Lymphoma – nodular sclerosis, might be more frequent than what is commonly observed, suggesting that pulmonary inflammation and time remodelling can be similar to EBV lymph node infection.

PS-11-032
Comparative histopathological and digital scoring between microfluidic and standard immunohistochemistry for p40 and TTF1 on non-small cell lung carcinoma
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Background & objectives: Microfluidic-based immunohistochemistry (IHC) for the non-small cell lung carcinoma (NSCLC) differential diagnostic markers p40 (squamous cell carcinoma) and TTF1 (adenocarcinoma) was previously optimized.
Here, we aim to prove its non-inferiority with respect to standard assay for NSCLC differential diagnosis.
Methods: Comparative scoring of p40 and TTF1 immunoreactivity between the two techniques was assessed on a NSCLC tumour microarray (TMA) cohort (160 resected patients, two cores each). The QuPath software was trained by manual annotation for cancer cell identification and employed for digital quantification of p40 and TTF1 signal intensity, reported as average score of tumour cells' nuclei per TMA core.
Results: The microfluidic-based IHC for p40 and TTF1 was previously optimized to achieve an analytical performance comparable to standard staining, while shortened to 26 minutes - including the antigen retrieval step.
The concordance rate between the microfluidic (LabSat®) and gold-standard (BenchMark® ULTRA) IHC staining technique was 100% for both p40 (n=194 cores, 126 patients) and TTF1 (n=175 cores, 119 patients) when visually scored as positive or negative as routinely done in the histopathological practice.
Furthermore, comparison of digitally quantified staining intensity on the same NSCLC TMA for p40 and TTF1 resulted in a very strong positive correlation for the two techniques with a Pearson coefficient of 0.94 and 0.95, respectively.
Conclusion: Overall, the microfluidic-based IHC assay represents an equivalent approach to the standard chromogenic staining, allowing for NSCLC classification into squamous cell carcinoma or adenocarcinoma by automated, rapid and accurate detection of p40 and TTF1, respectively.
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PS-11-034
Two unexpected and overlapped endobronchial benign lesions
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Background & objectives: Benign neoplasms comprise less than 10% of tumours involving the bronchi. Primary Pulmonary Leiomyoma (PL) is very rare and usually solitary. In the other hand, solitary squamous cell papillomas (SSP) are exceedingly rare and account <1% of all lung neoplasms.
Methods: We present a 57-year old man presented with a several month history of cough. The bronchoscopy image showed an obstructive upper left bronchial lobe mass. Histology revealed an squamous epithelial exophytic-papillary tumour with acanthosis and a submucosal proliferation of monomorphic cells arranged in whorls and fascicles with spindly nuclei. No necrosis or mitotic activity.
Results: PL are uncommon both in adults and children, constituting 2% of benign lung tumours, symptoms are due to partial/complete airway obstruction, can simulate asthma or be complicated (bronchiectasis and recurrent infections), besides that, endobronchial growth can cause cough, wheeze, haemoptysis. There are four types of respiratory papillomas: recurrent respiratory papillomatosis, solitary squamous papilloma, solitary glandular papilloma and mixed papilloma. They are 3 times more common in men that are usually in their 6th decade of life, presented with obstructive symptoms and up to 25% could be asymptomatic. CT scan reveals endobronchial plaques, nodules or thickening. They are usually central and endobronchial. The size range is 0,7 to 9 cm.
Conclusion: PL are the rarest benign neoplasms of the respiratory tract and treatment should be conservative but as SSP`s local recurrence-transformation into squamous cell carcinoma is uncertain, surgical and more aggressive manage is recommended. We present this overlapped benign endobronchial lesion case due to their low incidence, the fact that SSP could be misdiagnosed as a carcinoma and the need of diagnostic/manage algorithms to avoid unnecessary thoracotomies and wedge resections.

PS-11-035
Proposition of a morphological score to predict the STK11 variation status in lung adenocarcinomas without genotyping
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Background & objectives: STK11 is the third mutated gene in lung adenocarcinomas (LUAC). STK11-mutated LUAC are resistant or poor responders to immunotherapy. Our objective was to build a morphologically predictive score that could assess STK11 mutation status before genotyping.
Methods: LUAC surgical specimens resected during a 2-year period were included. Twenty-eight morphological criteria were assessed. Among them, 2 criteria, i.e. presence of mucinous contingent and presence of lymphoid nodule at low magnification, seemed more frequent in STK11-mutated LUAC. A morphological score was built attributing one point to the presence of these 2 criteria: minimum 0 and maximum 2.
Results: Forty-eight STK11-mutated and 235 STK11-wild type LUAC were morphologically evaluated. With a threshold defined at 1, our morphological score showed a sensitivity of 94%, a specificity of 34%, a negative predictive value of 95% and a positive predictive value of 29%. Of note, lymphoid nodules are usually associated with a better response to immunotherapy. In STK11-mutated LUAC, immune response seemed to be impaired, explaining this paradoxical finding.

Conclusion: In a recent study using deep learning-image analysis, STK11 mutational status was predicted using only morphological criteria, which were not determined.
Our good results, using a 2-criteria morphological score, warrant further validation in a larger muticentre series of LUAC.

PS-11-036
Cryobiopsy in lung transplant patients: diagnostic yield and long-term mortality
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Background & objectives: Transbronchial biopsy (TB) is a routine procedure to assess rejection in lung transplant patients. Cryobiopsies are a kind of TB that provides more tissue with few complications. We report the diagnostic yield and long-term mortality in our series.
Methods: We have reviewed the 429 cryobiopsies' diagnosis and follow-up of 256 patients transplanted at Vall d'Hebron University Hospital between April 2011 and April 2016.
Results: Of the 429 cryobiopsies analysed we could reach a multidisciplinary diagnosis in 421. All-cause 5-year mortality was 25.8% (n=66). Three patients died within 30 days (1.2%). Only one of these cases (0.2%) was directly related to the procedure (pneumothorax). Nine patients died within 90 days (3.5%) and 29 patients died within 360 days (11.3%).
Conclusion: Safety of cryobiopses has been recently questioned in terms of long-term mortality in patients with difuse parenchymal disease. We can say that this observation is not true for transplanted patients. Our series has a high diagnostic yield and a 5 years mortality rate that is halve the observed in lung transplanted patients demonstrating that cryobiopsies are safe and can potentially improve patients' outcomes.

PS-11-037
Pluripotency factors in mesothelioma
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Background & objectives: Pluripotency factors and PI3K-AKT pathway regulate tumour differentiation status and could be responsible for local and distal spreading of the tumour, resistance to therapy and other unfavourable characteristics of malignancy. We tested their expression in mesothelioma and mesothelium.
Methods: We tested samples of 66 patients diagnosed with Epitheloid Malignant Pleural Mesothelioma. Of them male (93%), with median age of 62 (27- 82) at the time of diagnosis. Pathohistological samples have been analysed and subclassified into 6 subtypes: solid (23 cases, 34.8%) , tubulopapillary (18, 27.7%), pleomorphic (12, 18.1%), trabecular (8, 12%), micropapillary (3, 4.5%) and microcystic (2 cases, 3%).
Results: Kaplan-Meier survival curves showed median overall survival of 15 months (95% CI 10.2- 19.7), but without statistical significance between various histological subtypes (chi square 9.176, p=0.102). Immunohistochemical staining was performed to determine expression of pluripotency factors Sox2, Oct-4, Akt and Nanog as well as the Pi3k-bcl 2 signalling pathway in mesothelioma histological subtypes. Sox 2 expression was high in all MPM samples, while the expression of oct-4 was negative regardless of subtype. Other proteins had moderate to high expression. Correlation between transcription factors expression and overall survival time was calculated. Nanog (Pearson corr. 0.282, p=0.022) and Sox-2 (0.281, p=0.023) suggesting correlation significance.
Conclusion: Human mesothelioma exhibits enhanced expression of NANOG, SOX2 and AKT proteins and reduced expression of BCL2 representing the basis for further pluripotency studies.
Funding by: HRZZ Grant

PS-11-038
Recurrent respiratory papillomatosis with extensive lung involvement in a young woman with juvenile-onset form
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Background & objectives: Recurrent respiratory papillomatosis(RRP), human papilloma virus(HPV–mostly 6 and 11) related, is characterized primarily by laryngeal papillomatous lesions rarely affecting the nasopharynx, tracheobronchial tree(2-5%) and pulmonary parenchyma(1-3.3%). Juvenile-onset form (JORRP) develops before 20-years-of-age (mean 3-5.5 years) mainly due to vertical transmission.
Methods: We report the case of a 28-years-old female, non-HPV vaccinated, non-smoker, with JORRP since 3-years-of-age, submitted to dozens of larynx papillary lesions endoscopic CO2-laser excisions. Lastly, tracheal lesions were discovered and CT-scan revealed several bilateral (mostly inferior lobes) lung cavitated lesions(4-24mm) and a 12mm inferior right lung lobe solid lesion, consistent with RRP imaging findings. The solid lesion was biopsied.
Results: All the larynx lesions previously removed were histologically compatible with squamous cell papillomas with HPV infection cytopathic signs and some with areas of mild dysplasia. The current lung biopsy revealed intra-alveolar nests of squamous epithelium (consistent with RRP lung involvement) with focal necrotic and degenerative aspects that were suspicious but not sufficient for a malignancy diagnosis. HPV genotyping of one of the most recent larynx lesions and of the lung biopsy revealed infection with HPV11.
In this case, histopathological findings were consistent with RRP with lung involvement and the scarcity of material prevented the conclusion of malignant transformation.
Conclusion: JORRP is generally more aggressive than adult form with multiple papillomas, high recurrence rate and need of several surgeries, increasing downward/lung dissemination possibility. HPV11, age-of-onset and multiple recurrences represent risk factors for aggressiveness (our case) and malignant transformation (<1% of cases).

PS-11-039
The role of pulmonary collapse in radiation-induced lung injury
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Background & objectives: Radiation therapy is used for the treatment of cancer but it has a severe effect on other organs. The goal of this study is to find out the morphological characteristics of pulmonary collapse after a single dose of X-ray exposure.
Methods: For this study, two groups of Wistar male rats, aged between 8-9 weeks, were used. The main group of rats received a single dose of X-Ray. In both groups, surfactant phospholipids were checked. At various time points, each of the rats were sacrificed and lung samples were analysed through light and electron microscopy.
Results: On days 1 - 3, changes in the lung tissue could only be observed by electron microscopy in the subpleural areas. We discovered signs of endothelial and type II alveolocyte's damage, such as oedema, disturbances in the location of the organelles, osmiophilic bodies and destruction of the surfactant. At the end of the first week, partial atelectasis were seen by light microscopy. Moreover, during this time, zones of pulmonary collapse expanded from the subpleural area to the lung's root. Between 2 and 7 weeks, there was a noticeable change in the lung and

constriction of the bronchus was widespread. After 7 weeks, a 'honeycomb' pattern and pulmonary fibrosis was observed.
Conclusion: This study showed that after a single dose of X-ray exposure, atelectasis starts from the distal, subpleural areas and moves down. There are different causes of pulmonary collapse, including surfactant damage, hypoxia, the destruction of the epithelium cells and bronchial constriction.

PS-11-040
The oxidative stress and endothelial dysfunction in radiation-induced lung injury
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Background & objectives: Irradiation of organs of the thoracic cage to treat malignancies causes frequent complications that manifest as radiation pneumonitis and fibrosis. The purpose of this study is to evaluate oxidative stress and endothelial dysfunction in radiation induced lung injury(RILI).
Methods: Two groups or the Wistar-male-rats were used. One group had been irradiated by a single dose 12Gy of X-ray on the right lung. Non-irradiated group had been instilled with a saline solution into trachea. Animals from both groups were sacrificed on the different days after the beginning of the experiment and their lungs specimen had been analysed.
Results: Signs of the endothelial dysfunction were discovered by electron microscopy in the lung's capillaries such as spasm, endothelial dystrophy and neoangiogenesis in the first hours after the start. IHC showed the reduction of the endothelial function markers (CD31, CD34, CD117, VEGFR1, VEGFR2, e-NOS) but their activity had been recovered in a few weeks. The local maximum of the residual fluorescence identified on the spectrum of the specimens is conditioned by toxicity of– OH radicals, superoxide anion radicals – O2 and some quantity of – CH3 radicals in the tissues. Superoxide anion radicals reduced the amount of nitrogen oxides converting them into peroxynitrites (ONOOH).
Conclusion: The results show that signs of oxidative stress and endothelial dysfunction could be detected within the first 24 hours after the initiation of the experiment by electron microscopy. Raman-fluorescent shows peaks by the 3rd day and the activity decreases by the 50th day of the experiment. Free radicals play the key role in oxydative stress and mediate the extent and intensity of the endothelial dysfunction.

PS-11-041
The use of multigene next generation sequencing to improve accuracy of lung cancer staging in multiple tumours
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Background & objectives: In patients with multiple lung carcinomas, pathological staging depends upon whether these are considered independent. Molecular profiling has value in making this distinction. We reviewed a case series in which multigene sequencing was performed and assessed the impact on staging.
Methods: We searched the case database of the Sarah Cannon Molecular Diagnostics laboratory to identify patients with multiple synchronous lung carcinomas which had undergone NGS. The histopathology reports from these cases were reviewed alongside the tumour mutational profiles to determine evidence of clonality and whether the staging of their lung carcinoma was affected following the results of NGS.
Results: The patients included in the study were all diagnosed with lung adenocarcinoma, and the tumour nodules showed similar histologic types. Seven patients were identified and for 5 of these cases the tumours showed differing somatic mutations indicating that these are likely to be independent primaries. In the remaining 2 patients, there were overlapping variants in the detected mutation profile, indicating that these are highly likely to represent separate nodules of the same tumour. TNM stage was altered in 2 cases overall as a result of the molecular profiling.
Conclusion: The integration of multigene molecular profiling alongside conventional histopathological reporting can improve the accuracy of TNM staging in multiple pulmonary tumours.

PS-11-042
Clinical and economic impact of the current testing scenario for ALK rearrangements in Spain compared to a hypothetical no-testing scenario
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Background & objectives: Biomarkers play an essential role in diagnosis, treatment, and management of lung cancer. The aim of this study is to assess, for the first time, the clinical and economic impact of current ALK testing scenario in Spain.
Methods: Estimate the cost-health outcomes of NSCLC patient comparing current testing scenario vs no-testing scenario. A panel of expert established the assignment of the target treatment (true and false positive-negative). 3-states Markov model was developed, where progression free-survival and overall-survival curves were parameterized using exponential extrapolations to model transition of patients among health states. Only medical direct costs were included (€2019).
Results: A target population of 7,628 NSCLC (non-squamous and never-smoker squamous) patients was estimated. Over a lifetime horizon, the current ALK testing scenario produced additional 4,291 life years and 3,120 quality adjusted life years (QALYs), compared with no-testing scenario. More analyses such as the incremental cost-effectiveness ratio (ICER) (9.855 €/QALY), effect of increasing the testing rate and sensitivity analyses, to confirmed the robustness of the base-case results, were carried out.
Conclusion: The resulting ICER shows that performing molecular testing to the appropriate population of NSCLC patients is a cost-effective strategy in Spain.
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PS-11-043
Analysis of frequency of EGFR and ALK mutations, and PD-L1 expression in patients with lung adenocarcinoma in Bosnia and Herzegovina
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Background & objectives: Molecular testing of lung adenocarcinomas has become a standard and required part of pathological report. We analysed the EGFR, ALK-mutation status, and PD-L1 expression in a representative cohort of patients with lung adenocarcinomas in Bosnia & Herzegovina and correlate with clinical data.
Methods: Newly diagnosed patients within 12 months with histological proven primary lung adenocarcinomas were included. Mutational analyses for EGFR mutations were performed on a Cobas z 480 analyser. ALK immunohistochemistry was performed using the D5F3 clone on Ventana Ultra Benchmark instrument, and PD-L expression data obtained with Antibody DAKO 22C3.
Results: Of the 158 patients, 61,4 % (97) were male. Median years was 61, range from 29 to 84 years. Most of the patients were current or former smokers (95%). EGFR mutations were found in 12% of the patients, and of these mutations, exon 19 deletion was the most common (45.1

%). ALK mutation were present in 3,8% of the patients. The EGFR was more often detected in women and non-smoking, while ALK mutation had no gender predilection. Analysis of PD-L1 expression showed that 21% had a PD-L1 tumour proportion score (TPS) < 1%, 33 % had a PD-L1 TPS of 1–49% and 46% had a PD-L1 TPS of ≥50%.
Conclusion: The detected mutation rates demonstrated expected prevalence of EGFR-mutations and ALK-gene rearrangement, in comparison with the rates in other European countries, while PD-L1 expression was some higher than previously reported, but it maybe be ascribe to high percentage of smokers.

PS-11-044
Histopathologic features of the pulmonary sarcomatoid carcinoma
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Background & objectives: Pulmonary sarcomatoid carcinoma are poorly differentiated cancers. The current classification includes pleomorphic carcinoma (PC), spindle cell carcinoma (SCC), giant cell carcinoma (GCC), carcinosarcoma (CS) and pulmonary blastoma. Our goal is to determine the histological features of sarcomatoid carcinomas.
Methods: Sarcomatoid carcinoma cases reported in our pathology laboratory over the last decade have been scanned. Histopathological features of the cases were evaluated.
Results: A total of 70 cases were detected. In cases, 53 PC, 3 SCC, 3 GCC, 9 CS, 2 pulmonary blastomas were found. In CS, carcinoma component was 6 squamous cell carcinoma, 2 adenocarcinoma, 1 nonsmall cell carcinoma. Sarcoma component was 5 chondrosarcoma, 2 osteosarcoma, 1 synovial sarcoma. Lymphovascular invasion was detected in 48 cases. Nodal involvement was found in 17 cases at N1 level and 7 at N2 level.
Conclusion: Pulmonary sarcomatoid carcinomas are a heterogeneous tumour group containing different histological components. This tumour group has its own spesific histologic profile.

PS-11-045
The decline of surgical lung biopsy in interstitial lung disease: a tertiary centre experience 2009-2019
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Background & objectives: High-resolution computerised tomography (HRCT) is increasingly used as a non-invasive diagnostic tool in interstitial lung disease (ILD). The aim of this analysis was to examine the impact of HRCT on annual rates of histological ILD diagnosis over the last decade.
Methods: A search of the laboratory information management system was performed to identify cases diagnosed between 2009 and 2019 at Southampton General Hospital. Paediatric cases were excluded. The remaining reports were examined, and only those in which ILD was the primary or favoured diagnosis were included in the final count.
Results: A total of 503 cases were identified, 462 of which were in adults. Of these, 202 had a diagnosis appropriate for inclusion in analysis. Over the 10-year period, the number of annual diagnoses was variable (range 7-32). However, the overall trend was a decrease in the annual rate of ILD cases diagnosed at histology, down 50% in 2019 from 2009. In contrast, the number of annual referrals to the ILD team has increased approximately fourfold.
Conclusion: The use of HRCT by specialist thoracic radiologists, together with specialist chest physicians, has obviated the need for diagnosis on surgical biopsy: the majority of cases can be diagnosed on the basis of clinical and imaging features. However, there is a subset of cases with overlapping features where histology plays a pivotal role in determining the diagnosis and accordingly, management.

PS-11-046
Pulmonary carcinoid tumours with elevated proliferation rates – should there be a grade 3 subgroup of neuroendocrine tumours (NET)?
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Background & objectives: The current WHO classification of pulmonary neuroendocrine tumours (NETs) includes low-grade typical carcinoid (TC) tumours to intermediate-grade atypical carcinoid tumours (AC) to high-grade large cell neuroendocrine tumours (LCNEC) and small cell carcinomas (SCC).
Methods: We wished to review of an emerging group of tumours that have histologic features of carcinoids but mitotic counts exceeding 10 per 2 mm2 which by the current WHO 2015 criteria are classified as LCNEC. We performed a retrospective analysis of 50 neuroendocrine tumour cases diagnosed at our institutions between 2005 – 2020.Detailed microscopic review was undertaken.
Results: Of the 50 cases reviewed,14 cases (28%) showed histological features of carcinoids but mitotic counts exceeding 10 per 2 mm2.Three cases showed combined AC and LCNEC morphology and one case showed combined AC and SCC morphology. In all included cases, the highest mitotic count was >10 per 2mm2.The median highest mitotic count was 19 (IQR 15.5 -31.0).In eight out of fourteen cases, the Ki67 proliferation index was >20 (IQR 13.7 – 40).
Conclusion: A subgroup of NETs exists with morphology closer to carcinoid than non-small cell carcinoma, but with a raised proliferation rate 10 per 2 mm2. These may be better classified in alignment with carcinoids than LCNEC.

PS-11-047
Plastic bronchitis: expanding clinical associations and identifying specific histologic characteristics compared to other intraluminal casts
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Background & objectives: Plastic bronchitis is a rare condition in which airway casts develop in the tracheobronchial tree causing airway obstruction. Casts may be expectorated or lead to asphyxiation. Patients with casts can clinically be divided into those with allergic bronchopulmonary aspergillosis (ABPA) and plastic bronchitis (PB).
Methods: The PB group may be subdivided into post-operative cases including those following congenital, paediatric, adult or transplant surgery. We wished to determine whether there is a "primary" PB subgroup and, if so, did it have specific histopathological features. We performed a retrospective analysis of 30 consecutive-cases diagnosed at our institutions between 1999-2019.Clinical history was reviewed to classify the cases. Relevant histological features were semi-quantitatively scored.
Results: The 30 cases reviewed were classified as follows: APBA (12), postoperative (6) and "primary" PB (12).M<F (11:19). Median age:38 (2 months – 82 years). Casts from the "primary" PB group contained significantly more lymphocytes compared to neutrophils (p=0.0037) and increased lymphocytes compared to the ABPA group casts (p=0.0292). All "Primary" PB casts comprised loose fibrillary material which was only seen in 1/6 post-operative cases (p=0.0007) and none of the ABPA cases which all comprised thick mucin (p=0.0001).
Conclusion: Five cases showed clinical evidence suggestive of abnormalities in lipid metabolism. We have identified a group of "primary" plastic bronchitis casts with distinct microscopic features, in some cases associated with abnormal lipid metabolism.

PS-11-048

Upregulation of phagocytosis in senescence cells in UIP and COPD to supplement their metabolic need, and their interaction with immune cells

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Background & objectives: Senescence cells (SeC) were demonstrated in usual interstitial pneumonia/idiopathic pulmonary fibrosis (UIP/IPF), driving the fibrotic process. They upregulate LDH and Glut1 to keep with hypoxia. How senescent cell interfere with the immune system has not been studied.
Methods: Tissues from patients with UIP of different aetiologies and COPD were investigated. Sections were incubated with antibodies for phagocytosis activation markers tartrate-resistant acid phosphatase, Rab7, and LAMP1. The tissues were evaluated for CD47, an inhibitor of phagocytosis. SeC/p16+/p21+ were evaluated for the inflammatory mediators TNF , iNOS, and VEGF. To elucidate the interaction of SeC with the immune system.
Results: Macrophages and lymphocytes were analysed using antibodies for CD4, CD8, CD20, CD68, CD206.Senescent cells are found in remodeling areas in UIP and COPD. They express positivity for p16 and p21, upregulate autophagy, and express phagocytosis markers.
They are negative for CD47. The cells secrete inflammatory molecules, and thus drive the repair process inducing proliferations of myofibroblasts, finally resulting in fibrosis.
Conclusion: Senescent cells secure their metabolic needs by phagocytosis, and to keep with hypoxia activate alternative metabolic pathways by LDH and GLUT1 upregulation, either for anaerobic glycolysis, or using the Warburg effect of glycolysis in hypoxia.
They also influence the polarization of macrophages, whereas the distribution of lymphocyte subtypes are not influenced.

PS-11-049

Mature cystic teratoma of the lung: an exceptional disease

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Background & objectives: Teratomas are tumours composed of tissues derived from more than one germ cell line. Intrathoracic teratomas are usually seen in the mediastinum; they rarely occur in the lung as intrapulmonary teratomas. The criteria for pulmonary origin are the exclusion of a gonadal site or other extragonadal primary sites and the exclusive origin of the tumour from the lung. This case aims to demonstrate the clinicopathological description of a teratoma mimicking a lung mass querying aspergilloma.
Methods: A retrospective review was conducted. The case was obtained from the Pathology archives at the Muhimbili National Hospital, Dar es Salaam, Tanzania. Age, gender, the clinical presentation was recorded. Histopathological diagnosis was confirmed by gross examination and hematoxylin and eosin sections, characteristics of mature cystic teratoma was seen.
Results: A 32-years-old woman presented with long standing cough for over 13 years and episodes of hemoptysis and chest pain, no weight loss. She has been treated with anti TB with no improvement. CT showed left sided upper heterogeneous mass with areas of calcification. A 7x8x6cm specimen was received at histopathology showed cysts and calcifications grossly, and microscopy revealed a tumour with mature tissue from all the 3 germ cell layers.
Conclusion: The diagnosis has to rely on the radiologic imaging, which demonstrates calcification, cavitations, and peripheral translucent areas and confirm by histopathology. Patients present with chest pain, cough, hemoptysis and trichoptysis. Surgical removal is the curative treatment of this condition.

PS-12 Autopsy Pathology

PS-12-001

Incidental lung hamartomas

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Background & objectives: Lung hamartomas or pulmonary chondromas or pulmonary chondromatous hamartomas are considered rare benign tumours. We report two cases of lung hamartomas incidentally discovered in the necroptic examination, in a man of 58 years and a woman of 61 years old.
Methods: Necroptic examination has been associated to collection of tissue specimens for microscopy. Paraffin-embedding, followed by routine hematoxylin-eosin (HE) and Masson's trichrome stainings have been performed.
Results: One case revealed, in a bronchial wall, a circumscribed incidental lesion, of approximately 10 mm and another had a parenchymal nodule, of approximately 13 mm diameter. They consisted in mature, disordered hyaline cartilage, containing areas of ossification, in one case, along with variable amounts of adipose tissue, smooth muscle, and entrapped clefts of respiratory epithelium, corresponding to the features of lung hamartomas. No cellular atypia has been observed. Lung hamartomas may occur as a component of Carney triad, a rare non-hereditary condition with young women prevalence that also includes gastrointestinal stromal tumours and extra-adrenal paragangliomas, which has been excluded in our cases.
Conclusion: Despite their rarity, lung hamartomas should be considered in the differential diagnosis of lung cancers or benign tumours, such as lipoma, leiomyoma, myxoma, and fibroadenoma. They may be incidentally discovered during necropsy and microscopic examination may certify the diagnosis.

PS-12-002

Developmental hepatic lesions in forensic pathology

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Background & objectives: Developmental hepatic lesions are attributed to abnormal growth of the biliary tree. The aim of our study is to evaluate the necroptic findings of developmental hepatic lesions from our files.
Methods: The reports from autopsies performed in the last 5 years in our Department, have been reviewed and 7 cases of developmental hepatic lesions, with age distribution between 50 to 73 years old, 4 male and 3 female, have been selected. These cases have been investigated by routine paraffin-embedding, followed by haematoxylin-eosin (HE) and Masson's trichrome stainings.
Results: The microscopic exam revealed multiple large cysts associated with renal cysts, in 3 cases, diagnosed as polycystic liver disease, small or dilated bile ducts surrounded by fibrous stroma, characteristic features for incidental biliary hamartoma ("von Meyenburg complex"), in 2 cases, and incidental simple solitary hepatic cysts, in other 2 cases. Differential diagnoses included pseudocysts, infection pathology, neoplastic diseases, and traumatic-related lesions.
Conclusion: Developmental hepatic lesions are relatively rare, occur as simple cysts, biliary hamartomas, polycystic liver disease, as reported in our files, along with Caroli disease and ciliated hepatic foregut duplication cyst, reported in literature, their differential diagnosis being important in forensics.

PS-12-003

Case report: post-mortem diagnosis of eosinophilic myocarditis

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Background & objectives: Eosinophilic myocarditis is a form of myocardial inflammation, characterized by eosinophilic infiltration of the myocardium and often accompanied by eosinophilia. We present a case of a cardiorespiratory arrest with histologic evidence of eosinophilic infiltrate of the myocardium during the autopsy.
Methods: A medico-legal autopsy, toxicological laboratory exams and a histological diagnosis were conducted.
Results: A 48-year old, female patient with no relevant background history presented cardiorespiratory arrest, with previous complaints of interscapular pain. Laboratory findings revealed elevated levels of d-dimer, troponin I, reactive protein C and creatine kinase and no peripheral eosinophilia. Imagiological testing and coronary angiography, excluded aortic dissection, pulmonary embolism as well as, an acute coronary syndrome. Organ support was suspended because of the presented instability and an unknown reversible cause. Macroscopic appreciation, during autopsy revealed a slight heterogenic coloration of the myocardium, and no other apparent causes of death. The histology revealed interstitial haemorrhage of the heart and an eosinophilic infiltrate of the septal subendocardic myocardium.
Conclusion: The clinical presentation of Eosinophilic myocarditis varies from paucisymptomatic to acute fulminant myocarditis. It is often fatal with high in-hospital mortality, in particular when it presents as fulminant form. Eosinophilic myocarditis is probably under-recognized and frequently discovered on post-mortem examination. We present a case of EM discovered on post-mortem examination were no associated systemic disorder was identified, as such considered an idiopathic/undefined EM.

PS-12-004

Correlation of digital and invasive post-mortem examinations

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Background & objectives: Invasive autopsy is the gold standard for determining cause of death (COD). Digital autopsies have been used in the Sefton Coroner's jurisdiction since August 2018. We compared proposed digital COD with invasive COD and compared assessment of coronary artery disease.
Methods: All autopsies that had both digital and invasive examination at Whiston Hospital between August 2018 and January 2019 (6 month period) were included. Reports were interrogated for major and minor discrepancies along with coronary artery disease assessment. The data was compiled in Microsoft Excel and analysed in both Microsoft Excel and IBM SPSS.
Results: A total of 303 autopsies were digitally scanned of which 134 proceeded to invasive post-mortem examination. A total of 51 minor discrepancies were identified, which would not affected cause of death not were otherwise significant. There were 6 major discrepancies identified that would have altered cause of death. 57% had similar estimations of coronary artery disease. Only 64% of cases had no discrepancies between the radiological and invasive examinations.
Conclusion: Our cohort population is significantly different from those of previous studies. Often due to lack of clinical information there are many unanswered questions remaining after DA, so invasive PM is required. The use of digital autopsies has to be refined based on appropriate case selection since some COD cannot be detected or are likely to be missed on radiological examination.

PS-12-005

Acute fatty liver disease of pregnancy: a difficult diagnosis in a case of maternal death

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Background & objectives: Acute fatty liver disease of pregnancy (AFLP) is a rare condition and an obstetric emergency with high rates of severe maternal morbidity and mortality. We present a case of a 29-years old female, who died shortly after the delivery.
Methods: She presented in emergency department with abdominal pain, nausea, and vomiting five days after her first delivery. She died shortly after due to liver failure. To establish the cause of death, a full autopsy was performed at the Institute of Forensic Medicine of Targu Mures, Romania.
Results: On autopsy examination, massive oedema of the lungs and fatty appearance of the liver were seen. At microscopy, the lungs exhibited acute extensive oedema and pulmonary capillary congestion. The liver presented microvesicular fatty infiltration of the hepatocytes visible only in the central and mid zonal parts of the lobule. The fat droplets surrounded centrally located nuclei with a foamy appearance of the cytoplasm. The fatty infiltration spared a thin rim of cells around the portal tracts.
Conclusion: The histological aspect of the liver was consistent with AFLP. The differential diagnosis with hemolysis, elevated liver enzymes and low platelets syndrome (HELLP) is difficult, since there are some clinical, biochemical and pathological overlapping. Some of the authors consider these entities as different stages of the same disease.

PS-12-006

CMV pneumonia mimicking lung tumour - an autopsy case report

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Background & objectives: Viral infections may cause acute exacerbations in patients with usual interstitial pneumonia. Cytomegalovirus (CMV) pneumonia ranges from mild interstitial infiltrates to diffuse alveolar damage and can sometimes mimic a lung tumour on macroscopy and Hodgkin's disease on microscopic examination.
Methods: We present a case of a 46-year-old woman, previously diagnosed with usual interstitial pneumonia (UIP), suffering progressive worsening of respiratory function, brought by ambulance into the emergency department. Chest CT scan showed ground glass appearance and multiple nodules in her lungs, suggestive of acute respiratory distress syndrome. The patient died several hours after admission.
Results: Autopsy showed multiple confluent firm tumour-like gray-white nodules in the middle and lower lobes of the right lung, encasing hilar structures, with yellow-gray areas of necrosis and associated pleural and pericardial retraction. Dark red areas of haemorrhage were also seen. Frozen section examination during autopsy raised suspicions of malignancy, but permanent sections showed no malignant cells. Pneumocytes were large and displayed a single basophilic intranuclear inclusion, surrounded by a clear halo, resembling Reed-Sternberg (RS) cells. We also found the honeycombing pattern characteristic of UIP and interstitial lymphocytic infiltrate, focal hyaline membranes, areas of hemorrhagic necrosis with central neutrophilic response and histiocytes within the airspaces.
Conclusion: On immunohistochemistry, the RS-like cells were pan-cytokeratin positive, TTF-1 and LCA negative and stained for anti-CMV antibody. CD15 was positive in some RS-like infected cells, but CD30 was negative.This case illustrates the diagnostic pitfalls in CMV pneumonia, mimicking a tumour, both macroscopically and histologically, and highlights the challenges pathologists face in autopsy examination.

PS-12-007
Video documentation in autopsy practice
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Background & objectives: Video documentation devices for personal use have become widely available in the last decade, many of whom are able to record the point of view of the pathologist and serve as aids in protocol finalization and educational tools for students.
Methods: Five separate wearable devices for video documentation were used in the standard autopsy practice of a single pathologist – two sport cameras, a pair of camera glasses and two pairs of smart glasses – Cloud-I II and Google glass – XE V2. The five devices were compared for their individual pros and cons and feasibility in autopsy and educational practice.
Results: A total of 50 consecutive autopsies, performed by a single pathologist were recorded for the period of one year. Only the sports cameras and Google glass provided sufficient resolution to be considered efficient aids. Ten of the autopsies were recorded simultaneously with the two devises, with the sports cameras performing superiorly in providing the proper point of view, due to their adjustable nature, video-resolution and audio quality, together with sufficient battery life. As of February 2020, however, Google glass XE V2 is no longer supported and is no longer a viable oprion.
Conclusion: Video documentation of autopsies using new generation wearable devices is a feasible option for both individual autopsy cases and educational purposes of both students and young pathologists.

PS-12-008
Differential heart weights in diabetics and hypertensives compared to apparently healthy adults - a post-mortem review
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Background & objectives: Diabetes mellitus (DM) and hypertension are insidious chronic disease conditions associated with multiple end-organ damage. This study investigated the effects of these two conditions, individually, and as comorbidities, on heart weights at post-mortem compared to apparently healthy decedents.
Methods: Eleven-year (2008-2018) Postmortem records were reviewed for apparently healthy, diabetic, hypertensive, and hypertensive-diabetic decedents aged 18 to 70 years. Absolute heart weights (without the pericardium), gender, body length and age were documented. The difference in mean heart weight and predictors of heart weight were determined using Kruskal Wallis (with post hoc test) and multivariate regression statistics on SPSS version 20.
Results: Two hundred and thirty-three cases from 159 males and 74 females met the inclusion criteria comprising of 85 apparently-healthy, 29 diabetic-only, 43 hypertensive-diabetic and 76 hypertensive-only decedents with mean heart weights of 296.9±44.1g, 349.0±121.4g, 404.8±111.0g, and 434.7 ±129.2g, respectively. The observed difference in mean heart weights was significantly different across groups (p <0.0005).On post hoc test, this significant difference was sustained between diabetic-only and apparently-healthy (p = 0.032), diabetic-only and hypertensive-diabetic (p = 0.006), apparently-healthy and hypertensive-only (p <0.0005), but not between hypertensive-diabetic and hypertensive-only (p = 0.305) groups. Hypertension and male gender were predictors of heart weight significantly (p <0.05), whilst age, and DM did not reach statistical significance.
Conclusion: Hypertensive individuals
(including hypertensive-diabetic) have significant differential heavier hearts compared to apparently healthy and non-hypertensive diabetic individuals. The possible effect of DM on heart weights seen between diabetic and apparently healthy decedents waned on multivariate analysis. Hence, its role remains unclear.

PS-12-009
Fibrinous pericarditis as cause of death in chronic kidney disease: study of a series of clinical autopsy cases
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Background & objectives: The need to determine the causes of underdiagnosed fibrinous pericarditis (FP) makes autopsy a fundamental tool for its study. Our goal is to describe a series of cases and draw conclusions about the pathogenesis and its link with other entities.
Methods: We review 219 clinical autopsies, selecting cases with diagnosis of FP.
Results: Seven patients, 4 women (57.2%) and 3 men (42.8%). Mean age: 71±9.6 years. Chronic kidney disease (CKD): 6 cases (85.7%).
High urea and creatinine in all cases. Shock during hemodialysis in 2 cases, exitus before 24 hours in 3, acute bronchopneumonia in 6, liver cirrhosis in 3. The pericardial exudate was sterile in 6 cases.
Enterococcus faecium was isolated in a patient with chronic liver disease due to congestive heart failure.
Conclusion: This study emphasizes the importance of clinical autopsy in the diagnostic of FP as cause of death in CKD. Capillary hyperpermeability due to uremic toxins coinciding with infections is probably related to its aetiology. Liver disease can decline the prognosis.

PS-12-010
Autopsy examination in sudden cardiac death
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Background & objectives: In sudden cardiac death autopsy is the essential step in establishing a diagnosis of inherited cardiac disease and identifying families that require cardiac screening.
Methods: To evaluate aspects of post-mortem practice in Europe a questionnaire was designed and circulated to both clinical and forensic pathologists. There was a 48% response rate. The results, which were from a total of 14 countries, showed a wide variety in the management of sudden cardiac death, with a general tendency towards a lack of thorough investigation.
Results: In up to 40% of cases autopsies were not performed in subjects less than 50 years who may have died from cardiac disease. Reasons for this were lack of finance and lack of interest from police, legal authorities and doctors. Only 50% of pathologists followed a standard protocol for autopsy examination. Lack of expertise and/or training were reasons for this.
Conclusion: The results of our questionnaire suggest that although the standard of practice during autopsy in many centres is appropriate in many centres, the results indicate that many more cases should be submitted for autopsy, especially in sudden cardiac death in the young. On a positive note when autopsies were performed histology and toxicology were almost always performed, genetic studies were generally available and retention of the heart for specialist study was permitted in most cases.

PS-12-011
Suspected tuberous sclerosis complex in a foetus in the third trimester of the gestation: pathological and genetic findings
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Background & objectives: Tuberous sclerosis complex (TSC) is a multisystemic neurocutaneous genetic condition with autosomal dominant inheritance, characterized by hamartomatous lesions in multiple organ systems. TSC is caused by mutations of either of the following tumour suppressor genes, TSC1 (9q34) and TSC2 (16p13.3).
Methods: A complete foetal autopsy and a mutational analysis of the genes TSC1 and TSC2 by Sanger method were performed. Foetus blood sample, for genetic study, was obtained from cordocentesis.
Results: Foetal cardiac tumours were diagnosed by routine sonographic study in utero at 32 weeks. Subsequent foetal brain MR imaging at 33 weeks showed multiple nodules. The combination of both findings suggested the diagnosis of tuberous sclerosis complex. Therefore, late termination of pregnancy was decided and autopsy performed. Cardiac rhabdomyomas and brain cortical tubers were histologically confirmed.
A heterozygous TSC2 mutation c.5024C>T (p.Pro1675Leu) was identified in the genetic study. This variant is classified as pathogenic in the literature.
Conclusion: The clinical suspicion of tuberous sclerosis complex was confirmed by pathological and genetic findings.
The progenitors of the foetus were a healthy nonconsanguineous couple with an unremarkable family history. However, genetic study of the parents is recommended to rule out that they are carriers in mosaicism of the pathogenic variant. If positive result, there would be risk of recurrence in future pregnancies.

PS-12-012
Features of the diagnosis of intravital fracture of ribs
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Background & objectives: Fractures of ribs are accompanied by mixture of fragments with continued breathing, friction occurs on the surfaces of fragments of ribs and appearance of traces that make it possible to judge the duration of the post-traumatic period and the lifetime.
Methods: To study the morphological picture of traces of friction of fragments to determine the intravital origin of the fracture.56 materials from corpses with chest injuries were studied by stereoscopy.
Results: It has been established: with continued breathing, a rigid surface with a rough relief is introduced into a less rigid surface. Therefore, at the beginning of friction on a less rigid surface there are multiple tsar-pins in the direction of movement of fragments. Experiment: for the formation of traces, about 25 respiratory movements are necessary, which corresponds to the duration of the agonal period. Further friction of fragments on a softer surface gives the marginal fracture site the appearance of a shiny site and corresponds to a post-traumatic period of up to 6 hours.
Conclusion: Signs of friction initially appear on the surface of the rib, which experienced a tensile stress during the formation of a fracture. On extensor fractures, these signs are more pronounced.

PS-12-013
Malignant neoplasms in clinical autopsies: the importance of the autopsy – a 13-year retrospective study in a tertiary hospital
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Background & objectives: Technology improvements have contributed to increase life expectancy; however, in 20% of clinical autopsies (CA) neoplasms are the cause of death.
We pretend to identify malignancies in CA and compare the data from autopsies with diagnostic hypotheses proposed during medical care.
Methods: Clinical and anatomopathological data were collected from reports at our institution, over a 13-year period (January/2007 to December/2019).
Staging was determined according to the 8th edition TNM/AJCC.
Discordance rate was established between clinical data and autopsy diagnoses.
A total of 238 cases were reviewed, of which 17 correspond to malignant neoplasms.
Results: Our cohort included 17 cases with a median age of 61 years (34-86 years) with a slight male predominance (9M/8F).
The most requesting department was Internal Medicine (41%).
Most of our tumours were carcinomas (41%) and lymphomas (41%) and the remaining (18%) were chondrosarcoma, glioblastoma and melanoma, all in advanced stage, mostly with multiorgan involvement (29%).
Primitive location of carcinomas was: lung (1), pharynx (1), thymus (1), breast (1), pancreas (2) and prostate (1).
The discordance between clinical and autopsy diagnoses of malignant neoplasms was 41%, mainly due to suspected infection conditions.
Conclusion: The discrepancies between clinical and autopsy diagnoses continue to occur and confirm the importance of the post-mortem examination.
Autopsy examination would allow a better understanding of the evolution course of the disease and it remains a useful tool, enabling the identification of occult neoplasms, clinically unknown.

PS-12-014
Cystic fibrosis (F508del / W1282X): clinical and morphological analysis of a 23-year-old patient
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Background & objectives: Patient U., 23 years old, is admitted to the hospital with bronchopulmonary infection. Receives antimicrobial and antifungal treatment without effect. The patient died of respiratory and renal failure.
Methods: A clinical anatomical analysis of the case of cystic fibrosis with multiple continuously recurring infectious complications in a 23-year-old patient was carried out. The diagnosis of AA amyloidosis with kidney damage with severe nephrotic syndrome was morphologically verified.
Results: At autopsy: The filling of the bronchi of all calibers is determined up to bifurcation of the trachea with a viscous purulent secretion. In the interstitium of the lungs, interstitial fibrosis, bronchial and bronchiolectasis.
In the kidneys, the border between the cortical and medulla is not distinguishable. Spleen 12x8x5 rocky density
Desquamative bronchitis, goblet cell hyperplasia, papillary proliferation and squamous metaplasia of bronchial epithelium are microscopically determined. The lumens of the bronchi are filled with purulent contents mixed with desquamated epithelial cells and cellular detritus. Amyloid deposition is noted in the kidneys. Intrafollicular deposition of amyloid masses in the spleen.
Conclusion: This clinical and anatomical observation demonstrates a rare genetic disease of cystic fibrosis (F508del \ W1282X: heterozygous mutation), which is practically untreatable, leading to multiple complications in the form of secondary amyloidosis and death.

PS-12-016

Analysis of medical students' previous knowledge about autopsy

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Background & objectives: Autopsy is an essential procedure for identifying the cause of post-mortem death; however, contact with medical professionals usually occurs only after graduation. Evaluate the general knowledge of medical students about the concepts related to the practice of an autopsy.
Methods: Cross-Sectional epidemiological study performed with medical students from seventh (7th) and eighth (8th) semesters of a University, the first and the second after finisnh pathology that are passing and already passed by of pathology, through the application of a questionnaire using the google forms platform.
Results: The sample consisted of 85 students, 61 (71.8%) from the 7th and 24 (28.2%) from the 8th. In the 7th semester, when asked about the definition of autopsy, only 9.83% answered correctly, 80.3% knew the instructions for sending cases to the Death Verification Service (DSV) and 52.5% to the Institute of Legal Medicine (ILM), however 100% did not know the autopsy techniques. As for the students of the 8th semester, 87.5% knew the concept of autopsy, 100% knew the instructions for sending cases to the DSV and 87.5% to the ILM and regarding the autopsy techniques 54.17% knew at least two.
Conclusion: This study shows that the importance of teaching autopsy in medical school.

PS-12-017

A "lost generation" of patients with AAA - lessons from the mortuary

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Background & objectives: Abdominal aortic aneurysms (AAA) are localised dilatations of the abdominal aorta. AAA are usually asymptomatic unless they rupture, with a mortality rate ~80%. The UK AAA screening programme aims to reduce AAA-related-mortality, inviting men aged 65+ for a "one-off" ultrasound.
Methods: An electronic database (CoPath) was searched to ascertain cause of death for all post-mortem examinations performed in a tertiary hospital from 2013-2019. AAA-rupture deaths were identified and patient demographic data collected. The UK AAA screening programme (NAAASP) database (SMaRT) was cross-checked to interrogate screening-status and to categorise causes of non-screening.
Results: There were a total of 105 cases where death occurred as a result of ruptured AAA (66%men, 35%women). Only 6 patients were known to any screening program; of these, 1 declined attendance, 1 died prior to attendance, 1 did not attend and 1 was screened out-of-region. Only 2 patients underwent ultrasound locally. The mean age of the male cohort was 77.6 years (SD 7.81). Only 5 deaths (4.8%) occurred in patients aged <65 years old.
Conclusion: This autopsy-based study identifies a potential "lost-generation" of elderly patients at risk of fatal AAA rupture. More work is needed to investigate the disease burden in this un-screened population. Research should focus on the suitability of these patients for intervention, particularly in light of draft NICE guidelines restricting endovascular aneurysm repair (EVAR) in un-ruptured AAA.

PS-12-018

Sudden death secondary to schistosomiasis, case report and literature review

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Background & objectives: Report a case of sudden death secondary to schistosomiasis. Schistosomiasis is caused by a parasitic trematode worms. The parasite has a complex life cycle that includes contamination of water by excreta, specific fresh water snails as intermediate hosts and mammalian water contact. Acute schistosomiasis is generally benign and self limited, whilst the chronic form causes major morbidity. This case report aims to highlight autopsy findings in sudden death secondary to schistosomiasis and suggest possible pathogenesis thereof.
Methods: This is a case report to highlight an unusual clinical presentation of schistosomiasis in a previously healthy 32 year old female who collapsed suddenly and became unresponsive. Emergency medical unit investigations revealed ventricular fibrillation. Despite resuscitation, the patient demised. Consent for autopsy was granted. Patient's record review, autopsy examination and literature review was undertaken as part of the work-up.
Results: Following the review of the literature and the index case histopathological findings comprising parasitic pulmonary arterial embolization with minimal to absent tissue reaction, urinary bladder fibrosis and transmural schistosome ova and clinical history of ventricular fibrillation, pulmonary hypertension secondary to schistosomiasis was suggested as the aetiology of abnormal cardiac electrical activity. Other systems including heart, liver, kidneys, spleen, brain and thymus were unremarkable.
Conclusion: Parasitic arterial embolisation as an exclusive cause of pulmonary hypertension and sudden death is unusual, hence more studies are warranted in understanding the pathogenesis of schistosomiasis associated pulmonary hypertension.

PS-12-019

Schistosomiasis as an autopsy diagnosis in a patient with massive digestive haemorrhage

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Background & objectives: To report a case of schistosomiasis diagnosed at autopsy.
Methods: Review of medical record and autopsy report.
Results: A 33-year-old man arrived at the hospital with a massive episode of hematemesis. An urgent high digestive endoscopy showed a large amount of clots in the esophageal lumen, and massive active bleeding from thick varicose cords. During the endoscopic examination, the patient presented cardiac arrest. Cardiopulmorary resuscitation maneuvers were performed for 30 minutes, but vital signs did not return. At the autopsy, the patient presented areas of periportal fibrosis and an abundant presence of blood throughout the entire gastrointestinal tract, due to active bleeding from the distal oesophagus. Microscopically, Schistosoma mansoni eggs were identified in the liver and in both lungs (Loeffler syndrome), clarifying the aetiology of portal hypertension.
Conclusion: Schistosomiasis is a rare disease in southeastern Brazil. In the present case, this pathology leaded to portal hypertention and the patient died due to hypovolemic shock in consequence of massive upper gastrointestinal bleeding.

PS-12-020

Mortality pattern in children in a Nigerian tertiary hospital: an autopsy study

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Background & objectives: Childhood mortality is high in developing countries and, under 5 mortality is highest in sub-Saharan Africa. Autopsies validates cause of death. This study retrospectively reviewed post-mortem records observing the causes of death and paediatric autopsy trend in our institution.
Methods: Post-mortem records of children 17yrs and below between 2008 to 2017 in our institution were reviewed. All post-mortem examinations were duly consented. The causes of death were classified using ICD-10. The data was analysed using SPSS 23. $P \leq 0.05$ was considered significant.
Results: There were 89 paediatric cases representing 8.2% of the 1092 autopsies done within the study period. Infections (34.8%), and malignancies (12.4%) were major cause of deaths. Infections accounted for 50% of under 5yr mortality. Pneumonia is the most common infectious disease with 48.4% of all infections followed by bacteria sepsis of newborn at 9.7%. Malignancies were commoner in children above 10yrs old accounting for 36% of causes of death within this age group. The modal age was the first year and early neonatal deaths constituted 40% of this group. There is 33.8% decrease in autopsy request rate in the later 5yrs of study period.
Conclusion: This study shows that a major cause of childhood mortality in our environment is infection with majority of under 5 children dying from infections which is majorly pneumonia. Better hygiene and infection control with prompt adequate management might be lifesaving.

PS-12-021

Hepatic necrosis in haemophagocytic lymphohistiocystosis

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Background & objectives: A 41 year old man died of multi-organ dysfunction after admission to intensive care. His only previous illness was chronic lymphocytic leukaemia (CLL). His white count (36 X 109/l) was stable and he was receiving no specific treatment for this.
Methods: A full autopsy was performed including detailed histology, immunohistochemistry and molecular studies.
Results: The premortem ferritin level was > 60,000mg/l. The most striking post mortem finding was substantial liver enlargement (4.1kg) with extensive hepatocyte necrosis. There was paraaortic lymphadenopathy with widespread histiocytic phagocytosis of erythrocytes. Histological sections from the spleen and lymph nodes confirmed CLL. No other form of lymphoma/leukaemia was identified. There was no autopsy evidence of sepsis or acute lung injury. The heart was enlarged (560g) but there was no evidence of myocardial pathology.
Haemophagocytic lymphohistiocystosis (HLH) was diagnosed histologically. HLH is a poorly understood condition associated with viral and bacterial infections, some lymphoid malignancies, solid neoplasms, various multi-system disorders and genetic abnormalities. CLL is not specifically associated with HLH.
Conclusion: No underlying cause for HLH was found. The cause of the florid hepatocytic necrosis was not established but it was beyond what would be expected in multi-organ failure. Whether it was the cause or consequence of HLH is uncertain.

PS-12-022

Hydroxychloroquine-induced cardiomyopathy with endomyocardial fibrosis of unknown cause

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Background & objectives: The differential diagnosis of Systemic Lupus Erythematosus (SLE) affecting the heart is Hydroxychloroquine (HCQ) Cardiotoxicity.
Endomyocardial Fibrosis (EMF) can be confused with other hypertrophic cardiomyopathies (HCM).
We raised the possibility that EMF could be related to compounds of valvular prosthesis.
Methods: A 41-year-old female with SLE and mitral valvulopathy with mechanical prosthetic and HCQ treatment. She was admitted with decompensated heart failure and fever. Echocardiogram showed functional worsening and presence of fibro-calcified areas. The patient was died, a partial clinical autopsy was requested.
Lungs and heart were studied. Genetic studies were ordered, and biochemical studies of cardiac tissue and prosthetic material.
Results: In gross view, the transversal section of the heart showed extensive areas of white and partial calcified fibrosis in the endocardium of left ventricle, that had diffusely thickened the lining of the chamber and involved the papillary muscles
Microscopically, the heart tissue showed alterations of HCM. An intense subendocardial myocyte vacuolization (MV) was observed, which also affected the sinus node.
Genetic study was performed by massive sequencing to overrule Fabry Disease, resulting in negative non-identified pathogenic genetic variants. However, two uncertain significance variants were found.
The prosthesis has been analysed with semi-quantitative Wavelength X-ray fluorescence, and heart tissues analysed by Inductively Coupled Plasma Mass Spectrometry High Resolution
Conclusion: The histopathologic features are diagnostics of HCQ-induced cardiomyopathy. However, EMF remains of unknown aetiologies.
The results obtained in the high-resolution molecular biochemical techniques could support the hypothesis of the relationship between inert compounds of the valvular prosthesis and EMF.

PS-12-023

Ante-mortem and post-mortem diagnoses of pulmonary infections in HIV/AIDS patients in a tertiary hospital in Ghana

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Background & objectives: HIV/AIDS patients suffer from opportunistic infections with pulmonary infections being the commonest cause of morbidity and mortality. The study aimed to investigate the burden of pulmonary infections HIV deaths in Ghana, and the drug susceptibility of the causative organisms.
Methods: 95 consecutively consented HIV/AIDS-related deaths were prospectively included. Standard autopsy procedure was followed with review of record of deceased. Lungs were sampled with two representative specimens taken from each lobe, and then processed with histology-stains and cultures for micro-organisms. Drug susceptibility testing was performed. Baseline characteristics

using Pearson, chi-squared, Fisher's exact and student t tests were applied where appropriate.
Results: Bacterial pneumonia was the most common cause of death (66.3%) followed by TB (35%). The ante-mortem clinical diagnosis of TB compared to confirmed-autopsy diagnosis was 78.8% sensitive (95% CI 62.2-89.3) and 67.3% specific (95% CI 54.1-78.2). Of culture-proven M. tuberculosis cases, 23.8% failed to identify TB as an ante-mortem clinical cause of death, of which 20% were rifampin mono-resistant. Bacteria and fungi cultures resulted in several isolates. E. faecalis, E. coli, K. pneumonia, Staphylococcus species and Candida species are among the organisms identified. Gram-negative bacteria are most susceptible to cefoxitin but highly resistant to cefuroxime sodium whereas, the Gram-positives are highly susceptibility to vancomycin but resistant to flucloxacillin.
Conclusion: Our findings emphasize that pulmonary TB and pneumonia are major causes of death in HIV/AIDS patients. A significant percentage of missed TB-infections demonstrated drug resistance. There is the need for heightened awareness coupled with aggressive TB screening amongst HIV/AIDS patients.
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PS-12-024
When the association gets ambiguous – VACTERL in a new-born autopsy – case report
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Background & objectives: To present an autopsy case-report of VACTERL association (vertebral; anal atresia; cardiac; tracheo-oesophageal fistula; renal; limbs) in a new-born with 33 weeks of gestation, with ambiguous sexual development.
Methods: A 34-years old woman, from Angola, presented at our emergency department in spontaneous labour. The previous ultrasound showed oligohydramnios and foetal malformations (cardiac, spinal, genitourinary and gastrointestinal). The delivery occurred without incidents (33 weeks of gestation). The new-born died within 3 days and an autopsy was performed.
Results: The gross examination showed a new-born with 33 weeks anthropometry; 2350g weight; a slight lumbar kyphosis, male external genitalia (micropenis with hypospadias and scrotum); faeces in the urethral meatus and imperforate anus. The internal examination showed: right atrium, right ventricular and ascending aorta dilatation; bilateral pulmonary hypoplasia; medium oesophageal atresia with tracheo-oesophageal fistula; inverted colonic rotation with distal colon/rectum dilatation and recto-vesical fistula; polycystic fused kidneys with horse-shoe conformation (larger right kidney) and dilated right ureter. Both ovaries and Fallopian tubes were present without evidence of uterus. There were no alterations in the limbs.
Conclusion: VACTERL association is rare (incidence of 1:10.000-40.000) and most cases are sporadic. There are few cases with ambiguous genitalia. It should present at least three of the six anomalies described and it overlaps with other entities, namely, the CHARGE syndrome.

PS-12-026
Hypophosphatasia: a rare metabolic genetic disease: an autopsy study
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Background & objectives: Hypophosphatasia is a rare metabolism bone disease, caused by a mutation with loss of function in the Alkaline phosphatase, tissue-nonspecific isozyme (ALPL).This genetic disorder produces a deficiency throughout the body being more severe in the liver, kidney and bone.
Methods: We present an autopsy study of a 15+4-week foetus, resulting from a legal interruption of pregnancy, with prenatal diagnosis of bone dysplasia. The foetus weighed 79.8 g and presented anthropometric measurements at the lower limit of normality for its gestational age.
Results: Externally, it drew attention to the shortening and deformity of the lower and upper limbs. These alterations were corresponded radiographically and in the macroscopic examination with multiple fractures in the diaphysis of the long bones. Histologically, it is characterized by the pathological persistence of columns of hypertrophic chondrocytes 2-3 in the metaphysis and adjacent diaphysis of long bones with absence of bone trabeculae and osteoid matrix. In this case, the mutation was positive for the ALPL gene. Later studies showed that the mother is a heterozygous carrier, so we would be facing an autosomal recessive inheritance pattern.
Conclusion: Hypophosphatasia is a rare disease with a large clinical variability. It needs to be suspected by a compatible clinic and confirmed by a genetic study. Differential diagnosis will be mainly made with rickets and imperfect osteogenesis (most common skeletal dysplasia)

PS-12-027
Causes of death of cancer patients in the emergency hospital
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Background & objectives: The peculiarity of medical care in the emergency hospital is prevalence of severely decompensated patients, among which there are patients with malignant tumours.
Objective: to analyse the complications in cancerous patients in emergency hospital.
Methods: Out of 1519 autopsy reports (2017-2019) 207 cases were death due to cancer, misdiagnosed in 50% in hospital; only 9,2% patients already had diagnosis of malignant tumour. Cancer of colon, stomach, pancreas and also heamoblastoses were dominant. Usually the patients had a set of complication, among which it was very difficult to extract a fatal one.
Results: 41,5% patients had cancerous cachexia; 34,8% cases had decompensated obstruction of hollow organs due to tumour grow; 29,0% had secondary pneumonia; 31,9% died because of toxic shock due to tumour destruction; 27,7% had posthemorrhagic anaemia (half cases due to tumour decay and another half – due to bleeding fromsymptomatic erosions in GIT). 15%cases had paraneoplastic coagulopathy,manifested by pulmonary embolism or ischemic stroke.
Conclusion: Dealing with the patients of advanced cancer in emergency hospital clinician must be ready to face a complicated case with overlapping complications, blurring the clinical picture. Pathologists also may be stumpted looking for the immediate cause of death during autopsy.

PS-12-029

Regulation of clinical autopsies in Russia

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Background & objectives: Clinical autopsies still play an important role in healthcare. In different countries they are regulated quite differently. In Russia there is long-term tradition in autopsy pathology and a set of documents regulating this work.
Methods: Brief concise presentation of the basic documents and results of their use according the federal law N323 (accepted on the 21.11 2011) of Russia procedure of clinical autopsies is determined by Ministry of Healthcare and special order of the federal ministry 6.06 2013.
Results: Procedure of autopsy and the forms of record (common and perinatal: foetus, stillborn or new-born). Clinical autopsy has to be conducted when patients died from diseases. In cases of death due external causes and in absence of documents - legal investigation. In RF autopsy is obligatory if there is suspicion on violent death, impossibility to formulate exactly the final clinical diagnosis, hospitalization for less than 1 day, possible relationship with therapeutic or diagnostic medicaments, in cases related to medical interventions, infectious diseases (including suspect), oncology without histology, results of ecological catastrophes, pregnant, in childbirth, new-borns in age till 28 day, stillborn. Clinical autopsies were divided in 5 categories of difficulty
Conclusion: According to reports from regions of Russia in 2018 were done approximately 469000 autopsies. The percentage of discrepancies between clinical and pathological diagnosis – 6,3 % (from 1,2% to 12,1% in different years) we consider not to be objective.

PS-13 Endocrine Pathology

PS-13-001

Utility of fine needle aspiration cytology in the distinguishing between parathyroid and thyroid lesions

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Background & objectives: Fine needle aspiration (FNA) smears of parathyroid glands is often confused with thyroid. Thus, majority FNA of parathyroid glands is unintended. However, ultrasound guided FNA is increasingly used to localize parathyroid glands in abnormal location and in hyperparathyroidism.
Methods: 91 patients underwent parathyroid FNA either unintended during the sampling of thyroid nodules (36 patients) and suspicions metastatic lymph node (7 patients) or specifically to localize parathyroid lesions (48 patients). In addition to cytological examination, measurement of parathyroid hormone in the needle washouts (FNA-PTH testing) was performed in all examined patients and immunocytochemical examination (IC) on 16 FNA specimens.
Results: The most frequent cytological features included: stippled chromatin (34), scattered naked nuclei (30), loose clusters (22), large crowded clusters (17), oxyphilic cytoplasm (13), cribriform or trabecular architecture (10) and follicular pattern (7). Cells with small, dark nuclei and colloid-free background was another sign suggestive of parathyroid origin. 87 FNA smears were correctly diagnosed as parathyroid lesions in conjunction with FNA-PTH testing and/or IC.
Conclusion: The architectural pattern and cellular features help to distinguish between parathyroid and thyroid in the FNA smears. FNA-PTH testing in conjunction with FNA is the most useful adjunct to determine whether the FNA specimen represents parathyroid or thyroid lesions. In addition immunocytochemical examination increases the diagnostic accuracy of the FNA.

PS-13-002

Clinicopathological impact of C228T mutation of telomerase reverse transcriptase promoter in follicular cell-derived thyroid carcinoma

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Background & objectives: C228T mutation of telomerase reverse transcriptase promoter (TERTp) has been identified as specific for malignancy in thyroid and indicative of poorer prognosis.
Objective: to determine the prevalence and prognostic value of C228T TERTp mutation in thyroid malignancies of our institution.
Methods: From 1993 to 2017, 147 cases of thyroid follicular cell-derived carcinomas were identified with histological material available, corresponding to 122 women and 47 men, with age range between 7 and 83 years. C228T TERTp mutation was determined by pyrosequencing. Histopathological and clinical data were recorded. Follow-up was available in 143. Statistical analysis for variables of clinical interest was performed.
Results: The mutation was identified in 18 of the 147 cases (12.2%), with higher percentages in poorly differentiated carcinomas and well differentiated carcinomas with a poorly differentiated component than in well differentiated carcinomas (37.5% vs 7.3%), with statistically significant difference. None of the cases of anaplastic carcinoma held the mutation. It was more prevalent in stages II to IV vs stage I (25.8% vs 8.62%), in cases that presented recurrence or persistence vs cases that did not (25.9% vs 9.56%), and in cases with death due to disease or persistent disease at follow-up vs cases free of disease (28.57% vs 9,83%), with statistically significant differences in all of them ($p<0,05$) .
Conclusion: C228T TERTp mutation was more prevalent in poorly differentiated thyroid carcinomas and carcinomas with poorly differentiated component, and in cases with higher stage, persistence and / or recurrence of the disease and worse prognosis. These associations suggest that the presence of this mutation could indicate a more intense treatment or a closer follow-up.
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PS-13-003

NIFTP vs FVPTC: a cyto-histo morphological study with clinical correlation and diagnostic challenges

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Background & objectives: NIFTP , introduced in WHO 2016 classification of endocrine tumours is an indolent lesion distinct from FVPTC with strict diagnostic criteria. It's cytological features aren't clearly defined.
To study the cyto-histo morphological features and uncover useful morphological clues to distinguish them.
Methods: Retrospective study (Jan 2016- Dec 2019). All cases of NIFTP and FVPTC diagnosed during this period are included. The FNAC smears were reviewed for: cellularity, nuclear features (9 parameters) and architectural features (11 parameters). Gross details (5 parameters) and Histopathology (9 parameters) were documented for each case.
Results: NIFTP: 12 cases, FVPTC: 14 cases. FNAC: Nuclear membrane irregularity, chromatin margination, atypical bare nuclei

was more frequent in FVPTC (40%, 10%, 50%) than NIFTP (14%, 0%, 29%). Gross: FVPTC was more multifocal (36% vs 0%). Haemorrhage on cut-section was seen more in NIFTP (67% vs 21%). Histopathology: Capsule thickness >2mm was more frequent in FVPTC (57% vs 25%). Mitosis <1/10hpf was common in NIFTP (67% vs 29%).
Conclusion: Although cytomorphological overlap does exist between NIFTP and FVPTC, there do exist certain features on FNAC, gross and histopathology that can differentiate the two convincingly.

PS-13-004
Increase of thyroid cancer in the area of Santiago de Compostela (northwest Spain)
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Background & objectives: The incidence of thyroid cancer (TC) is increasing worldwide. The aim of this study was to analyse the incidence of TC in Santiago de Compostela (northwest Spain) during the period of 1990-2015. This is a population-based cross-sectional study.
Methods: 905 cases of TC were diagnosed in the area of Santiago de Compostela between 1990-2015. Mean age at diagnosis was 51.96 years, and 79.9% were women. The histological types were: 78.8% papillary carcinoma (ca) (PTC), 8.7% follicular ca (FTC), 5.5% Hurthle cell (oncocytic) ca (HCC), 2.5% medullary ca, 1.7%, anaplastic (undifferentiated) ca, 1.5% poorly differentiated ca, and 1.3% other.
Results: A significant increase in the incidence of TC was observed: 2.14 per 100,000/year (1991-1996) to 16.88 per 100,000/year (2011-2015). This increase was mainly due to PTC, which increased from 1.34 to 14.30 per 100,000/year (from 0.95 to 5.52 per 100,000/year, when excluding papillary microcarcinomas). There was also an increase in the incidence of FTC from 0.19 to 1.12 per 100,000/year and in HCC from 0.09 to 0.77 per 100,000/year.
Conclusion: Our data confirmed an increasing trend in the incidence of TC in the area of Santiago de Compostela, Spain. PTC was the most common histological type found, and the increase of incidence was mainly due to PTC, with FTC and HCC also playing a role.
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PS-13-005
Clinicopathologic analysis of pulmonary and gastroenteropancreatic large cell neuroendocrine carcinoma
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Background & objectives: Large cell neuroendocrine carcinoma (LCNEC) is a rare and aggressive neoplasm, representing a histologically and biologically heterogeneous group of tumours. The aim of this study was to evaluate clinico-morphological features, the immunophenotype, genotype, and follow-up of LCNEC of different locations.
Methods: We studied 39 surgically resected LCNECs of pulmonary and extrapulmonary origin. Clinical data was retrieved from medical records. The mean patient age was 54.2 years (range, 28 to 81 y), and the male/female ratio was 1.2. Pathological analysis included morphological study, re-evaluation of tumour proliferation rate (mitotic count) and differentiation, immunohistochemistry (chromogranin A, synaptophysin, SSTR-2A, p53, Ki-67) and sequencing (TP53).
Results: In the whole cohort, 18 patients had tumours that originated from the lung and 21 patients were of the gastroenteropancreatic (GEP) location. Neuroendocrine differentiation was confirmed in all cases with Ki-67 index 40%-80%. SSTR-2A expression was seen in 19% of GEP cases and in 11% of the lung tumours. p53 protein was strongly expressed in 64% of the cases, including 72% of lung LCNECs and 57% of GEP LCNECs. Eigh of the 18 lung LCNECs were additionally sequenced for TP53 exons 4, 5, 6, 7, and 8. Only one case showed exon 5 missense mutation of the TP53 gene. P53 and SSTR2A were not found to be a prognostic markers.
Conclusion: Our results suggest that abnormal p53 expression is a more frequent event in LCNECs of the lung than in GEP location. There was no correlation between mutant form of p53 protein and morphology or prognosis. Lower Ki-67 index correlated with normal/wild-type p53 pattern and positive SSTR-2A expression. Further studies are needed to compare genetic information with p53 protein immunoreactivity and other possible prognostic biomarkers such as SSTR-2A for LCNEC patients.

PS-13-006
Thyroid needle core biopsy: usefulness and improvement in its efficiency with the gross management by histotechnicians
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Background & objectives: Thyroid pathology is very prevalent in Spain. Our aim is to show the percentage of unsatisfactory thyroid needle core biopsies (TNCB) and diagnostic delay (DD) depending on the gross sampler (pathologist or histotechnician) and the correlation between TNCB and thyroidectomy.
Methods: We reviewed the TNCB reports from January 2013 to February 2020. The TNCBs were performed with a 18G core. Until April 2019 the sampling was made by pathologist and later by histotechnicians.
DD was defined as the dates from biopsy registry day to signing the pathology report.
Results: In this time were performed 794 TNCBs, being 82 (10.33%) unsatisfactory, with an average DD of 6,37 days.
In the first lapse there were 701TNCBs, being 73 (10.41%) unsatisfactory, with an medium DD of 6,68 days. In the second time there were 93 TNCBs being 9 (9.68%) unsatisfactory, with a mean DD of 4,03 days.
Comparing both periods of time, the unsatisfactory biopsies and the DD has been reduced in a 7.01% and 39.67%, respectively.
The global correlation between TNCB and thyroidectomy is a 74.64%. In Bethesda ≥ III it grows up until 80.00%.
Conclusion: TNCB show some advantages:
a) It has a low percentage of unsatisfactory results.
b) The sampling by histotechnicians improve the efficiency.
c) TNCB possesses a robust correlation with thyroidectomy.
Take everything in account TCNB is an efficient alternative to FNA.

PS-13-007
Prognostic implications of CD10 and CD15 expression in papillary thyroid carcinoma
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Background & objectives: Patients with papillary thyroid carcinoma (PTC) have excellent survival, however, recurrence remains a major problem in the management of PTC. We aimed to determine

the prognostic impact of the expression of CD10 and CD15 on patients with PTC.
Methods: Immunohistochemistry for CD10 and CD15 was performed on the tissue microarrays of 515 patients with PTC. Clinical significance of MME (CD10) mRNA and FUT4 (CD15) mRNA expression was analysed in 454 PTC patients using the Cancer Genome Atlas (TCGA) data.
Results: CD10 and CD15 expression was detected in 201 (39.0%) and 295 (57.3%) of 515 PTC cases, respectively. Extrathyroidal extension and BRAF V600E were associated with the expression of both CD10 and CD15. Recurrence was inversely correlated with CD15 expression ($p = 0.034$) but not with CD10 expression. Patients with CD15 expression had an adjusted hazard ratio of 0.509 ($p = 0.027$) for recurrence-free survival and an adjusted odds ratio of 2.511 ($p = 0.028$) for predicting no clinical evidence of disease. CD10 expression was not associated with clinical outcomes. In the TCGA dataset, the expression level of CD15 mRNA was higher in the low/intermediate-risk group than the high-risk group.
Conclusion: Taken together, CD15 expression was an independent prognostic marker for improved prognosis in PTC patients.
This study was supported by a grant (2017R1D1A1B03029597) from the Basic Science Research Program through the National Research Foundation of Korea.

PS-13-010
Synchronous DIPNECH and paraganglioma in PALB2 mutation carrier: just a coincidence?
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Background & objectives: Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia(DIPNECH) and paraganglioma are both rare neuroendocrine tumours. While paraganglioma harbour well-known germline/somatic mutations, the genetic background of DIPNECH remains unknown.
We herein report for the first time their coexistence and discuss the genetic results.
Methods: A 56-year-old female with a previous history of papillary thyroid carcinoma and breast ductal carcinoma, was found to have multiple lung nodules (from 4mm to 9mm) in a follow-up CT scan. Biopsies disclosed a neuroendocrine tumour. Subsequently, a Ga-68 DOTANOC PET/CT was performed disclosing a mass (20mm) near the left carotid artery that was removed before the lung surgery.
Results: Cervical lesion was a paraganglioma and lung lesion was a carcinoid tumour with associated tumourlets and neuroendocrine cell hyperplasia (DIPNECH). Genetic study for mutations in SDHAF2, SDHB, SDHC, SDHD, MEN1, MAX, TMEM127 and VHL genes was negative. A variant of unknown significance in the PALB2 gene (c.1408A>G) was found in the peripheral blood while a genetic cause for the breast cancer was being pursued. This genetic variant was also detected in one close relative with breast cancer at younger age. The patient is symptom-free over two years of follow-up.
Conclusion: It´s well-recognized that DIPNECH may be associated with malignancies like breast and thyroid carcinomas, however its association with paraganglioma has never been reported. Mutations in PALB2 might be the key to explain this unique case of synchronous DIPNECH and paraganglioma.

PS-13-011
Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP): report of an institutional experience
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Background & objectives: The diagnostic criteria for non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) was recently proposed. The frequency of this new entity is unknown. The aim of this study was to report our institutional experience with NIFTP.
Methods: Thyroid tumours diagnosed as follicular variant of papillary thyroid carcinoma (FVPTC) or NIFTP between 2005 and 2019 were identified using our data base. Information regarding patient demographics, clinical presentation, fine-needle aspiration (FNA) results, multifocality, pathology stage, type of surgery, lymph node, systemic metastasis and follow-up were recorded, and the archived slides of the cases were reviewed.
Results: 13 patients (median: 50,3 years) were identified and classified as NIFTPs representing 5,4% of all cases of thyroid carcinomas. The FNA results were indeterminated including AUS/FLUS (33,3%) and suspicious for follicular neoplasm (33,3%), benign (25%) while malignant (8,3%) was les common. Treatment consisted of lobectomy (n=9) and total thyrodectomy (n=4). None of them had prophylactic cervical lymph node dissection. All the patients were free of disease in the follow-up.
Conclusion: NIFTP comprises a significant fraction of cases previously diagnosed as PTC. Typically, most NIFTP were diagnosed as indeterminated in cytology. None of our patients developed metastases or recurrences. Establishment the correct diagnosis of NIFTP requires adequate macroscopy examination protocol and rigorous morphologic criteria in order to avoid unnecessary overtreatment of these tumours.

PS-13-012
Adrenocortical carcinoma prognostisation with digital pathology
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Background & objectives: Adrenocortical carcinoma (ACC) is a rare malignant tumour with hardly predictable prognosis. Weiss-score (WS) defines malignancy criteria, while ENSAT and Helsinki score might be used for prognostisation. We aimed to introduce digital pathology methods for the precision work-up of ACC.
Methods: HE, Ki-67 and Phospho-Histon H3 (PHH3) stained slides of 34 ACC-cases were digitized and analysed with Pannoramic 250 Scanner and Pattern/HistoQuant Softwares (3DHistech, Hungary). For Digital Prognostisation Index (DPI) following variables were measured on whole slides: size and shape of tumour cells, necrosis, Ki-67 proliferation Index and PHH3 (for mitotic count). Results were correlated with data from clinical follow up.
Results: ENSAT-stage (Stage2:35 versus Stage 3-4:15 months, p=0,09), correlated better with modified Weiss-score and both showed moderate impact on survival. The presence of necrosis (threshold at 1%) resulted in lower overall survival (21,5 versus 39 months, p=0,08). WS, mWS and ENSAT stage could predict 18-month survival in less than 60% of cases. Ki-67 proliferation index defined by pathologists and by Digital Image Analysis correlated well (Spearman: 0,804), but PHH3, Ki-67, size and shape of tumour cells did not have prognostical impact alone on overall survival. If we combined above mentioned data into a Digital Prognostisation Index, it could predict 18-month overall survival in 21 of 27 (78%) cases.
Conclusion: Helsinki and ENSAT score can tell something about the metastatic spread of ACC, but ACC still remains a disease with hardly predictable survival or outcome. Our study shows that thorough morphological examination with digital image analysis might bring some increase in the accuracy of predicting overall survival. Though more studies involving more patients are still needed for validating our findings.

PS-13-013
Study of the role of NEUROD1, Nkx2.2, Isl1 and somatostatin in congenital hyperinsulinism
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Background & objectives: Objective: a morphological study of the NeuroD1, Nkx2.2, Isl1, somatostatin in various forms of congenital hyperinsulinism (CH).
Methods: Materials and methods included immunohistochemistry examination with NeuroD1, insulin, somatostatin, ChrA, Nkx2.2, Isl1, and morphometric analysis of pancreas fragments from 18 CH children and 9 normal pancreases.
Results: The number of cells with the expression of ChrA, Isl1, Nkx2.2 and NeuroD1 was significantly higher than in the normal pancreas in contrast to somatostatin. The level of Isl1expression corresponded to Nkx2.2 expression. NeuroD1 was expressed in 58,4±9,7% and 83 ±4,7% of endocrine cells in diffuse CH and in focal CH respectively. This transcription factor was observed in 65,5±7,4% and 77,3±9,4% of exocrine cells accordingly.
Conclusion: The expression of the studied transcription factors in the endocrine part of the pancreas with any form of CH is significantly higher than in the normal pancreas. The most significant marker of CH is NeuroD1.

PS-13-014
Distribution of sex hormones and lymphocytes in reproductive woman with thyroid papillary carcinoma and Hashimoto's thyroiditis

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Background & objectives: The aim of our study was to analyse the expression of hormone receptors, lymphocytic infiltration and thyreocyte/lymphocyte proliferation index in thyroid papillary carcinoma and in Hashimoto's thyroiditis.
Methods: Study included 115 formalin-fixed and paraffin-embedded tissue material from the teaching, research and diagnostic laboratory of Tbilisi State Medical University. Study material was divided into following groups: normal thyroid gland (n=15), Non-invasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP) (n=15), classic papillary carcinoma (CPC)(n=20), follicular variant of papillary carcinoma (FPC) (n=17), cylindric-cell variant of papillary carcinoma (CCPC)(n=9), Hashimoto's thyroiditis (HT) (n=25) and the co-occurrence of Hashimoto's thyroiditis and papillary carcinoma (HTPC) (n=14). Standard immunohistochemistry was used to detect ER, PR, Ki67, CK19, CD56. In addition, lymphocytic infiltration was evaluated in H&E stained specimens.
Results: Study results showed that ER and PR expression is higher in FPC, CCPC and HTPC compared to CPC ($p<0.001$), whilst lymphocytic infiltrate is lower in FPC and CCPC compared to CPC ($p<0.05$). In addition, ER and PR expression is higher in HTPC compared to HT only (<0.001). The thyreocyte/lymphocyte proliferation index is increased in FPC and CCPC compared to CPC and it is also higher in HTPC compared to only HT ($p<0.05$).
Conclusion: Increased expression of hormone receptors may represent the risk factor for the development of thyroid papillary carcinoma and immune regulation plays an important role in this process.

PS-13-015
Morphological, molecular and outcome characteristics of non-invasive follicular thyroid neoplasms with papillary-like nuclear features in a Romanian population: a retrospective, institutional study

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Background & objectives: The aim of our study was to assess the morphological, molecular and outcome characteristics of NIFTPs (non-invasive follicular thyroid neoplasm with papillary-like nuclear features) in a Romanian population.
Methods: All cases of non-invasive encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC) registered at Târgu-Mureş Pathology Department between 2008-2015 with available follow-up data were reviewed by two pathologists and re-classified as NIFTPs in accordance with the WHO 2017 diagnostic criteria. All NIFTP cases were subjected to RT-PCR amplification targeting the BRAFV600E and RAS (KRAS, NRAS, HRAS) somatic mutations.
Results: Our study included 66 cases. More than half of the cases occurred in patients younger than 55 years-old (68.2%), with a significant female predominance (86.4%); the mean tumour size was 28.65±15.29. RAS mutations were identified in 22 (33.3%) cases, with the following distribution: HRAS (11 cases), NRAS (10 cases) and HRAS (1 case). Any NIFTP case was associated with BRAFV600E mutation. The mean follow-up period was 53 months. Most of the patients (n=61 cases, 91.4%) were treated with total thyroidectomy and received RAI (I131 therapy) (90.9%). All cases had a disease-free status at the last clinical assessment, including 5 cases treated with lobectomy only.
Conclusion: RAS mutations are common among NIFTPs, being identified in 1/3 of the cases included in our study, whereas BRAFV600E mutation is absent. Our follow-up data highlight the indolent behaviour of non-invasive EFVPTCs reclassified as NIFTP

PS-13-016
Adaptive alterations of pinealocytes after the long-term influence of heavy metal salts on the body

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Background & objectives: Epiphysis and parathyroid glands take part in the regulation of the adaptive capacity of the body. The aim was to study of morphological and immunohistochemical features of epiphysis's pinealocytes and parathyroid cells under heavy metal salts influence.
Methods: The experiment was conducted on 24 rats aged 5-6 months (1 control and 1 experimental group). Animals received normal drinking water for 30 days after a 90-day exposure to a combination of heavy metal salts: zinc, copper, iron, manganese, lead and chromium. To reveal the neuroendocrine cells, the immunohistochemical study of Chromogranin A, using the rabbit monoclonal antibodies, was performed.
Results: Heavy metal salts cause the morphological and immunohistochemical alterations in all structural components of the epiphysis and parathyroid glands. Perivascular oedema, significant vascular plethora, thickening and impaired permeability of the vascular wall with the formation of diapedesis haemorrhages were observed. The vast majority of pinealocytes had signs of significant cytoplasmic vacuolation with an increase of Chromogranin A expression compared to control animals. The number of neurosecretory cells in the peripheral areas of the gland was especially increased, while the pinealocytes of the control animals were spread evenly throughout the gland. At the same time the amount of parathyroid cells and their Chromogranin A accumulation were decreased.
Conclusion: The change of Chromogranin A expression and amount of pinealocytes and parathyroid cells indicate their disturbed secretory activity, at the same time the evacuation of hormones inside the vessels has impaired as a result of pathological alterations of vascular wall.

PS-13-017
Dyshormonogenetic goiter: a study of 3 cases

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Background & objectives: Dyshormonogenetic goiter is a genetic thyroid hyperplasia secondary to an enzyme defect in hormonal synthesis. Malignant transformation is one of the complications, rarely reported in the literature. We aim to analyse the clinicopathological and prognostic aspects of this rare entity.
Methods: In our pathology department, three cases of dyshormonogenetic goiter were diagnosed between 2012 and 2019.
Results: Patients were all males aged from 18 to 40 years. All patients presented with a goiter and one of them was followed for congenital hypothyroidism. A total thyroidectomy was performed in all cases. Sectioning demonstrated multiple nodules measuring from 0.2 to 5 cm. Histologically, the thyroid presented a marked nodular architecture formed by microfollicles or trabecular structures, separated by thick fibrous bands with foci of haemorrhage, necrosis and calcification. The follicles were lined by thyrocytes with eosinophilic or clarified cytoplasm and an enlarged nucleus with conspicuous nucleoli. There was no vascular or capsular invasion. In one case we identified 2 micro-nodules (0.2 and 0.4cm) fulfilling the criteria of papillary microcarcinoma.
Conclusion: Dyshormonogenetic goiter is a rare entity characterized by an architectural and cellular pleiomorphism which can mimic neoplasia and cause diagnostic difficulties.

PS-13-018
Myelolipoma of the adrenal gland
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Background & objectives: Myelolipomas of the adrenal gland are rare, benign neoplasms, without any known gender predilection, mostly asymptomatic and an incidental finding. We will study 4 cases to obtain addition relevant information and compare to what is already known on these lesions.
Methods: We present 4 cases of myelolipoma of the adrenal gland, diagnosed in our department over the course of 5 years. We evaluated the morphology (relative proportions of mature fat to haematopoietic elements), clinical presentation, differential diagnosis, lab results, image studies and any additional relevant medical information that we were able to obtain regarding these patients.
Results: Three of the patients were female, one was male, ages between 35 and 74 years. All patients had complaints of abdominal discomfort and occasional pain, one had dyspnea, one presented through the ER. Three of the neoplasms were located in the right adrenal gland. The fourth myelolipoma was associated with a splenic cyst. One patient had an associated adrenal adenoma, one had cortical hyperplasia.
Conclusion: Our microscopic observations regarding the composition of these neoplasms showed no significant differences between all four cases. All four myelolipomas were morphologically identical and composed of predominantly fat with scant haematopoietic elements. The main clinical differential diagnosis of these neoplasms is retroperitoneal lipoma, although on gross examination liposarcoma can also be suspected.

PS-13-019
Comparison of risk stratification scores and predictors of metastasis in pheochromocytoma: a 14-year institutional case review
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Background & objectives: Pheochromocytoma is an adrenal medulla tumour whose behaviour cannot be reliably predicted by clinical, histological, molecular or biochemical parameters alone. We aimed to compare two commonly used risk stratification scores and correlate them with the patients' follow-up.
Methods: A senior pathologist and a pathology resident reviewed all primary pheochromocytoma cases diagnosed in a tertiary healthcare institution over a 14-year period, from 2001 to 2014, and determined their "Pheochromocytoma of the Adrenal Gland Scaled Score" (PASS) and "Grading system for adrenal pheochromocytoma and paraganglioma" (GAPP) score. Clinical records and the National cancer registry were assessed for metastasis during follow-up.
Results: Of the 27 cases examined, 17 showed a PASS equal or greater to 4, while 10 and 1 cases showed GAPP scores of 3-6 (moderately differentiated type) and over 6 (poorly differentiated type), respectively. There was a 50% concordance in risk stratification out of the 20 cases rated as intermediate to high-risk by at least one of the scores. Of the cases with metastatic disease, one had scored over 4 with PASS (6) and was of the moderately differentiated type by the GAPP score (3), while another had a PASS over 4 (17) and was graded as poorly differentiated with the GAPP score (8).
Conclusion: Although risk stratification through both scores is not always consistent, they can still help select the cases in which a closer follow-up is warranted.

PS-13-020
Large discrepancies between pre-operative biopsy and surgical resection diagnosis in pulmonary carcinoids
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Background & objectives: Neuroendocrine pulmonary carcinoids can be classified into typical and atypical carcinoids based on mitotic count and presence of necrosis in surgical resection specimens. Objective was to assess the reliability of carcinoid classification on pre-operative (transbronchial/transthoracic) biopsies, which guide treatment decisions.
Methods: We have analysed all pulmonary carcinoid diagnoses established in the Netherlands between January 2003 and December 2012 using both the Dutch Pathology Registry (PALGA) and the Netherlands Cancer Registry (IKNL). Paired biopsy-resection specimens were available in 330 cases of which we have compared the pre-operative biopsy specimen diagnosis with the surgically confirmed diagnosis using pathology report conclusions.
Results: In total 160 typical carcinoids (TC), 88 atypical carcinoids (AC) and 82 carcinoid not otherwise specified (N.O.S.) were diagnosed on resection specimens. Results showed that in 57% (189/330) of the patients the pre-operative biopsy specimen diagnosis did not match with the paired resection diagnosis. This was in 36% of TC, 40% of AC, and 65% of carcinoid N.O.S., respectively. Moreover, 24% of pre-operatively diagnosed TC were subsequently classified as AC in the resection specimen.
Conclusion: In conclusion, biopsy specimen diagnosis of pulmonary carcinoids is unreliable and should not be used in decision making for type of surgery (e.g. sparing vs complete). Our results indicate the necessity for additional (molecular) markers to guide pulmonary carcinoid biopsy classification.
Funding: Dutch Cancer Society (KWF)

PS-13-021
RB expression in relation to survival in pulmonary neuroendocrine neoplasms with well differentiated morphology but high proliferation index
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Background & objectives: It is unclear if pulmonary neuroendocrine neoplasms (NENs) with well-differentiated morphology but high proliferation index should be regarded as large cell neuroendocrine carcinoma or high-grade carcinoids. We analysed 9 of these cases for pRb expression in relation to overall survival.

Methods: Cases with well differentiated morphology, but MI >10/2mm2 and/or Ki-67 proliferation index >20% were selected based on pathology reports of consecutive pulmonary NENs in our university medical centre (Maastricht UMC+, 2007-2018) and confirmed by pathological review. Immunohistochemistry was performed to assess pRb expression.
Results: Nine cases were included in this study. Median overall survival in stage IV was 8 months (95% CI 4-12 months). Cases with preserved pRb expression (4/8) had an increased survival compared to cases with loss of pRb expression (4/8) (45 months vs. 5 months, p=0.042).
Conclusion: A subgroup of pulmonary NENs with well differentiated morphology but high proliferation index likely exists. pRb staining might be helpful to predict prognosis, but clinical relevance remains to be studied.
Funding: Dutch Cancer Society (KWF)

PS-14 History of Pathology

PS-14-001
A wet specimen of "sarcoma of the orbit" from the pathology museum of Turin at the dawn of radiotherapy
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Background & objectives: The Pathology Museum of Turin houses specimens dating back between the late 1800s and the early 1900s. Among these specimens there are 10 cases of ENT pathology. A case labelled as "sarcoma of the orbit" was selected for the study.
Methods: The wet specimen is a case of sarcoma of the orbit dating back to the year 1920. The label shows the autopsy number and an archive research was carried out.
Results: The wet specimen was collected performing an autopsy on a 50-year-old male. The autopsy report also describes his clinical history: he had a neoplasm at the basis of the orbital cavity which was treated with roentgen therapy. After the treatment the neoplasm was reduced. Later the patient had vertebral metastases and spinal cord compression with paraplegia. He died for purulent cystitis with fistulas.
Conclusion: This case shows one of the historical first attempt to cure sarcomas with roentgen therapy in Turin. Therefore, it is of historical interest since it shows the outcomes of a first treatment with a new therapy.

PS-14-002
Dry congenital arterial anomalies in the museum
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Background & objectives: Stroke is a major cause of morbidity and mortality. Arterial congenital malformations, namely of vertebral arteries, is pointed as a promoting ætiological factor. The authors aim to draw attention to the issue, using the resources of historical museums.
Methods: A retrospective study of the specimens – human liquid-fixed and dehydrated (dry) ones, as well as wax and clay artificial models – of an historical Anatomo-Pathological Museum was performed, searching for anomalous vertebral arteries. Photographies of the specimens were taken. The literature was reviewed.
Results: Three (n=3) dehydrated (dry) specimens from adult/elderly autopsies were found. Each item presented a left vertebral artery with anomalous origin – emerging directly from the aortic arch, between the brachiocephalic trunk and the left common carotid artery ostia.
Conclusion: Reported congenital anomalous origin of vertebral arteries range 6.7%. The most usual anatomical variant matches our findings. It acquires relevance in acute cerebro-vascular events, sudden death, surgical, traumatic settings. Historical, Anatomo-Pathological University Museums fulfil their didactic mission using such specimens.

PS-14-003
Historical overview of the development of the haematopoietic stem cell concept
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Background & objectives: The haematopoiesis was first discovered as blood islands in extraembryonic tissues (area opaca/ yolk sac).In 1846 a liver role was discovered by Weber and Kölliker. In 1868, the bone marrow was identified as source of haematopoiesis by Neumann and Bizzozero.
Methods: Early blood staining techniques were developed by Ehrlich and refined by Pappenheim, allowing them to study the maturation sequence of blood cell lineages. Subsequently in the XX century, techniques of radiation biology provided experimental tools to distinguish among the dualistic and unitarian theory on haematopoiesis of the two scientists. Later on, radiation biology techniques extended to bone marrow transplantation research.
Results: P. Ehrlich and A. Pappenheim came to different conclusions, the first proposing a precursor marrow cell for the myeloid series and a lymphatic-derived precursor for lymphocytes (dualistic theory), and A. Pappenheim proposing that a primitive mononuclear cell he identified was precursor of all blood cells (unitarian theory). The blood stem cells were investigated by the scientists E. Neumann and A. Pappenheim both in physiological haematopoiesis and in various forms of leukaemia. A. Pappenheim was aware that 'stem cells' ("Stammzelle")"or 'mother cells' (Mutterzellen) had the potential to differentiate into diverse cell lines. From the early 1960s the studies on stem cells in haematopoiesis led to the beginning of modern stem cell research
Conclusion: The concept of Stem cells includes both positive meanings of common heritage and normal development as well as a negative significance as potential source of cancer. In the second half of the XX century the history of leukaemia research considered stem cells both as a 'biological force for good' in the framework of bone marrow transplantation as well as having a 'dark side' through the concept of cancer stem cell.

PS-14-004
Evolution of intestinal metaplasia definition (term) as reflection of history of medicine
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Background & objectives: Metaplasia is the replacement of one differentiated somatic cell type with another differentiated somatic cell type in the same issue. Historically, the development of ideas about metaplasia (and, in particular, intestinal metaplasia) was accompanied by a significant semantic modification.
Methods: Content analysis through systematic review of publications (PubMed, Embase) using key words metaplasia and intestinal metaplasia was carried out. Substantial evolutionary modification of these terms was noted from Rudolph Virchow (he coined the term "metaplasia" at the VIIIth International Medical Congress in Copenhagen in 1884) to the present time. A comparative method and a substantial analysis of sources were used.
Results: The main evolutionary stages of terms modification were identified and designated: general biological approach, pathology and epidemiology-based approach, association with stem cells and genetic regulation. Each period was associated with basic values and features of the development of medical knowledge. The forecast of the further evolution of the term based on the current ideas of modern pathology was indicated. Expanding on earlier discussion that metaplasias can develop when mature cells dedifferentiate and pro-

liferate the modern aspects of this process is discussed about contribution of huge number of associated factors and conditions. There are numerous similarities between gastric and esophageal intestinal metaplasia,suggesting an idea that the mechanisms would be identical.
Conclusion: The main feature of metaplasia is changing in cellular identity associated with transcription factors that inhibit and/or maintain cellular characteristics. Improved surveillance of metaplasia might lead to cancer prevention. All elements in terminology system affect each other with the following changes of conceptual apparatus (metaplasia-transdifferentiation). It means changing not only the terminology itself, but significantly affects the assessment of the pathological process: its diagnosis and the development of therapeutic strategies.

PS-14-005
Pathology museum: the old way for learning medicine on modern times
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Background & objectives: Learning pathology is fundamental for a successful medical practice. Nowadays, new methods of teaching have been developed, leading pathology museums to be obsolete Hereby, we present a collection of macroscopies existing in our Pathology Department.
Methods: We want to highlight the importance of pathology museums, given than they are part of the history of medicine, and extremely useful for teaching Pathology. We counted the macroscopic samples, group them in the different body systems and finally these samples were catalogued taking into account the nosological entities they represented: inflammatory, vascular and degenerative processes, tumours, amongst others.
Results: We have 1275 specimens placed in sealed formalin bottles. The majority of them represented pathologies of gynaecological, digestive and respiratory system (18,5 % 16% 9,5%). The most frequent illnesses are neoplasms, except in: cardiovascular system, spleen and thyroid, for which inflammatory diseases, infarcts and goiter were prevalent.
Conclusion: This presentation is important to seize this learning material to teach medicine. It represents the illness in an extremely tangible state and allows to make a correlation between clinical, imagenologic, and pathological findings. It's our duty to ensure that the contribution of macroscopic material to pathology museums is carried out in a consistent and continuous way. By doing so, they will endure over time and will continue being an invaluable source of teaching for the generations to come.

PS-15 Molecular Pathology

PS-15-001
Reliability and interrater agreement of tumour purity estimate in frozen tumour tissues: comparison between a panel of pathologists and copy number variation-based algorithm
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Background & objectives: Heterogenous structure of tumour tissues leads to mixed sequencing signals. Microscopic examination to estimate "tumour purity" before sequencing ensures high-quality data. We aim to estimate the level of consistency among pathologists and their agreement with CNV-based algorithms for tumour purity.
Methods: We selected 40 of 450 sequenced oesophageal tumours from the Mutographs study, through clustering by country of origin, method of preservation, and post-sequence assessment of purity. Four pathologists examined frozen sections and scored them for quality, percentage of tumour and inflammatory cells and necrosis. Inter-rater reliability (IRR) was estimated for the consistency among pathologists and their agreement with bioinformatics measurements.
Results: Average and individual IRR (95%CI) of purity estimates among pathologists was 0.73 (0.61 – 0.81) and 0.40 (0.28 – 0.52) respectively. The average IRR for inflammation and necrosis were 0.69 (0.56 – 0.79) and 0.37 (0.09 – 0.57). Modified weighted kappa for agreement between pathology and CNV-based methods ranged from 0.66 (0.44 – 0.87) to 0.51(0.29 – 0.73). When the quality of samples was accounted for, agreement improved to 0.72.
Conclusion: Microscopic examination of frozen tissues is applicable for purity estimation in NGS-era and higher quality improves the estimate. We observed moderate to good reliability among pathologists and a moderate but variable agreement with post-sequencing measurement. This variation could not be explained solely by the quality of samples or differences in non-tumoral components. Harmonizing the method of estimation of cellular elements and regular communication between pathologists and bioinformaticians in case of disagreement might help to ameliorate this practice.
Funding: CRUK Grand Challenge Program

PS-15-003
Utility of national next generation sequencing-based cancer profiling tests: experience from a series of 172 patients in a large private laboratory in Brazil
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Background & objectives: Gene panels based on next-generation-sequencing (NGS) have been increasingly used as a tool to improve individualized care in cancer patients. Herein we present the results of the application of two in-house gene panels (ONCOFOCO) in a reference centre in Brazil.
Methods: Two gene panels using NGS technology were applied to 172 patients: 113 patients were submitted to a 366-gene panel and 59 patients to a 72-gene panel. The presence of single nucleotide variations (SNV), copy number variations (CNV), and insertion-deletions (Indels) was assessed, as well as microsatellite instability (MSI) and tumour mutation burden (TMB).
Results: The most common tumour types submitted to our gene panels were biliopancreatic adenocarcinoma (n=23;13.4%), breast carcinoma (n=23;13.4%), colorectal adenocarcinoma (n=22;12.8%), lung adenocarcinoma (n=18;10.5%), ovarian carcinoma (n=17;9.9%), sarcomas (n=13;7.6%) and carcinomas with unknown site of origin (n=9; 5.2%). Pathogenic somatic variants were identified in all the major tumour types evaluated, and actionable variants were identified in all major tumour types except sarcomas. One case of lung adenocarcinoma presented high TMB. Cases of lung adenocarcinoma presented a higher frequency of detection of actionable variants when compared to the remaining major tumour types (47.1% vs. 19.4%, p=0.026), and cases of colorectal adenocarcinoma presented more commonly variants associated with drug resistance (59.1% vs. 6.8%,p<0.001).
Conclusion: Our in-house gene panels (ONCOFOCO) were able to successfully detect actionable variants in most of the major tumour types evaluated, with greatest output in cases of lung and colorectal adenocarcinoma.

PS-15-004

Variant detection with the ion torrent Genexus Integrated Sequencer and Oncomine Precision Assay across multiple sites

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Background & objectives: The objective of this study was to evaluate performance of the Genexus Integrated Sequencer in detecting genomic variants relevant to cancer using the Oncomine Precision Assay across multiple sites in Europe.
Methods: The same set of commercially available and custom developed controls were analysed and used for cross-site calculations such as reproducibility and correlation. Each site then selected their own set of clinical samples, both FFPE and liquid biopsy, previous characterized by NGS or other technologies. The results to the previously obtained to determine concordance across the different genomic variant types.
Results: The cross-site analysis with control materials showed correlation and reproducibility ranging from 97% to 100% across all variant types. Concordance to pre-characterized samples showed results ranging from 90% to 100% across all variant types. No statistically significant difference was observed between the different extraction methods or the results derived from FFPE or liquid biopsy samples.
Conclusion: The concordant and reproducible results demonstrate that the Genexus Integrated Sequencer and Oncomine Precision Assay are a complete and reliable molecular profiling solution that can be adopted by molecular diagnostic laboratories for testing of variants relevant for cancer treatment in an automated and fast manner.

PS-15-005

Personalised mapping of tumour development in synchronous colorectal cancer patients

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Background & objectives: Synchronous colorectal cancers (syCRCs) are defined as two/more primary tumours identified simultaneously in a patient. Previous studies report high inter-tumour heterogeneity between syCRCs, suggesting independent origin and potential different treatment responses. No specific guidelines are currently available rendering management challenging.
Methods: We performed an in-depth characterisation of 12 tumours from 3 treatment naïve syCRC patients by analysing histopathological, whole genome sequencing and RNA-sequencing data. We assessed the extent of genetic overlap between syCRCs and examined associations between clinicopathological information and the molecular, microbial and immune features of each tumour genome.
Results: We found mixed microsatellite status between and within patient tumours. Synchronous lesions within patients harboured distinct mutations in the same known CRC genes, although overlaps of known driver mutations such as BRAF V600E did occur. DNA analysis of gut microbial organisms revealed the presence of Fusobacterium nucleatum species in BRAF mutant, hypermutated, microsatellite unstable tumours. Quantification of tumour immune infiltration showed varying immune responses between syCRCs. Inter-tumoral transcriptomic heterogeneity classified each tumour into different consensus molecular subtypes. High genetic heterogeneity between syCRCs suggest these tumours originate independently while accessing the same mutational processes.
Conclusion: The importance of personalised genome/transcriptome sequencing of synchronous lesions is highlighted. Potential drug targets will vary depending on the mutational status in synchronous tumours from the same patient. This may aid in therapy decisions and improve management of syCRC patients.

PS-15-006

Classification of central nervous system tumours in cerebrospinal fluid based on cfDNA methylation profiling

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Background & objectives: Genome-wide DNA methylation profiling allows for tumour classification of central nervous system (CNS) tumours. The aim of this study is to determine the feasibility of liquid biopsy methylation array analysis for the diagnosis of CNS tumours.
Methods: 34 cerebrospinal fluid (CSF) samples (0.05–9.5ml per case) from adult and paediatric patients with a primary central nervous system (CNS) tumour were evaluated for their eligibility for methylation profiling based on cfDNA quantity. Of these, eight samples with at least 15ng cfDNA were analysed using the Infinium EPIC BeadChip 850k methylation array and the DKFZ brain tumour classifier tool.
Results: In this cohort, no correlation was observed between the quantity of cfDNA and the volume of CSF sample per patient. We found that methylation profiling using minimally 15ng cfDNA can lead to a correct histomolecular diagnosis in 63% (5/8) of the samples. Of note, 15 ng cfDNA from the CSF samples would have been available of 98% of the patient samples in case >7ml CSF would be submitted per sample.
Conclusion: Methylation profiling of CNS tumours based on CSF liquid biopsy is feasible. More in depth study is needed to determine how this minimally-invasive approach can be used in clinical practice for the diagnosis of primary CNS tumours.

PS-15-007

Molecular pathology testing for non-small cell lung cancer: which information on the test request and result report is essential to make a solid choice of therapy?

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Background & objectives: For patients with non-small cell lung cancer (NSCLC), targeted therapies are becoming part of the standard treatment. It is questioned which information the clinicians provide on test requests and how the laboratories adapt test conclusions to this knowledge and regulations.
Methods: This study consisted of two components; checking the presence of pre-defined elements (administrative and key for therapy-choice) on completed requests and corresponding reports in Belgian laboratories, both for tissue- and liquid biopsy (LB)-testing and opinion analysis from Belgian pathologists/molecular biologists and clinicians during national pathology/oncology meetings. Data from 4 out of 6 Belgian laboratories with ISO-accreditation for LB-testing were analysed.
Results: On the scored requests (N=4), 12 out of 19 ISO-required elements were present for tissue and 11 for LB-testing. Especially relevant patient history, such as line of therapy (for LB), tumour histology and the reason for testing were lacking. Similarly, 11 and 9 out of 18 elements were present in the reports (N=4) for tissue and LB, respectively.
Elements that pathologists/molecular biologists (N=18) were missing on requests were the initial activating mutation, previous therapies, clinical question and testing-related information. For reporting, an important item for both groups is the clinical interpretation of the test result. Clinicians (N=28) indicated that they also wish to read the tumour load for tissue testing.

Conclusion: Communication flows between the laboratory and the clinician, together with possible pitfalls were identified. Based on the study results, templates for complete requesting and reporting were proposed.
The project was financially funded by AstraZeneca Belgium.

PS-15-009

Contribution of cytogenetic study in a series of foetal losses: genetic and autopsic correlation

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Background & objectives: Foetal loss is sometimes poorly understood due to the difficulty or impossibility to determine the cause. Our objective is to evaluate the contribution of the cytogenetic study to establish the cause of death and to correlate it with autopsy findings.
Methods: Retrospective cohort analysis of spontaneous foetal losses from 12th to 40th gestational weeks, from 1999 to 2018. Analysed data included: gestational age, genetic studies, foetal autopsy and histopathological examination of the placenta. Cytogenetic study was made by chorion villi, amniotic fluid, placental tissue or foetal cartilage. Abnormal results of karyotype, foetus and placenta were classified using Tulip and CODAC classifications.
Results: During 19 years of the study period, there were 755 foetal losses. Successful karyotyping was possible in 614 cases (81.3%). In 82 cases (13.4%) karyotype was abnormal. Parents gave consent for foetal autopsy in 39 cases (47.6%) of the 82 cases with abnormal karyotype. Chromosomal abnormality was the only finding in 11 cases (28.2%); in the other 28 cases (71.8%) a cause that justifies foetal loss by itself was found. Placental pathology was the first cause of death, followed by infections. 12 cases (30.8%) had structural chromosomal defect. In 18 cases (46.1%) the autopsy did not detect phenotypic expression of the genetic alterations.
Conclusion: Chromosomal abnormality has been the only finding detected in 11 cases (28.2%). Karyotype adds complementary information in the other 28 cases (71.8%) in which other cause has been found at autopsy study. Understanding the aetiology of foetal loss enables classification of recurrence risk, improves the management of future pregnancies and facilitate the development of preventive strategies. We recommend the integration of the genetic analysis in the study of foetal losses.

PS-15-011

Prognostic significance of substance P/ neurokinin 1 receptor and its association with hormonal receptors in breast carcinoma

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Background & objectives: To evaluate the expression and Immunolocalization of Substance P (SP)/ Neurokinin-1Receptor (NK-1R) in Breast Carcinoma (BC) patients and it's association with routine proliferative markers (ER, PR, HER2/ neu and Ki-67).
Methods: There were 23 cases of group A (Grade III), 8 of group B (Grade II) and only 3 cases of group C (Grade I). HE, ER, PR, HER2 and Ki-67 staining was performed as routine biomarkers. Samples were then processed for immunomarkers study of Substance Pand NK-1R immunohistochemistry was performed for few cases.
Results: 61% of group A, 88% of group B and 67% cases of group C were SP positive. Overall, strong staining (≥ 10% tumours cells), labelled as "3+", was observed in 9/14 (64.2%) cases of group A and 1/8 (12.5%) case of group B. Moderate staining labelled as "2+" (in ≥ 10% tumour cells) was observed in 3/14 (21.4%) cases of group A, 4/8 (50%) cases of group B.
Conclusion: SP and NK-1R is overexpressed in breast carcinomas and there is significant association between grade of tumour and their over expression. It may serve as a novel bio-marker for grading of BC. We also suggest that NK-1R antagonists as a potential therapeutic strategy to inhibit and manage BC.

PS-15-012

Next generation RNA sequencing assay for comprehensive gene fusion detection in solid tumour samples using FusionSync detection technology

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Background & objectives: Gene fusions can play a critical role in oncogenesis making them useful biomarkers in solid tumour samples. We developed an Oncomine targeted RNA sequencing assay for fusion detection using FusionSync detection technology that combines three different approaches for improved sensitivity.
Methods: The assay includes amplicons designed to target >1200 recurrent known fusions in 49 driver genes. They also enable detection of non-targeted fusion isoforms (i.e., novel combinations of drivers and partners genes). We also included amplicons across the exon junctions of ALK, RET, FGFR2, NTRKs to detect novel fusions using 3'/5' expression imbalance. We developed algorithms to detect targeted and novel fusions.
Results: We tested the assay using the Ion GeneStudio S5 sequencer with Seraseq formalin fixed paraffin embedded (FFPE) V4 fusion mix and identified the 18 expected fusion isoforms including MET Exon 14 skipping isoform and EGFRvIII deletion. We sequenced a penta-fusion control sample mixed with cell-lines positive for ALK, RET, ROS1, FGFR3 and NTRK1 fusions and detected all the fusion isoforms with 100% sensitivity and specificity. We tested the exon tiling method for ALK, RET and NTRK1 genes with the penta-fusion sample and observed concordant results. We sequenced 10 FFPE and 10 total RNA negative samples and detected no known fusion isoforms or novel fusions thus confirming high specificity of the assay.
Conclusion: We developed a highly multi-plexed RNA assay using Ion AmpliSeq targeted sequencing chemistry for comprehensive, sensitive and specific fusion detection in FFPE samples with sample input as low as 10ng. For research use only. Not for use in diagnostic procedures.

PS-15-013

Prognostic value of BRCA mutations in triple-negative breast cancer

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Background & objectives: Triple-negative breast cancer (TNBC) is characterized by its aggressiveness. TNBC patients lack directed therapies and chemotherapy is the standard treatment. Nevertheless, they might benefit from PARP inhibitors as 15-20% of them display BRCA alterations that should be studied.
Methods: Next-generation sequencing was performed to analyse BRCA1 and BRCA2 genes in DNA extracted from paraffin-embedded tumours resected from 30 TNBC patients. The Oncomine™ BRCA Research Assay (ThermoFisher) was used, with a total coverage of all the exons. The association between the molecular and clinico-pathological variables was performed by SPSS statistical package, considering a median follow-up of more than 7 years.
Results: A percentage of 30% of the TNBC patients displayed mutations (Types 3 to 5), being 44.4% present in BRCA1 and 55.6% in BRCA2. There was an association between the presence of BRCA mutations and the presence of metastasis (p=0,0318). BRCA mutated patients displayed a worse prognosis than BRCA patients without BRCA mutations independently of the presence of metastasis, although the statistical value did not reach significance (p=0.116). More studies with numerous populations are needed to address this issue.
Conclusion: - Analysis of the BRCA mutational status in TNBC patients is of prognostic significance.

- Additional studies to evaluate the prognostic and predictive value of these alterations are needed.

PS-15-015

Tracking tumour mutations in liquid biopsies from patients with metastatic melanoma using custom Ion Torrent AmpliseqHD NGS analysis

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Background & objectives: Ion AmpliseqHD uses single molecule tagging to allow for error correction and counting of individual DNA molecules. We tested performance of custom Ion AmpliseqHD NGS panels to track mutations in ctDNA from patients with metastatic melanoma.
Methods: Patients undergoing SOC therapy were enrolled to a IRB approved study (29-450 ex 16/17). Liquid biopsy samples were collected in Streck tubes, ctDNA was extracted by Promega Maxwell and NGS was performed with two custom Ion Ampliseq HD panels covering hotspots in BRAF, CTNNB1, CYSLTR2, EIF1AX, GNA11, GNAQ, HRAS, KIT, KRAS, MAP2K1, NRAS, PIK3CA, PLCB4, PTEN, RAC1 and SF3B1.
Results: Primary tumour FFPE tissue was analysed with Ion Torrent Ampliseq to obtain initial mutation profile. Subsequently, liquid biopsy specimens were collected at defined intervals during targeted and immune therapy. A total of 159 plasma samples were analysed. ctDNA amounts were generally above 5ng/ml plasma and only marginally influenced by hemolysis. AmpliseqHD libraries were generated from 10 ng DNA and sequenced with at least 3mio reads. Analysis was successful in 100% of cases, molecular depth was 1000-2000 molecules per amplicon. Analysis revealed patients without detectable mutations, patients with mutations detectable only in the baseline LBx, and patients with levels of mutated plasma ctDNA correlating with treatment.
Conclusion: Custom Ion AmpliseqHD analysis is able to track mutations during extended treatment periods with high specificity and sensitivity. Using Streck tubes, Promega Maxwell and Ion Torrent Ampliseq HD allows to reliably analyse large numbers of relevant mutation hotspots in liquid biopsy samples collected in a real-world clinical setting. Mutations were detectable in LBx of the majority of patients and variant allele frequencies closely followed treatment events.
Funding: Novartis Pharma GmbH, Stella-Klein-Löw-Weg 17, 1020 Vienna, Austria

PS-15-017

Transcriptome signature associated with tmprss2-erg molecular subtype in prostate cancer

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Background & objectives: In 40% of cases, prostate cancer (PC) is represented by the *TMPRSS2-ERG*fusion-transcript molecular subtype. In this work, we aimed to compare the results of qPCR testing with whole-transcriptome analysis of signature introduced by the active expression of *TMPRSS2-ERG*fusion-transcript.
Methods: RNA-Seq analysis of 74 locally advanced PC samples was performed with Illumina NextSeq500 system. qPCR detection of *TMPRSS2-ERG*fusion transcripts (T1:E4, T2:E4, T1:E2, etc.) was done on 7500 Real-Time PCR Systems with using TaqMan Gene Expression Assays kits.
Results: qPCR analysis detected *TMPRSS2-ERG*fusion-transcript in 39 of 74 (52%) PC samples (mainly T1:E4), but only 26 of 39 samples (67%) demonstrated *TMPRSS2-ERG*-associated transcriptomic signature (overexpression of *ERG*, its downstream targets and other genes). The overexpressed genes included: *ERG*, *PLA1A*, *TDRD1*, *PLA2G7*, *ATP8A2*, *GUCY1A1*, *MYO6*, *FZD8*, *CACNA1D*, *ALOX15*, *PEX10*, *TBX1*, *KCNH8*. Additionally, we detected *TMPRSS2-ERG*breakpoints directly in Illumina reads, and this method gave the most similar results to the RNA-Seq expression analysis. In 3 samples, we did observe the transcriptome signature, but qPCR gave negative results.
Conclusion: The study showed that not all *TMPRSS2-ERG*-positive PC samples (according to qPCR), demonstrate *TMPRSS2-ERG*-associated transcriptome signature, and this phenomenon requires further investigation. The detected transcriptome signature should be considered as an additional tool to clarify the molecular subtype of *TMPRSS2-ERG*in PC.
This work was funded by the Russian Science Foundation grant no. 18-75-10127.
This work was performed using the equipment of EIMB RAS "Genome" centre (http://www.eimb.ru/ru1/ckp/ccu_genome_c.php).

PS-15-018

Differentially methylated CpG sites as potential prognostic markers in prostate cancer

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Background & objectives: The search for informative markers for choosing the best therapeutic concept for patients with high-risk prostate cancer (PC) is an urgent task. The aim of this study is to search for prognostic markers among differentially methylated CpG sites.
Methods: The study included PC samples methylation data of The Cancer Genome Atlas. The cohort was divided into two groups: patients with biochemical relapse (19 cases) and relapse-free patients (66 cases). To analyse differential methylation BiSeq package was used. The Mann-Whitney test, beta-regression and logistic regression models were used for statistical analysis.
Results: In total, 611 differentially methylated CpG sites were identified potentially associated with biochemical relapse in PC. The most interesting CpG sites are those in promoter regions. Hypermethylated CpG sites: cg22663872 (chr7: 149120266 in ENSR00000219606), cg11536940 (chr8: 97658076 in ENSR00000227434), cg07576175 (chr19: 59049843 in ENSR00000111888), cg21446511 (chr2: 179316481 in ENSR00000126971), cg22343001 (chrX: 100914848 in ENSR00000423862). And hypomethylated CpG sites: cg13691599 (chr9: 74863413 in *GDA* gene promoter), cg07286253 (chr5: 111496047 in ENSR00000185293).
Conclusion: Were found out differentially methylated CpG sites in several promoter regions: cg22663872, cg11536940, cg07576175, cg21446511, cg22343001, cg13691599, cg07286253. These methylation changes in promoters could affect gene expression *GDA*, *CPQ*, *PRKRA*, *ARMCX2*, *ZBTB45*, and also ncRNA *SNORA13*, *EPB41L4A-AS1*.
This work was financially supported by the Russian Foundation for Basic Research, grant no. 17-29-06083.
This work was performed using the equipment of EIMB RAS "Genome" centre (http://www.eimb.ru/ru1/ckp/ccu_genome_c.php).

PS-15-019

Circulating micrornas, potentially associated with progression during therapy in castration-resistant prostate cancer

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Background & objectives: CRPC develops is a molecular events result that lead to resistance emergence of tumour cells to therapy and to further progression. The aim of study is to search for predictive markers during therapy, based on circulating exosomal microRNAs of plasma.
Methods: From the plasma exosomes of the patients in periods of remission and progression (12 time points in each group), total RNA was isolated, on the basis of which microRNAs libraries were prepared, followed by high-throughput sequencing on the Illumina platform. Next, the bioinformatic analysis of differential expression between groups in statistical environment R was carried out.
Results: As a result of the comparison of the groups (progression and remission), the following differentially expressed microRNAs were found that were potentially associated with the progression of CRPC: -221-3p, -99b-3p, -145-5p, -375-3p, -20a-5p, -21- 5p, -451a, -199a-5p, -183-5p, -let-7i-5p, -let-7f-5p, -451a (p-value < 0,05). Identified microRNAs have previously established oncogenic significance in various types of cancer.
Conclusion: Thus, identified miRNAs are aberrantly expressed in the studied progression group and can be considered for subsequent validation by qPCR as potential predictive markers for CRPC.
The reported study was funded by RFBR, project number 17-29-06085. This work was performed using the equipment of EIMB RAS "Genome" centre (http://www.eimb.ru/ru1/ckp/ccu_genome_c.php).

PS-15-021
Investigation of NTRK fusion in solid tumours
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Background & objectives: Neurotropic tyrosine kinase (NTRK) fusions are oncogenic drivers of solid tumours and detection of it has a clinical importance due to efficacy of targeted therapy. We present our results with RNA based sequencing in different solid tumours until February 2020.
Methods: Recent guidelines prefer NGS based RNA sequencing. RNA was extracted from biopsies, cytology smears, and formalin-fixed paraffin-embedded tissues. A maximum of 100 ng of RNA was used. The assay was performed on an IONTORRENT S5 SYSTEM using the Ocnomine Focus panel kit. Data was evaluated using IONRIPORTER SOFTWARE.
Results: 123 cases of solid tumours were analysed: 74 lung, 25 salivary gland, 9 soft tissue, 8 gastrointestinal, 4 thyroid, 1 breast, 1 neuroendocrine, 1 kidney tumour.
NTRK fusion was confirmed in 2 cases: secretory carcinoma of the parotid, and myofibroblastic sarcoma. Other mutation of clinical significance were also detected: 6 cases of Met exon skipping, 4 cases of ALK translocation in lung adenocarcinoma, 1 case of KIF5B(15)-RET(12) fusion in non small cell carcinoma. 109 cases were negative.
Conclusion: The advantage of NGS is that it allows multiple genes to be tested. NTRK fusion was identified only in two typical tumour types. The assay was advantageous especially for lung cases, with that in mind that it detects all fusions with clinical relevance.

PS-15-022
Differential expression of DNA methyltransferases and demethylases among the various subtypes of testicular germ cell tumours
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Background & objectives: Very distinct DNA methylation profiles characterize the most common subtypes of testicular germ cell tumours(TGCTs), seminomas (SEs) and non-seminomas (NSs), pointing towards differential expression of DNA methyltransferases(DNMTs) and demethylases(TETs). We aim to characterize the expression of such players in TGCTs.
Methods: An in-silico analysis of The Cancer Genome Atlas database was performed to select the most relevant enzymes of each family. Transcript levels were assessed in four TGCT cell lines. Findings were further validated in our own patient cohort, by real-time quantitative PCR and immunohistochemistry.
Results: DNMT3B was significantly more expressed in NS-related cell lines, while the inverse was seen for TET2. Significantly higher mRNA expression levels of DNMT3A/B were observed in embryonal carcinoma, indicating a role of de novo methylation in reprogramming. Significantly higher protein expression of TET2 was observed in SEs, indicating active demethylation as contributor to the demethylated background. All enzymes were differentially expressed among the various subtypes, related to differentiation.
Conclusion: DNA modifying enzymes are differentially expressed in TGCT subtypes and seem to influence phenomena like reprogramming and differentiation. Better understanding of these patterns may be helpful in designing protocols for experimentation with novel targeted therapies for TGCT patients.
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PS-15-023
Designing a model for predicting informative liquid biopsy-based microRNA biomarkers in germ cell tumours: insights from in vitro, in vivo and patient-derived data
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Background & objectives: Liquid biopsy-based biomarkers, such as microRNAs, represent valuable tools for patient management. However, often these candidate microRNAs do not make it to integration in the clinic. In this work, we aim to explore these issues in the setting of germ cell tumours, for which novel biomarkers are needed.
Methods: We describe a model for predicting clinically relevant microRNAs for germ cell tumour patients, using both in vitro (cell lines) and in vivo (mouse model) data, employing a high-throughput pipeline. Initial wide screening of microRNAs is performed (Taqman Low-Density Array cards), followed by targeted analyses, in several bodily fluid patient samples.
Results: We describe a model for predicting clinically relevant microRNAs for germ cell tumour patients, using both in vitro (cell lines) and in vivo (mouse model) data, employing a high-throughput pipeline. Initial wide screening of microRNAs is performed (Taqman Low-Density Array cards), followed by targeted analyses, in several bodily fluid patient samples.
Conclusion: Our approach is informative to identify the best candidate microRNAs to pursue in liquid biopsies. A patent application was filed covering the finding of using miR-885-5p as molecular marker for teratoma and the effect of miR-885-5p on the P53 pathway.
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PS-15-026
Detection of KRAS, BRAF, PIK3CA by microarray technology for targeted therapy in patients with pancreatic cancer: a single centre experience
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Background & objectives: In the carcinogenesis of the pancreatic carcinoma, one of the early events is the mutation of the oncogene KRAS, which is found altered in 20% of pancreatic intraepithelial neoplasia and this percentage increases with progression to invasive carcinoma.
Methods: We tested 46 patients with diagnosed pancreatic adenocarcinoma for the frequency and type of mutations in KRAS, BRAF и PIK3CA on paraffin-embedded surgical tissue specimen, by using Multiplex PCR amplification on Randox Platform. We correlated the type of mutation with the clinical stage and histological grade of the tumour, and with the histological type of the tumour.
Results: Twenty-eight of the cases diagnosed pancreatic carcinoma were males and 19 cases were females. The mean age of the group was 62.2 y. Seven of the patients were in stage I, 14 of the cases were in stage II, 7 of the cases were in stage III and 8 patients were in stage IV. Ten of the cases were with an undetermined clinical stage. The molecular analyses revealed alteration of the KRAS in 22 of the patients and in one patient was found combined alteration of the KRAS and PIK3CA. The patients with present alterations of the KRAS were almost equally distributed accordingly to the clinical stage.
Conclusion: KRAS is a late event in the development of pancreatic carcinoma and probably has a role in tumour progression. Testing of the pancreatic carcinoma tissue by a `larger panel of oncogenes with the next sequencing techniques should be done.

PS-15-027
Predictively significant mutational analysis of routine NSCLC biopsy samples: a pilot study comparing conventional gene by gene and NGS tests
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Background & objectives: FFPE samples of adenocarcinoma NSCLC (ADC) were conventionally tested for alterations of EGFR, ALK and ROS1 genes rearrangement by CE-IVD techniques. The retrospective study was performed to verify sensitivity and specificity of DNA/RNA analyses using NGS of identical samples.
Methods: 81 samples with known EGFR status were tested for DNA analyses and 78 with known status of ALK and ROS1 for RNA with AmpliSeq™ for Illumina® Focus Panel (Illumina, CA, USA) using bioinformatical software Finalist Dx (IAB, Czechia) for DNA and RNA Amplicon App. Version2.0.1 (Illumina, CA, USA) for RNA samples. The results were compared with those of conventional approach.
Results: The comparison showed 100% specificity and sensitivity for DNA analyses and 100% specificity for RNA analyses. The sensitivity was 100% for ROS1 rearranged and 76.5% for ALK rearranged cases. The discordant cases by conventional testing showed 100% agreement with IHC for ALK positive and 100% agreement with FISH results for ROS1 positive cases.
Conclusion: The implementation of NGS allows precise understanding of molecular background of ADCs and therapeutical management of individual patients. The cases showing lower sensitivity will be further reanalysed using more complex NGS analyses.

PS-15-028
Microfluidic-based automated chromogenic RNA in situ hybridization
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Background & objectives: The RNAscope® in situ hybridization (ISH) assays allow for single RNA molecule detection at cellular resolution within tissue and cellular morphological context. Here, we aimed to automate the RNAscope® 2.5HD-BROWN chromogenic ISH (CISH) assay on the Lunaphore's microfluidic device LabSat®.
Methods: Deparaffinization of the formalin-fixed paraffin-embedded (FFPE) specimens was performed manually. Each CISH protocol step was optimized separately on LabSat®, while performing the rest of the assay manually according to Advanced Cell Diagnostics' (ACD) datasheet. Slides were scanned using bright-field microscopy and analysed using the RNAscope® scoring system.
Results: The full RNAscope® 2.5HD-BROWN protocol, from pretreatment to counterstaining, was successfully automated on LabSat®, a pressure-driven system allowing for rapid and uniform delivery of reagents on a tissue section in a temperature-controlled closed reaction chamber via the fast-fluidic exchange (FFEx) technology. The RNAscope® assay, based on ACD's technology for signal amplification and background suppression, was optimized on LabSat® to result in well-preserved morphology, uniform staining with excellent signal-to-noise ratio and readily detectable punctate signal dots - comparable to the manual assay on mouse and human FFPE samples. Concomitantly, the assay turn-around time was shortened with respect to the manual and other automated CISH protocols.
Conclusion: Overall, we have proven the capability of the microfluidic platform LabSat® to automate the RNAscope® 2.5HD-BROWN CISH assay with reproducible staining results. The microfluidic platform brings the benefits of a shorter run time and reliability of a compact desktop system.

PS-15-029
The role of molecular tumour board in lung cancer: current practice
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Background & objectives: The use of a Molecular Tumour Board (MTB) may become a useful tool to provide personalized assessment of lung cancer patients in high stages with molecular studies. We aim to characterize the patients discussed in our MTB.
Methods: We retrospectively analysed data collected from 588 patients presented on the MTB since September 2017 to August 2019. The MTB took place on wednesdays every week and involves different medical professionals (oncologists, pathologists, biologists, bioinformatics, technicians, palliative care and residents).
Results: We found out that 405 (69%) were newly diagnosed cases with metastatic disease, 82 (14%) were patients with progressive disease with a known molecular marker, 62 (10.5%) patients with molecular results were received from outside (external laboratory, clinical trials), 20 (3.5%) were cases with possible disease progression, pseudoprogression or hyperprogression after immunotherapy, 12 (2%) patients that stored material for new diagnostic studies/techniques. 7 (1%) patients undergo surgery with multifocal disease that require definitive staging.
Conclusion: MTB gathers all sources of information in order to create specific strategies for each patient also giving a rich opportunity to increase the understanding and knowledge for all medical professionals, boosting research of new molecular techniques and clinical assessment.

PS-15-030
Pan-cancer multiomics analysis of TC2N suggests its important role(s) in tumorigenesis of many cancers
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Background & objectives: Role of TC2N in carcinogenesis has been largely unfathomed until recently when it was identified as a novel oncogene in lung cancer. We present first report on pan-cancer multiomics-analysis of TC2N, highlighting TC2N as an important player in cancer-circuits.

Methods: We investigated TC2N mRNA expression, its promoter methylation, effects on overall patient survival, somatic mutations in TC2N gene and correlation between TC2N mRNA expression and other cancer genes in pan-cancer by using data available from the Cancer Genome Atlas (TCGA) and the Genotype Tissue Expression (GTEx) databases.
Results: TC2N mRNA expression was upregulated in cholangiocarcinoma, ovarian-serous-cystadenocarcinoma, rectal-adenocarcinoma, stomach-adenocarcinoma and thymoma and downregulated in pheochromocytoma-&-paraganglioma, skin-cutaneous-melanoma, thyroid-carcinoma and uterine-carcinosarcoma. TC2N promoter was hypermethylated in most cancers while hypomethylated in head-&-neck-squamous-cell-carcinoma and kidney-renal-clear-cell carcinoma. TC2N transcription was positively correlated with transcription genes from Myc, cell-cycle, Nrf2, Wnt, PI3K, Hippo, Notch, TGFβ and RAS/RTK pathways. Poor prognosis was associated with higher TC2N mRNA levels in pancreatic-adenocarcinoma and brain-lower-grade-glioma and lower TC2N mRNA levels in kidney-renal-clear-cell-carcinoma, mesothelioma, sarcoma and skin-cutaneous melanoma. Highest pathogenic somatic mutation rates in TC2N were found in skin-cutaneous-melanoma, uterine-corpus-endometrial-carcinoma, colon-endocervical-adenocarcinoma, bladder-urothelial-carcinoma and breast-invasive-carcinoma.
Conclusion: This is the first report detailing pan-cancer multiomics analysis TC2N, unravelling various molecular players in cancer circuits.

PS-15-032
Prognostic value of liquid biopsy with determination of circulating tumour DNA in early diagnosis of metastases in patients with colorectal cancer
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Background & objectives: Liquid biopsy is a minimal invasive approach to obtain ctDNA that used for molecular profiling tumour cells. The possibility of using ctDNA for prognosis assessment and detection of minimal residual disease, monitoring of treatment efficacy therapies at CRC are studied.
Methods: The molecular testing performed by acPCR. liquid biopsy were collected at patients with mutated ras gene. ctDNA was detected on Idylla Biocartis automatic system. LB was performed in 35 patients with a primary diagnosis of CRC with a mutated RAS gene, after surgical treatment, prior to initiation of adjuvant chemotherapy. In all cases, there was a localized process (T2-3N0-1M0).
Results: Of the 1318 patients with CRC RAS mutations found in 689 cases. Of the 35 patients examined by the LB, ct DNA in peripheral blood was detected in only 5 (14,2%) patients with moderately differentiated intestinal adenocarcinoma. All patients within 6-8 months passed from 6 to12 courses of adjuvant chemotherapy. In the control CT examination in 7/35 (20%) cases, the progression of the process to the liver and lungs was noted against the background of adjuvant treatment, of them in 5 cases with a positive on ctDNA confirmed before the start of chemotherapy. One patient with a constant positive ctDNA after adjuvant treatments with a fatal outcome during the year.
Conclusion: Thus, the positive result at LB for ctDNA at the RAS study can be considered as a predictor of an unfavourable prognosis of the CRC , and in non-operable patients when tumour tissue is inaccessible, use it as a diagnostic predictive marker. The possibility of using ctDNA as a marker for monitoring of treatment efficacy therapies requires further study.
Funding: Scientific Medical Society of Kazakhstan and pharmaceutical company

PS-15-034
Pan-cancer multiomics analysis of S-phase kinase-associated protein-2
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Background & objectives: Dysregulated expression of S-phase kinase-associated protein-2 (SKP2) contributes to tumorigenesis in breast, prostate and lung cancers. However, exact mechanistic role of SKP2 in other cancers remains unfathomed. We present first report on pan-cancer multiomics analysis of SKP2 in all cancers.
Methods: We investigated SKP2 mRNA expression, methylation patterns, effects of SKP2 transcription on overall patient survival and somatic-mutations in SKP2 gene in pan-cancer by analysing data available from The Cancer Genome Atlas (TCGA) and the Genotype-Tissue Expression (GTEx) databases.
Results: SKP2 mRNA expression was upregulated in 12/33 TCGA tumour types. SKP2 promotor was significantly hypomethylated in most cancers while hypermethylated in colon-adenocarcinoma, oesophageal-carcinoma, kidney/renal-clear-cell-carcinoma, lung-squamous-cell-carcinoma and pancreatic-adenocarcinoma. Increased SKP2 transcript levels significantly reduce overall-survival in adrenocortical-carcinoma, uterine-carcinosarcoma, skin-cutaneous-melanoma, mesothelioma, lung-adenocarcinoma, liver-hepatocellular-carcinoma, brain-low-grade glioma and kidney-renal-papillary-cell-carcinoma. Low SKP2 expressions were significantly associated with short survival in thymoma, thyroid-carcinoma and ovarian-serous-cystadenocarcinoma. A total of 109 somatic mutations were found in SKP2 gene including missense mutations to be the highest. The highest somatic mutation rates in SKP2 were found in uterine-corpus-endometrial-carcinoma followed by lung-adenocarcinoma, head-and-neck-squamous-cell-carcinoma, skin-cutaneous-melanoma and bladder-urothelial-carcinoma.
Conclusion: Our findings unravel several unfathomed pathways related to the role of SKP2 in oncogenesis of several cancers, suggesting SKP2 as an important player in oncogenesis and a potential candidate for cancer-therapy.

PS-15-036
Microsatellite instability testing, a 7-year experience
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Background & objectives: The role of microsatellite instability(MSI) testing has expanded to include treatment prediction. We set out to assess the demand for MSI testing in our laboratory over a 7-year period. We also assessed whether there was change in positivity rates.
Methods: Beaumont Hospital/RCSI acts a referral laboratory for a number of molecular pathological tests, including MSI. Cases tested for MSI were selected using an in-house laboratory database search between January 2014 and December 2019. Information regarding a positive or negative test was collected.
Results: The total number of MSI tests request has increased by approximately threefold over the period of the audit (106 cases in 2014, 182 in 2015, 264 in 2016, 340 in 2017, 393 in 2018 and 342 in 2019). The percentage of MSI positive cases over this period was 31% in 2014, 19% in 2015, 16% in 2016, 15% in 2017, 18% in 2018 and 19% in 2019.
Conclusion: Overall, the demand for MSI testing has increased approximately threefold over the past 7 years. This likely reflects a broadening of the indications for testing. Although there has been an increase in the number of cases tested, positivity rates have remained quite stable during this period.

PS-15-037
Identification of gene fusions in non-small cell lung cancers using two diagnostic approaches - can we significantly improve the detection rate?
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Background & objectives: The fusion gene detection in several tumours, including NSCLCs, is currently crucial step in diagnostic and qualification to targeted therapies. The aim was to: identify the gene fusions and compare two testing approaches: the IHC/NGS vs NGS.
Methods: In total 763 solid tumours FFPE specimens from NSCLCs patients were analysed. The two-step IHC/NGS test (402 cases), included the IHC screening using a pan-receptor tyrosine kinase cocktail of antibodies targeting ROS1, ALK and NTRK proteins followed by an RNA-based anchored multiplex-PCR NGS assay in IHC positive specimens. In one step NGS analysis, all the 361 samples underwent NGS.
Results: Overall, we identified 56 gene fusions. In the IHC/NGS analysis, gene fusions were detected in 15 /402 samples, which gave detection rate of 3.7%. In the one step NGS analysis gene fusions in 41/361 samples were found, giving the detection rate of 11.3%.
Conclusion: The two-step IHC/NGS approach is regarded as cost-effective, but our results indicate that this strategy may omit several important fusions.

PS-15-038
NTRK gene fusion testing adoption readiness in three European countries
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Background & objectives: NTRK gene fusions occur in few rare cancer types and infrequently in some common cancers. To determine real-world laboratory readiness for NTRK adoption we investigated current methodologies used by 83 laboratories from three European countries for NTRK fusion testing.
Methods: This study used real-world pathology laboratory data from 83 laboratories in France, Spain and Italy performing NTRK testing. The Diaceutics proprietary global laboratory database was analysed for the described setting in the period between May and December 2019 to understand NTRK testing capabilities currently available in these laboratories.
Results: Table 1 – NTRK fusion testing adoption and testing methodologies in 83 labs from 3 European countries.

Country	Solid tumour pathology labs	NTRK testing adoption rates	Methodologies for NTRK fusion testing			
			NGS	RT-PCR	FISH	IHC
France	21	67%	86%	7%	7%	36%
Italy	33	45%	80%	20%	27%	67%
Spain	29	55%	69%	0%	19%	94%
Total labs	83	-				
NTRK testing labs	-	45				

Conclusion: NTRK gene fusion testing has been perceived as a new challenge by European laboratories. The agnostic nature of NTRK fusions leads to the use of different testing algorithms based on the type of tumour. There are differences between the adopted methodologies for NTRK gene fusion testing by the laboratories. This highlights the necessity for guidance and testing harmonization around the detection of NTRK fusions in the clinic.

PS-15-039
PIK3CA testing adoption readiness for breast cancer in nine European countries
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Background & objectives: PIK3CA represents a new molecular biomarker for HR+ HER2- BRCA- advanced breast cancer patients. Recently FDA approved the first PIK3 inhibitor with a RT-PCR CDx. Laboratory readiness for PIK3CA molecular testing adoption in Europe was accessed for 111 laboratories.
Methods: This study used real-world pathology laboratory data from 111 laboratories that test breast cancer samples in Austria, Belgium, Denmark, Finland, Netherlands, Norway, Portugal, Sweden and Switzerland. The Diaceutics proprietary global laboratory database was analysed in the period between January and July 2019. In addition, we compared RT-PCR uptake for solid tumour tissue testing versus NGS and Sanger sequencing, per country.
Results: Table 1 – Molecular methodologies for solid tumour testing in 111 laboratories from 9 European countries and PIK3CA testing adoption rates.

Country	Molecular methodologies for solid tumour testing			Total labs	PIK3CA testing adoption rates
	RT-PCR	NGS	Sanger Seq.		
Austria	65%	53%	6%	17	57%
Belgium	35%	65%	0%	17	65%
Denmark	100%	75%	0%	8	86%
Finland	40%	40%	0%	5	40%
Netherlands	71%	71%	6%	17	71%
Norway	20%	100%	0%	5	80%
Portugal	61%	39%	11%	18	33%
Sweden	67%	78%	0%	9	56%
Switzerland	47%	80%	27%	15	80%
Solid tumour labs by methodology	64	71	8	111	
PIK3CA testing labs by methodology	2	57	7	67*	

Conclusion: The existing testing landscape for PIK3CA appears to be supportive of the future launch of PI3K inhibitors in the nine European countries included in this study. Despite NGS is the preferred methodology for PIK3CA testing as the biomarker is included in panels for indications such as lung and colorectal cancer, single-gene testing by RT-PCR is highly adopted for solid tumours.

PS-16 Ophthalmic Pathology

PS-16-001
Pleomorphic adenoma of the lacrimal gland: a study of five cases with high proportion of myoepithelial component
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Background & objectives: Lacrimal gland tumours are similar to those in salivary glands. Pleomorphic adenoma is the most common. They are characterized by combining epithelial and mesenchymal elements. Different

patterns are found, but lacrimal gland tumours usually have higher proportion of myoepithelial cells.
Methods: We have reviewed 5 tumours of the lacrimal gland studied in our institution with diagnosis of pleomorphic adenoma. They corresponded to three women and two men with ages between 40 and 57 at the time of diagnosis. One of them was a recurrence but without evidence of malignant transformation. We used immunohistochemistry to assess myoepithelial and mesenchymal epithelial components.
Results: The five tumours studied presented a canalicular pattern with patent lights lined by cuboidal or columnar cells and surrounded by fusiform elements sometimes of clear cells. These cells expressed p63, GFAP, s100, and actin myoepithelial markers while the luminal cells were positive for keratins 5/6, 7 and 34βE12. In all cases Ki67 was expressed below 10% and in all, the myoepithelial component was superior to the epithelial. The mesenchymal component did not exceed one third of the tumour volume. None of the cases presented an absence of myoepithelial component, unlike many salivary tumours.
Conclusion: Although lacrimal pleomorphic adenomas reproduce the same patterns and elements as salivary, the proportion of myoepithelial component is more abundant and resembles biphasic patterns of epimyoepithelial carcinoma, so a denomination epimioepithelial adenoma would be representative of its more usual features.

PS-16-002
Prognostic role of immunoexpression of autophagy-related proteins in uveal melanoma
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Background & objectives: We studied the immunoexpression of autophagy-related proteins such as p62, Beclin-1 and ATG-7 in patients affected by uveal melanoma (UM) both with and without metastases, in order to assess the prognostic significance of autophagy in this rare neoplasm.
Methods: We retrospectively analysed clinical data and histological samples of 62 patients affected by UM (n= 35 free from metastases; n= 27 with metastatic disease) with the respective follow-up data. p62 and Beclin-1 were immunoexpressed both in the cytoplasm and in the nucleus of neoplastic cells, while ATG-7 only showed cytoplasmic staining.
Results: Stain intensity (IS) and percentage of immunopositive cells (Extent score; ES) were assessed as follows: IS was graded on a scale of 0–3 and ES on a scale of 0-4. IS was multiplied by the ES to obtain the intensity reactivity score (IRS; < 6 = low expression, > 6 = high expression). High Beclin-1, p62 and ATG-7 levels were observed in 30/35, 32/35 and 29/35 non-metastatic UMs, respectively. Kaplan-Meier survival analyses showed higher survival times free from metastasis in patients with high expression of the abovementioned proteins.
Conclusion: Autophagy role in cancer still remains controversial. We suggest that autophagy-related proteins might be considered promising positive prognostic factors of UMs. However, further investigations with additional markers involved in the autophagy process may be required to confirm our findings.

PS-16-003
Ocular melanoma: clinicopathological features of 7 cases
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Background & objectives: Ocular melanoma represents the most common primary intraocular malignant tumour in adults and the second most common type of melanoma. The aim of this report is to present a series of seven cases.
Methods: We conducted a retrospective review of all ophthalmologic pathology specimens received between 2005 and 2019, using department's database. From these records, sex, age, location, clinical presentation, and histologic type were analysed.
Results: The age varied from 35-84 years, with a mean age of 65 years. Of them, 85% were located in the uvea, and 14% in conjunctiva. Almost all of them (71%) debuted with visual loss, while the rest presented retinal detachment (28%). The majority were mixed type. None of them presented local recurrence, but 42% had hepatic metastases. At the time of this study, 71% had died, 57% from metastatic disease.
Conclusion: Ocular melanoma represents a rare and lethal clinical entity with a poor prognosis. Our findings agree with the reviewed literature. Uvea is the most frequent location and visual loss is the most common form of presentation. Hepatic metastases were the most prevalent and approximately 57% died with metastatic disease. In our series, the most common type was the mixed type in opposition to the reviewed literature. In conclusion, we found a higher lethal prognosis in relation with non-spindle-cell type.

PS-16-004
Histopathologic features of descemet membrane endothelial keratoplasty graft detachment
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Background & objectives: Descemet membrane endothelial keratoplasty (DMEK) is the selective replacement of posterior corneal layers. The major postoperative complication is donor graft detachment. The purpose of this research is to study morphologic features involved in graft detachment after DMEK.
Methods: In a prospective case series, 14 patients (14 eyes) with FECD underwent a primary DMEK. The mean age of the recipients was 68.5 ±9.5. Intraoperatively obtained recipients' endothelium-Descemet's membranes (EDMs) were investigated histologically (hematoxylin-eosin staining). The postoperative donor graft status was assessed as attached or detached by anterior segment optical coherence tomography (RTVue; Optovue, Inc, Fremont, USA).
Results: Local graft detachment occurred in 4 eyes (29%), which required a second intervention with SF6 gas injection in the anterior chamber performed on 6±3 days. Regarding histologic investigations, residual recipient' stromal collagen fibrils fixed to EDM were detected in all cases with graft detachment. In contrast, a complete removal of single EDM was observed in patients with adherent EDM grafts.
Conclusion: Deep disruption of recipient' posterior corneal stroma may induce graft detachment as a postoperative complication of DMEK.

PS-16-005
Histopathological pattern of conjunctival tumours, a single centre experience: a twelve-year review
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Background & objectives: Conjunctival tumours are either malignant or benign and constitute an important cause of morbidity and mortality. The histological spectrum of these tumours varies widely with prognostic implications. This study is a review of conjunctival tumours in a Nigerian tertiary institution.
Methods: This is a retrospective study conducted in pathology department of our institution. All conjunctival tumours from the records and files of the Department of Morbid Anatomy, over a 12 year study period spanning from January 1, 2003 to December 31, 2014 were reviewed and subsequently classified using World Health Organisation Histologic Classification of the Eye, Fourth Edition 2018.

Results: A total of 101 cases were retrieved. The patients' ages ranged from 1 to 84 years with a median age of 28 years. The age groups of 20 - 29 years and 30 – 39 years were most affected accounting for 24 (23.8%) and 28 (27.7%) respectively. There were 50 males (49.5%) and 51 females (50.5%), giving a ratio of 1:1.02. Conjunctival tumours show almost comparable frequency of 42 (41.6%) and 48 (47.5%) for benign and malignant tumours, while premalignant tumours accounted for 11 (10.9%). Squamous cell carcinoma 42 (41.6%) and squamous cell papilloma 18 (17.8%) were the most prevalent malignant and benign tumours respectively.
Conclusion: Conjunctival tumours affect all age group with a slight female predominance. Malignant tumours were commoner than benign tumours. Squamous cell carcinoma was the most prevalent tumours and closely followed by squamous cell papilloma.

PS-16-006
Clinicopathologic high risk features in retinoblastomas as seen in a tertiary hospital, south west, Nigeria
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Background & objectives: The role of histopathology in retinoblastoma is not necessarily for diagnosis as this is usually made clinically, histopathology is employed for staging, prognostication and evaluation in metastatic disease, hence the identification of high-risk clinicopathologic features in retinoblastoma is principal.
Methods: This retrospective, descriptive study was carried out utilizing records and blocks taken from patients with retinoblastoma who presented and were treated in our hospital between January 2007 and December 2018.The International Classification of Retinoblastoma (ICRB) as well as the Reese-Ellsworth (RE) classifications were used for the clinical staging while the high risk features were as documented in several large studies.
Results: Eight (8) cases of retinoblastoma were confirmed in our histopathology laboratory. All tumours were unilateral and there were no positive family history. Half of the cases were at clinically advanced stage. Five (62.5%) had tumour up to the optic nerve surgical margin as well as microscopic intraocular spread. Choroidal and intrascleral invasion were present in 5(62.5%) and 6(75%) respectively.3 years after conclusion of treatment, 5 were lost to follow up.
Conclusion: The morbidity of retinoblastoma(blindness) has drastically reduced with new treatment approaches, and cure rates of up to 100% have been achieved. In low and middle income countries however the morbidity and mortality is disproportionately high. Patients present at advanced stages of the disease requiring more invasive and expensive medical interventions with less favourable outcomes. The identification of high-risk clinicopathologic features will assist the clinician on the choice of adjuvant therapy required to reduce the occurrence of metastasis and subsequent mortality.

PS-16-007
Choroid melanoma with distant metastases and without them: peculiarities of intraorgan spread and cell renewal in the tumour
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Background & objectives: To characterize morphological and immunohistochemical peculiarities of the intraorgan spread of choroid melanoma and its cellular renewal depending on the presence or absence of distant metastases.
Methods: Surgical material (eye enucleation) from 31 patients with choroid melanoma served as the object of the study: Group 1 - observations with liver metastases (n = 14), Group 2 - without distant metastases (n = 17).
Results: The patients' median age in Group study 1 was 58.0 (51.75; 62.75), in Group 2 - 64.0 (57.0; 73.0). The differences in the number of tumour emboli with prevalence in Group 1 appeared to be statistically significant (p = 0.003). Immunohistochemistry revealed significant differences in the number of tumour cells expressing Bcl-2 and p53, with a predominance in the Group 2: in Group 1, the values of Bcl-2 and p53 were 26.0 (22.25; 48.0) and 8.0 (5.0; 16.0); in Group 2 - 56.0 (48.5; 58.5) and 25.0 (17.5; 32.5) respectively (p <0.0001 in all cases). No differences in the expression level of the Ki-67 marker were revealed (p = 0.856).
Conclusion: The number of tumour emboli in choroid melanoma and the expression rates of Bcl-2 and p53 tumour cells statistically differ significantly for metastatic tumours and neoplasms without metastases; so, they can be used as prognostic indicators of melanoma generalization.

PS-16-008
Primary lymphoma of ocular attachments - analysis of a retrospective cohort at the National Cancer Institute
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Background & objectives: Primary lymphomas of the ocular attachments (OAL) appear in places such as orbit, conjunctiva and lacrimal gland. The objective is to evaluate clinical, epidemiological and histopathological characteristics of patients with OAL, at the National Cancer Institute (INCA) for eleven years.
Methods: This is a cohort study, with data collection from the bank of the Division of Pathology (DIPAT) of INCA, with diagnosis of primary lymphoma of ocular attachments in the period from 1999 to 2019.
Results: According to the analysis of the DIPAT data, 98 cases were selected. 57.82% of the sample was female, 54.88% MALT lymphoma and 69.58% affecting the orbit. The most prevalent age group, with 58.80%, was 60 years or older. The diagnosis was made by biopsy of the lesion followed by histopathological and immunohistochemical exams. Diagnostic staging assesses the extent of the disease, with approximately 60 to 80% of lymphomas of the ocular attachments presenting as a localized disease at diagnosis.
Conclusion: Currently, there are no official data on the incidence and prevalence of primary ocular lymphoma in Brazil. Since INCA is a reference body in the treatment of neoplasms, it is estimated that the data collected may add information necessary for diagnosis and treatment, in addition to recording statistical and epidemiological data on the disease.

PS-16-009
Malignant orbital tumours in Gwagwalada / Abuja: histopathological analysis
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Background & objectives: Tumours of the eye and ocular adnexa have been reported to be more common in Africa than other parts of the world, making ophthalmic neoplasms a major cause of clinical morbidity and mortality on the continent.
Aim: To describe the pattern of malignant orbital tumour in our environment
Methods: This is a 5-year retrospective study of malignant orbital tumours diagnosed between 2005-2009 in the Department of Histopathology, University of Abuja Teaching Hospital, Gwagwalada, Abuja, Federal Capital Territory, Abuja, Nigeria. All the Haematoxylin &Eosin stained slides and paraffin embedded blocks were retrieved and studied.
Results: A total of 23 patients were studied during this review, 12 males and 11 females. The age range is 3-60 years, with the mean age of 31.5 years. The peak age in this study is in the fourth decade. The most common malignancy was squamous cell carcinoma (SCC) 78.2%, followed by retinoblastoma and adenoid cystic carcinoma each having 8.7% respectively and Kaposi sarcoma (4.4%).
Conclusion: The most common orbital tumour in this study is squamous cell carcinoma followed by retinoblastoma with one case each of adenoid cystic carcinoma and Kaposi sarcoma.

PS-16-010

Clinico-histopathological correlation of orbito-ocular lesions: a hospital based study

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Background & objectives: The orbital and ocular lesions, either non-neoplastic or neoplastic require correct preoperative provisional diagnosis along with series of investigations and clinical examinations for better treatment. However, the histopathological examination of the same remain as mainstay in confirmation of the diagnosis.
This study was aimed to analyse the histomorphological spectrum with clinico-pathological correlation of orbito-ocular lesions and to evaluate the need of ancillary techniques for confirmation of diagnosis.
Methods: Prospective cross sectional hospital based study conducted at Birat Medical College Teaching Hospital for a period of one year among orbito-ocular surgical biopsies obtained in the Department of Pathology, studied as per epidemiological, clinical and histopathological findings.
Results: Patients age from ten month-82 years, M:F=1.1:1. Orbito-ocular lesions were highest in < 20 years age group. Cornea-conjunctiva was commonly involved site. Clinical diagnosis was consistent with histopathological diagnosis in approximately 66% cases. Non-neoplastic, benign and malignant lesions were 36.75%, 33.51% and 29.72% respectively. SCC formed 50.90% of all malignant lesions followed by sebaceous carcinoma and melanoma. The special stains and immunohistochemistry study recommended for 19.45% and 11.35 % respectively.
Conclusion: Findings suggest HPE along with clinical findings correlation is useful for diagnosing the wide spectrum of orbito-ocular lesions. The clinicopathological diagnostic correlation was good (66%) along with recommendation of ancillary techniques like special stains and immunohistochemistry panel study was made.

PS-16-011

Retinoblastoma metastasizing to the ankle joint, case report from Kigali university teaching hospital

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Background & objectives: Retinoblastoma is the most common intraocular neoplasm in childhood representing 3% of all childhood malignancies. It rarely metastasizes to the soft tissue. We present a case of retinoblastoma that has metastasized to the ankle joint.
Methods: The case was obtained from the Pathology archives at the University Teaching Hospital of Kigali (CHUK), Rwanda. Age, gender, patient history, clinical presentation and imaging were recorded. Histopathological diagnosis was confirmed by hematoxylin and eosin (H&E) sections and immunohistochemistry.
Results: A 5-year and 6months old male presented at CHUK with left ankle painful swelling for 7 months on past history of bilateral retinoblastoma at the age of 5 months. Imaging found a soft tissue lesion and bone structures were intact. A small round blue cell tumour was noted on H&E stain and neoplastic cells were positive for CRX and Synaptophysin.
No other metastatic focus seen
Conclusion: Local spread with brain involvement are the most common in advanced retinoblastoma. Distant metastasis in the soft tissue may rarely be seen even after 5 years' post-chemotherapy. Symptoms are not specific and H&E alone is insufficient to make the diagnosis.

PS-16-012

Histopathological and molecular features of a conjunctival caruncular deep penetrating nevus

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Background & objectives: Lesions located at the lacrimal caruncle are uncommon and the differential diagnosis includes many different entities, because the caruncle harbours both skin and conjunctival elements. We describe the first presentation of a deep penetrating nevus (DPN) on the lacrimal caruncle.
Methods: Case report
Results: This lesion was seen in an 18-year-old woman presenting with haemorrhage of a long-standing pigmented caruncular mass, histopathologically revealing two different melanocytic components. The differential diagnosis, based on histological examination, was a conventional melanocytic nevus, a Spitz nevus or a combined melanocytic nevus. On the molecular level, both components harboured a BRAF V600E mutation, with one of the components revealing a mutation in the CTNNB1 gene encoding the β-catenin protein.
Conclusion: This presentation of a DPN of the lacrimal caruncle emphasizes the similarities of the caruncle with the skin and shows that molecular analysis might be necessary in rendering a correct diagnosis.

PS-16-013

Clinicopathological features of 51 cases of retinoblastoma cases from Sudan

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Background & objectives: Retinoblastoma is the most common childhood ocular neoplasm worldwide and in Sudan. Most patients is Sudan present with late clinical stage. The aim of this study is to investigate the clinicopathological features of 51 Retinoblastoma cases from Sudan
Methods: This is a Retrospective study investigating 51 cases of enucleation specimen received at Ibn Alhaitham Histopathology Laboratory serving the Mekka Opthalmic hospital at Khartoum /Sudan during the year 2019. Demographic data, clinical information, macroscopic and microscopic features and pathological TNM staging for all cases were collected and slides for all cases examined. Data were analysed using SPSS 31
Results: Fifty-one were studied, 30 (58.2%) were males &21(41.2%) females with mean age of 3 years. All cases presented with Leukocoria, there were 2 cases of bilateral tumours. the youngest patient was 3 months old. The mean size of tumours is 15mm. All cases (100%) show tumour invasion pf the anterior chamber, the posterior chamber and the vitrous. Pathological TNM staging for the tumours were as follows: 24 (47%) cases with PT4NXMX, 15 (29%) with stage PT1, 6 cases (11%) pT2 &2cases (11%) pT3.
Conclusion: Most cases in this series presented with advanced histopathological stage (47%) with extensive intra-orbital &extra-orbital tumour. The very late clinical presentation made vision salvage impossible Early detection and screening of Retinoblastoma cases in Sudan is highly recommended.

PS-17 Pathology in Favour of Developing Countries

PS-17-001

A 'triple edged sword'; high tumour budding, stromal desmoplasia and low host inflammatory response are associated with poor prognosis in pancreatic ductal adenocarcinoma: a review from a resource poor setting

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Background & objectives: Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive cancer that is not usually detected early and associated with treatment resistant/ failure. It has ability to rapidly disseminate to the lymphatics and distant organs. Most patients have advanced stage disease with median survival of less than one year. Pancreatic cancer is not common in our

environment; hence data on PDAC is limited. We review five cases of PDAC over a two-year period (2018-2019).
Methods: Five cases of diagnosed PDAC were retrieved, H&E and immunohistochemical stains (IHC) were performed using AE1/AE3 for tumour budding, tumour buds were defined according to ITBCC and were counted at x20 magnification (field area 0.785mm2) at the invasive front. CD 3 and CD 20 were used for the host immune microenvironment while stromal desmoplasia was accessed using SMA.
Results: The patient's ages were 40- 70 years respectively. The tumour was located in the head of pancreas in all patients. Three of the patients died within one month of surgical intervention. Histology showed marked desmoplastic stroma. Tumour budding was ≥10 in the invasive front, four of the patients showed few inflammatory responses with CD3+T cells and CD20+ B cells were mainly present at the peritumoral areas. One patient had tertiary lymphoid structures.
Conclusion: The dismal prognosis in PDAC especially in our environment includes but not limited to high tumour budding which entails present of epithelial mesenchymal transition (EMT), marked stromal desmoplasia and low host immune response.

PS-17-002
A histopathology reporting system for resource limited departments in low income countries
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Background & objectives: Modern histopathology laboratories rely on computer management systems (LIMS) for accessioning and reporting. Most laboratories in sub-Saharan Africa do not have the resources to afford a commercial LIMS. Open source cloud-based environments offer an alternative for providing essential LIMS functionality
Methods: A minimal specification was developed and an experienced software consultant produced a web based system using the Grails application framework with the data being stored in a PostgreSQL database. These are popular open source technologies. The system facilitates accessioning, reporting, authorisation, the production of supplementary reports, and basic workload statistics. A simple disease coding system is included to facilitate research.
Results: Total development time was approximately 120 hours. After commissioning the system has now run without outage for one year, accessioning 1400 surgical and 500 cytology cases. Patient demographics conform to local custom (two names, age and village). The number of steps involved in producing a report has been reduced and a printed or emailed PDF report is available immediately following electronic authorisation resulting in a reduction in turn-around-times. The system can be accessed via any modern internet enabled device (mobile phones, tablets and computers), is resilient in local power outages and complies with local data protection requirements. Running costs of the server are less than 800USD per year.
Conclusion: We have demonstrated practically of using a low-cost web-based system as a LIMS in a low resource environment. The system has been embraced by staff and could be adapted for use in any laboratory with internet access.
Funding: Path of Logic, Durango, CO a non-profit, has provided funds for the rental of the server.

PS-17-003
Starting a pathology explanation clinic in a tertiary care hospital of a developing country: a challenging but rewarding task
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Background & objectives: Pathology explanation clinic (PEC) is an innovative type of clinic where the pathologist interacts directly with the patient and discusses their reports and findings, providing direct insights to the patient regarding disease process, stage, grade, prognosis and other details.
Methods: A PEC was setup at Cantonment General Hospital which is located in Rawalpindi, Pakistan. A total of 150 patients were enrolled in the study and their histopathology reports were discussed with them by two expert consultant pathologists. Furthermore all of their queries were appropriately addressed. A feedback form was provided to be filled by the patients after consultation.
Results: 89% of patients reported better satisfaction and understanding of the reports when explained by the pathologist and 75% patients reported better communication with the clinician after pathology clinic consultation. None of the patients gave a negative feedback about the consultation.
Conclusion: PEC is a novel idea which may help to improve the concept of patient centered care and empower patients in integral decision-making process. However, the financial, logistic and administrative implications have to be sorted out.

PS-17-004
The evaluation of homegrown digital scanner as learning and assessment tool of haematoxylin and eosin stained slides in pathology
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Background & objectives: Digital scanning of glass slides in pathology is usually the purview of expensive, time consuming, labor intensive machines. In this study the Morphle a low-budget, cost-effective scanner is explored as an ideal tool for continued learning and assessment in pathology.
Methods: Six surgical-pathology glass slides sets (20) were scanned and evaluated by the pathology post-graduate students at SRMC. Each whole-mount scanned case-slide was presented as an interactive group discussion. Each slide-set had a post-slide review test as formative assessment. Sixty screen shots of the scanned images were evaluated as final summative assessment. Student feedback questionnaires and self-reflective learning documents were obtained
Results: The scanning of each twenty-slide-set took 2.5 hrs. Each session reviewed whole-mount scanned images that were zoomed to high power to demonstrate specific pathological findings in a stress-free, engaging, learning environment with simultaneous group/peer learning. The scanned images were also available digitally for individual/self-learning. The final summative review test scores demonstrated increased knowledge gain. All students liked this digital format of teaching as an exam preparatory tool in comparison to microscopic sessions and self-reported improved personal knowledge.
Conclusion: Digital scanning of pathology slides using Morphle is user-friendly and cost-effective. The real-time zooming of the whole mount scanned images is easy and of great clarity with high resolution that allows for assessment with just-in-time learning suitable for group/peer or individual self-learning. This low cost, time-sensitive scanner also provides a permanent digital resource for continued deep learning with the ongoing potential of real-time portability and knowledge sharing across digital divides

PS-17-005
An open-access atlas of cytology – a collection of 500 cases
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Background & objectives: Inspired by the experiences made during many years of the iPath-network, which enables contact with colleagues from countries with restricted resources and gives insights into their needs, we compiled this collection of cases as a resource for learning and teaching.
Methods: The specimens are from serous cavities (96), CNS (56), soft tissue and bone (46), cervical smears (40), pancreas/biliary tract (38), thyroid (29), breast (27), lymph nodes (22), liver (15), urine (12), ovary (10), adrenal gland (9), intestinal (9), mediastinum (9), salivary glands (8), joint spaces (7), pituitary gland (5), testis (4), kidney (4), skin (2), bone marrow (2), prostate (1).
Results: Each case is presented on two pages: On the first page, the cytological findings and the necessary clinical information are displayed. The second page reveals the final diagnosis together with a description of the morphology, differential diagnostic considerations, histological correlation (when available), and literature references. Cases were collected from all over the world (iPath-network), and the contributing institutions are located in Germany (336 cases), Switzerland (103 cases), Bangladesh (58 cases), Afghanistan (2 cases), and China (1 case).
Conclusion: To provide accessibility for everyone, with particular consideration of institutions with limited resources and developing countries, we choose the open-source internet platform WordPress. We intend to create a continuously expanding dynamic collection of special or characteristic cases. The platform will be maintained, and new cases will be added. The collection contains cases from digital consultations, classic educational examples, and unique cases with diagnostic pearls and pitfalls.

PS-17-007
Cancer incidence in a Nigerian tertiary institution
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Background & objectives: About 100, 000 new cancer cases occur yearly in Nigeria. There are, however, difficulties in sustaining cancer registration in developing countries. This is a retrospective study to review all malignancies received in our department from January 2005 to December 2017.
Methods: Records of patients with a histologic diagnosis of cancer made in the department were retrieved. These data were then classified and cumulated according to site (based on organ systems), age, sex and histologic type i.e. carcinoma, sarcoma, lymphoma, blastoma, melanoma and others not specified. These results were analysed in rank, percentage frequencies and presented in tables, charts and graphs.
Results: A total of 6540 malignancies were analysed during the study period. There was a general increase in cancer incidence over the 13 years of study. The male to female ratio was 1:2.2 for all the malignancies. The commonest cancers in this study are breast and cervical cancer amongst women; prostate cancer among men; and lymphoma among children. Carcinomas accounted for 86.1% of cases, sarcomas 5.7%, lymphomas 3.9%, blastomas 2.1%, melanomas 0.4% and other histologic subtypes accounted for 2.2%. The peak age of occurrence was in the 6th decade for men, 4th decade for women and under 5years for children.
Conclusion: More population-based cancer registries are needed in Nigeria. This is feasible despite the challenges. Studies like this could further strengthen the cancer surveillance of the existing cancer registries in the country for evidence-based planning for cancer prevention and control. An effective cancer screening programs will significantly reduce cancer morbidity and mortality in the countries because the most common sites of involvements especially, breast, cervix and prostate are easily assessable.

PS-17-008
Histopathological spectrum of solid cancers in childhood and adolescents: a single institutional experience from north-east Nigeria
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Background & objectives: Data systems on childhood cancers are required to drive quality improvement and policy decisions. The study aims to review the histopathological and epidemiological characteristics of solid cancers diagnosed in ATBUTH Bauchi, between 2014 and 2019, among children aged (0-19 years)
Methods: All cancer cases entered into the departmental records over a 6-year period (2014-2019) in the age group 0-19 years were extracted. The patients' request cards, case notes and histology slides were retrieved and relevant data extracted. Histological review of the slides was done and all the collected data were subjected to descriptive statistical tabulation and analysis.
Results: Childhood solid cancers constituted 3.9% of all solid malignancies seen during the study period. The histological spectrum included lymphoproliferative disorders (19.5%), small round blue cell tumours (19.5%) and Soft tissue sarcomas (excluding embryonal rhabdomyosarcoma)- (12.2%). Epithelial neoplasms ranged from colorectal, salivary gland, thyroid, conjunctival and skin cancers and were commoner in the older age group (15-19 years) where they constituted 60% of all malignancies diagnosed in that age bracket. The lymph nodes were the commonest site of tumour occurrence constituting 19.5% of all tumour locations and include Hodgkin lymphoma (50%), Non-Hodgkin lymphoma (20%) and Kaposi sarcoma (20%). Burkitt lymphoma occurred at relatively low frequency, constituting 4.9% of all tumours.
Conclusion: There is a wide spectrum of solid tumours in the paediatric age group. Some of these tumours (i.e. lymphomas) are potentially treatable and/or curable. For this reason, the provision of adequate diagnostic and treatment facilities for paediatric cancers is highly advocated.

PS-17-009
Patterns of hormone receptors and HER2/NEU status in Sudanese endometrial cancer cases: a single institution experience
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Background & objectives: Endometrial carcinoma (EC) is Sudan's third most common gynaecologic cancer. Hormone receptors and Her2/neu expression could be implicated in the prognosis and targeted therapy of EC. We aim to assess the unknown status of these receptors in EC among Sudanese women.
Methods: Samples of formalin-fixed, paraffin-embedded tissue of 40 patients with EC diagnosed at the university of Gezira Medical Laboratory between January 2018 and December 2019 were immunohistochemically studied for hormone receptors (ER,PR) and Her2/neu and the results correlated with histology.
Results: The patients median age was 60(range:35-80 years). Histologically, 27(67.5%) cases were type 1 EC and 13(32.5%) were type II EC; in type II EC, 11(27.5 %) cases were papillary serous carcinoma and the remaining two were clear cell and undifferentiated carcinoma. ER, PR, and Her-2/neu expression were positive in 26(65%), 23(57.5%) and 14(35%), respectively. of the ER positive cases 19(73%) were type 1 and 7(27%) were type II. of the PR positive cases 18(78.3%) were type 1 and 5(21.7%) were type II. of the Her2/neu positive cases 4(30.8%) were type 1 and 9(69.2%) were type II. 10(25%) cases were negative for all markers (triple negative). Her2/neu expression was associated with higher grades.
Conclusion: Our study provides important original data on the status of hormone receptors and her2/neu in Sudanese EC patients; This provides for better comprehension of the biology of the disease, and conforms with international literature the importance of implementing molecular diagnosis in EC.Multi-center studies with larger sample sizes and funds are essential to validate the findings of this study, as they may contribute to better management guidelines of EC in Sudan.
Funding: i have received the educational fellowship award from BDIAP.

PS-18 Uropathology

PS-18-001
Primary malignant melanoma of the urinary tract; case series with clinicopathologic and molecular insights

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Background & objectives: Primary melanoma of the urinary tract is rare and causes difficulties both in diagnosis and management. We aimed to present eight primary urinary case series with clinical, pathologic and molecular findings to add more insight to this challenging entity.
Methods: We documented retrospectively the eight cases from our archive of our department, and searched for clinical, treatment, prognostic data. Additionally, cases were evaluated for histopathologic, immunohistochemical and molecular findings.
Results: The mean age of the eight patients (five men, three women) was 67.25 years. The most common location was urethra (n=6), followed bladder and ureter one patient for each. Half of the cases were metastatic at diagnose. One case had local recurrence. Vertical growth phase, epithelioid and/ or spindle cell type, increased mitotic activity, necrosis was common. HMB45, Melan-A, S-100 were positive and Keratin was negative in all. Six patients' molecular results were available, and five of them revealed various mutations, including BRAF in two and KIT in one.
Conclusion: Awareness of nested growth pattern and in situ melanocytic component at the edges is helpful in histopathologic diagnose, especially in amelanotic or hypomelanotic tumours. Presence of genetic mutation may be related to metastasis, as well as an option for management.

PS-18-002
Alternations in cell proliferation and epithelial-mesenchymal transition (EMT) pathways with progression in recurrent non-muscle invasive bladder cancers

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Background & objectives: More than 2/3rd of bladder cancers are Non-Muscle Invasive (NMIBC) with high risk of recurrence. To understand the differences in cellular signalling in primary NMIBCs and their recurrences with/without progression, we studied the expression of molecules on tissue microarrays (TMA).
Methods: TMA of 106 NMIBCs (53 primary/53 recurrence) were constructed. Immunohistochemistry was performed for oncogenic (p53, p21/WAF1/Cip1), growth-factor signalling (Her2/neu), EMT (E-cadherin, Beta-catenin, vimentin), apoptosis (p53), cell proliferation (Ki-67, IMP3), angiogenesis (VEGF, VEGFR1), cell motility (MMP9) and immune tolerance (PDL1) pathways. Immunostaining was analysed by the semi-quantitative H-score (Histo-score, range 0-300) and differences in expression levels by the paired sample t-test.
Results: The mean time to recurrence was 30.3 months (range 3-109). p21 loss was defined as <10% nuclear expression and PDL1 positive when >5% cells showed membranous expression. Recurrent tumours showed higher p53, Ki-67, Her2/neu, PDL1, vimentin expression and p21 loss. 32 of 53 (60%) primary tumours showed progression in stage/grade/both at recurrence. Progressive tumours showed higher Ki-67 proliferation and expression of Her2, IMP3 and MMP9 and lower p21, beta-catenin, E-cadherin and VEGFR1 as compared to non-progressive tumours. Higher Ki-67 proliferation index and lower surface beta-catenin expression correlated with shorter time to progression. Two primary and four recurrent tumours were PDL1 positive. More recurrent tumours showed PDL1 positive tumour-infiltrating lymphocytes (TILs).
Conclusion: Recurrent and progressive NMIBCs acquire differences in expression of molecules of cellular growth and proliferation, EMT and in immunomodulatory pathways, which correlate with the time to progression.
Funding: Project funded by Government agency, Department of Biotechnology [Grant no. 6242-P2/RGCB/PMD/DBT/VAWL/2015].

PS-18-003
Low grade oncocytic tumour of the kidney: a review of 19 cases

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Background & objectives: Low grade oncocytic tumour (LOT) is an emerging entity with distinct morphology, characteristic immunoprofile, and indolent nature. LOT is diagnosed under several terminologies and poses a diagnostic challenge due to a lack of defined criteria, thus hindering definitive clinical decisions.
Methods: Institutional electronic database was searched between 2005 – 2020. It included all nephrectomies, partial resections, and biopsies performed during this period. A total of 7459 adult primary renal neoplasms were identified, and only tumours with characteristic LOT features were selected for the study. Age, gender, procedure type, surgery date, tumour stage, immunoprofile, and follow up data were recorded.
Results: 19 LOTs with CK7+/CD117- expression were identified. The median age was 67 years (range 47 - 84), and male/female ratio was 10/9. The median size was 4 cm (range 1.5 - 9.5 cm). All cases were confined except one with renal sinus invasion (pT3a). Nodal or distant metastases were not identified. 6 patients had long-term follow-up (median 43 months; range 24 - 93), and are alive without disease.
Conclusion: Renal oncocytic neoplasms are a diverse group of tumours. Recent data suggest that several distinct entities may exist within this group. LOT may particularly be confused with oncocytoma or eosinophilic chromophobe renal cell carcinoma. Strict morphologic criteria including eosinophilic oncocytoma-like morphology, solid growth with occasional archipelago-like tumour clusters with edematous stroma, diffuse CK7 expression with negative CD117 are mandated. These tumours display low malignant potential; however, due to limited reported cases, additional studies are required to further characterize its behaviour.

PS-18-004
Epithelioid trophoblastic tumour: a review of 10 cases

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Background & objectives: Non-choriocarcinomatous trophoblastic tumours are rare in testis. They are morphologically analogous to epithelioid trophoblastic tumour (ETT) and placental site trophoblastic tumour in females. Here we present the largest cohort of ETT in men with testicular cancer.
Methods: Trophoblastic tumours at our institution between 2013 - 2019 were retrospectively reviewed. ETT were identified based on their morphological features. Since most testicular ETT are associated with postchemotherapy and mixed germ cell tumours (MGCT); their differences and similarities to female tumours were recorded. Age, gender, procedure type, surgery date, tumour stage, immunoprofile, and follow up data were recorded.
Results: Median age was 34 years (19 - 59). One ETT was a primary testicular tumour. 2 cases had pure ETT, the remainder were part of the MGCT. 5 were identified in retroperitoneal lymph nodes, 4 were post-chemotherapy. Liver, lung, cervical lymph node, and posterior shoulder soft tissue were other sites. In 3/7 patients with follow-up, ETT occurred as late recurrence.
Conclusion: ETS has common association with teratoma, chemotherapy, and late recurrence. Limited data suggest that ETT has favourable

prognosis when compared to choriocarcinoma. Surgical resection remains the treatment of choice when only teratoma is present. No further recurrences of ETT recorded.

PS-18-005

PD-L1 expression in seminoma correlates with higher pathological stages

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Background & objectives: PD-L1 is not constitutively expressed in testicular tissue, but its presence in numerous tumours makes it a landmark in immunotherapy strategies.
This study evaluates PD-L1 expression in seminomas diagnosed at our Hospital during 2019, correlating its presence with pathological stage.
Methods: An experienced uropathologist determined PD-L1 expression - Tumour Proportion Score (TPS) - with Dako 22C3 antibody on all seminomas diagnosed during 2019. A 1% cut-off was applied for PD-L1 positivity. Data was analysed using IBM SPSS v24.
Results: Twelve seminomas were diagnosed during 2019. Median age at diagnosis was 39 (range: 23 - 66). Mean size tumour was 6,38 cm (0,7 - 18 cm).
Pathological stage: pT1 (6), pT2 (3), pT3 (2) and pT4 (1).
Seven cases showed PD-L1 heterogeneous expression within the tumour. All TPS-negative results were documented on pT1 stage seminomas, and all pT ≥ 2 tumours had TPS positive results. Accordingly, PD-L1 expression on tumour cells, measured by TPS, showed a statistically association with pathological T-stage ≥ 2 (Fisher's non-parametric test, p = 0.015).
Conclusion: In our series seminoma´s PD-L1 expression on tumour cells was statistically associated with ≥ pT2 staging, in line with published data advocating worst prognostic to PD-L1 expressing GCT.
Results from ongoing clinical studies are expected to demonstrate prognostic value and eventually therapeutically utility of PD-L1 expression, particularly in selected cases with higher stages or in patients not suitable or refractory to conventional therapies.

PS-18-006

PD-L1 expression in renal cell carcinoma – higher expression in higher WHO/ISUP grade

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Background & objectives: Renal cell carcinoma (RCC) represent 2-3% adult malignancies, and encompass different entities with variable morphologic and pathologic features. Programmed death receptor ligand 1 (PD-L1) pathway therapies are of the utmost importance, mainly in metastatic RCC.
Methods: We selected 80 random cases of surgical specimens of RCC diagnosed over a period of 2-years (Januray-2018/December-2019). Clinical and pathological data was analysed and PD-L1 immunohistochemistry (22C3 pharmDx, Dako Omnis) was performed in all cases. PD-L1 expression was evaluated by two experienced pathologists and was quantified as percentage of tumoral cells with membranous staining. Statistical analysis performed with SPSS software.
Results: Our cohort had a median age of 64±11.7 years-old (32-86), 23 female (28.7%) and 57 male (71.3%).
Regarding histologic types of RCC: clear cell (48.8%), chromophobe (25.0%), type 1 papillary (8.8%), type 2 papillary (8.8%), clear cell papillary (5.0%), MiT family translocation (2.5%) and mucinous tubular and spindle cell carcinoma (1.3%).
WHO/ISUP grades: G1 in 2.5% cases, G2 in 36.3%, G3 in 31.3% and G4 in 5%.
AJCC stages: I (68.8%), II (13.8%), III (15.0%) and IV (2.5%).
Considering PD-L1 expression: 0% (62.5%); 1-50% (28.8%) and >50% (8.7%).
We have found statistical significance between higher PD-L1 expression and higher WHO/ISUP grade (p=0.032), without association with stage or histologic type.
Conclusion: In this study we have found statistical significance between WHO/ISUP grade and PD-L1 immunohistochemical expression. Higher grade was associated with increased expression of PD-L1, what may suggest that these cases may benefit from immunotherapy, even without metastatic disease.
The aim of this study was to add some contribute for a greater knowledge of RCC and highlight some potential therapeutic targets, as PD-L1 pathway.

PS-18-007

Prostate amyloidosis: a rare finding usually associated with aging

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Background & objectives: Prostate amyloidosis (PA) is an unusual disease rarely reported in the literature. The amyloid deposits appear as thickening of small vessel walls. Changes may be focal and subtle. We present clinical, histological and immunohistochemical features of 7 cases of PA.
Methods: PA was diagnosed in seven cases studied in our department from 2015 to 2019. They were 5 prostate needle biopsies (performed because of raised serum PSA level), 1 transurethral resection and 1 prostatectomy. Immunohistochemistry for kappa and lambda light chains, amyloid A and transthyretin (TTR) was performed.
Results: The patients were aged 72-94 years (mean=82), without any rectal examination or transrectal ultrasound unusual findings. Histologically, amyloid deposits were inside arteriolar walls (sparse in 5 cases, extense in 2). Immunohistochemically the amyloid corresponded to lambda light chain in one patient (who had a monoclonal gammopathy of unknown significance), and TTR in the other 7 cases. They did not have familiar history or clinical manifestations attributable to amyloidosis. Most, but not all, of these cases correspond to TTR amyloidosis, concordant with a senile change.
Conclusion: Amyloidosis is a rare asymptomatic histological finding in the prostate.
The pathological finding of PA makes advisable complementary studies, at least immunohistochemistry to characterize the type of amyloid. Clinical evaluation to rule out systemic or haematological diseases could be considered.

PS-18-008

Grade group 2 and 3 prostatic adenocarcinomas with positive surgical margins

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Background & objectives: The surgical margin(SM) status after radical prostatectomy for prostate cancer is an important risk factor for biochemical recurrence(BCR).The aim of this study is to investigate whether tumour grade at the positive SM in score-7 group is significant to predict BCR.
Methods: The records of 3 university hospitals between 2006-2019 were searched for SM positive Gleason score-7 (3+4 or 4+3) prostatic adenocarcinoma with at least 12 months follow-up and no adjuvant therapy. Clinicopathologic features that may have prognostic value as well as

follow-up information were collected. Post-op PSA>0.2 ng/ml was accepted as BCR. Chi-Square test were used to correlate different variables and BCR.
Results: 138 patients were included into study. The mean patient age was 63 years (range: 45-77) and median follow-up was 30 months. 73.1% patients were grade group (GG) 2 while 26.9% were GG-3. Distribution of pathological stages: pT2=41, pT3a=66 and pT3b=31. BCR occurred in 45 patients (32%). The two parameters that significantly correlated with BCR were the largest diameter of positive SM (p=0,03) and presence of lymphovascular invasion (LVI) (p=0,013). Gleason grade at the margin did not appear as an independent risk factor for BCR.
Conclusion: In Gleason 7 (GG-2&3) tumours, existence of pattern 4 at the positive surgical margin does not have influence on BCR. The largest length of positivity and detection of lymphovascular invasion are two significant determinants of PSA recurrence.

PS-18-010
Immunohistochemical study of PD-L1 and CD8 in clear cell renal cell carcinoma
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Background & objectives: Clear cell renal cell carcinoma is the leading renal malignancy. In recent years immunotherapy with immune control point inhibitors has been introduced for its treatment, specifically anti-PD-1 and anti-PD-L1 antibodies, especially in metastatic renal carcinomas.
Methods: 49 cases were reviewed and immunohistochemical study performed, in a block of representative tissue fixed in formalin and included in paraffin, of PD-L1 (Clone 22C3, Agilent) using the EnVision FLEX visualization system in Autostainer Link 48 and CD8 (Clone C8/144B, Agilent). Both PD-L1 is titrated on tumour and inflammatory cells to potentially improve the assessment of patients treatable with immunotherapy.
Results: Increased immunohistochemical expression of PD-L1 in both, tumour cells and lymphocytes, in high histological grade of clear cell renal carcinoma. Positive association between the presence of CD8+ T-lymphocytes and the expression of PD-L1 in the same.
Conclusion: The immunohistochemical study of CD8 and PD-L1 could better reclassify patients with clear cell renal cell carcinoma as candidates for a greater response to immunotherapy. To do so, a correct immunohistochemical technique and subsequent evaluation is absolutely necessary.

PS-18-012
Microvascular proliferation in prostate cancer is associated with aggressive tumour features, recurrence and high contrast enhancement by multiparametric MRI
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Background & objectives: Angiogenesis is essential for carcinomas to grow and spread. Here, we studied the proliferation of immature microvessels in prostate cancer by Nestin/Ki67, focusing on relations to estimated in vivo blood flow from multiparametric MRI, clinicopathologic
phenotype, recurrence and survival.
Methods: Sections from 67 radical prostatectomies were immunohistochemically stained for Nestin/Ki-67. Vascular proliferation index (VPI), evaluated as the ratio between proliferating vessels (pMVD) and overall microvessel density (MVD), as well as the presence of glomeruloid microvascular proliferations (GMPs), were recorded. Anatomically corresponding blood flow imaging parameters from multiparametric MRI were acquired preoperatively.
Results: High pMVD, high VPI and the presence of GMPs were associated with high Gleason score, large tumour dimension, extraprostatic extension, high pathologic stage, and for GMP also positive surgical margins. By univariate survival analyses, high pMVD was associated with shorter time to biochemical- and clinical recurrence (p=0.044, p=0.052). Further, high pMVD and high VPI were associated with presence of high contrast enhancement on anatomically correlated areas from multiparametric MRI (p=0.025).
Conclusion: Proliferation of newly formed microvessels by Nestin/Ki67 is associated with increased blood flow by high contrast enhancement on multiparametric MRI and linked to aggressive tumour features and disease recurrence, unravelling potential prognostic and
therapeutic opportunities in prostate cancer.
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PS-18-013
Validation of ISUP grading of clear cell & papillary renal cell carcinoma on the digital pathology platform
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Background & objectives: Pitfalls in digital diagnosis require acknowledgement as pathologists adapt to digital reporting. In urological pathology one pitfall is said to be grading of renal cell carcinoma (RCC). We investigated concordance in grading between digital and glass slides.
Methods: 50 clear cell RCCs (CCRCC) and 10 papillary RCCs were assessed by three specialist urological pathologists who assigned an International Society of Urological Pathology (ISUP) grade on the digital images, and on the corresponding glass slides following a two week wash-out period. The pathologist's grade for each on digital and glass was recorded, and compared using Cohen's and Fleiss' kappa.
Results: Comparing ISUP grading on digital versus glass images for all 60 cases, agreement was 0.70, 0.57, 0.70 for each pathologist (concordance of 78%, 65%, 77% respectively), and for CCRCC alone, it was 0.72, 0.58, 0.75 (concordance of 80%, 66%, 80%). Agreement between the three pathologists on digital was 0.58 and on glass was 0.45, again with improved agreement for CCRCC alone (0.62 vs 0.50).
Conclusion: ISUP grading of RCC conveys prognostic information in CCRCC and papillary RCC, and potentially influences clinical trial entry. There was moderate to good agreement on ISUP grade between digital and glass for individual pathologists, agreement being slightly better if analysis limited to CCRCC. We therefore show that the concordance of ISUP grading between digital and glass appears acceptable, especially in the absence of evidence concerning reproducibility of the ISUP grade.
Funding: LB and CV are partly funded by the NIHR Oxford Biomedical Research Centre (Molecular Diagnostics Theme/Multimodal Pathology Subtheme)

PS-18-014
Xanthogranulomatous pyelonephritis confirmed histologically: a retrospective study of 10 cases
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Background & objectives: Xanthogranulomatous pyelonephritis (XGP) is an uncommon chronic inflammatory process of the kidney, resulting in renal destruction. It accounts for only 0.6% of all chronic pyelonephritis cases. Herein, we report the main clinical, biological, histological, radiological, and therapeutic features of XGP.
Methods: We carried out a retrospective study of XGP diagnosed and treated in the Urology Department, Sahloul Hospital, Sousse (Tunisia) during 2004-2019.
Results: A total of 10 patients was reported with a median age of 47 years, and sex-ratio of 1.5. The most common presentations were lower back pain 100%, isolated(n=4),febrile(n=4), associated with the biological inflammatory syndrome(n=6) and accompanied by lower urinary tract symptoms(n=6).Radiological-CT findings of the patients were non-functioning kidney with renal calculi(n=8), pyonephrosis(n=4), associated phrenic collection(n=1), and retroperitoneal abscess(n=2). The diagnosis of XGP was suspected only in one patient. Percutaneous deep pus drainage was performed four times. The germs identified were E.coli, P mirabilis, E.faecium, M.morganii, E.coli, and B.stercoris. Surgical procedures included nephrectomy(n=9) and partial nephrectomy(n=1). Perioperative complications included colostomy and abscess formation. Histology of all the specimens concluded to XGP.
Conclusion: XGP is an uncommon histologic variant of the kidney induced by recurrent bacterial urinary tract infection. Kidney cancer is the main differential diagnosis. Although the diagnosis can often be suspected based on imaging studies, the definitive diagnosis requires histological examination and early diagnosis and treatment is very important for decreasing morbidity and mortality.

PS-18-015

Recurrent KRAS mutation identified in papillary renal neoplasm with reverse polarity – a comparative study with papillary renal cell carcinoma

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Background & objectives: Comprehensive molecular analyses revealed that papillary renal cell carcinoma (PRCC) is a heterogenous entity. Papillary renal neoplasm with reverse polarity (PRNRP) is a subset of PRCC with characteristic histomorphologies such as low-grade nuclear features, inverted nuclear location, eosinophilic cytoplasm, and indolent clinical behaviour. We tried to define the molecular, clinicopathological, histologic, and immunohistochemical features of PRNRP by comparing them with type 1 PRCC (PRCC1) and type 2 PRCC (PRCC2).
Methods: A cohort of 30 PRNRP, 23 PRCC1, and 26 PRCC2 cases was used. Targeted sequencing of 90 cancer-related genes including KRAS was performed in 26 PRNRP tumour samples. PNA-mediated clamping PCR of KRAS was performed using paired normal and tumour DNA from 30 PRNRP, 23 PRCC1, and 26 PRCC2 cases.
Results: Recurrent mutations in KRAS were detected in 28 of the 30 PRNRPs. However, there were no KRAS mutations in any PRCC1 or PRCC2 cases. PRNRP exhibited distinct clinicopathological features: small tumour size, lower pathologic T stage, and no disease-specific death during the follow-up period. Histologically, peritumoral lymphoid aggregation, prominent papillary architecture (>80% of tumour), hyalinized papillae, inverted nuclear location, and lower nuclear grade were observed.
Conclusion: The findings suggest that PRNRP is a subtype of papillary renal neoplasm that is different from PRCC1 and PRCC2.

PS-18-016

Diagnosis of prostatic intraepithelial neoplasia and atypical small acinar proliferation in prostate biopsies: interobserver variation, and impact on patient management and follow-up diagnosis

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Background & objectives: With increasing use of multiparametric magnetic resonance imaging for prostate cancer diagnosis, the relevance of reporting prostatic intraepithelial neoplasia (PIN) and atypical small acinar proliferation (ASAP) in prostate biopsies (PBs), is questioned. The aim of this study was to determine reporting rates of ASAP and PIN between different uropathologists and determine the association between initial biopsy diagnosis and follow-up biopsy rate and diagnosis.
Methods: Diagnoses in PBs reported by three specialist uropathologists in a single tertiary centre over a three-year period (2016-18) were evaluated. The association between initial biopsy findings, re-biopsy rate and final diagnosis (12-48 month follow-up) was determined. 2941 PBs were reported during this period with 1602 adenocarcinomas, 652 benign, 42 ASAP, 525 PIN, and 107 PIN + ASAP.
Results: There was a significant difference between categories reported by the three uropathologists ($p<0.00001$) and the rates of ASAP and PIN diagnoses ($p=0.0156$). In contrast, there was no difference in the frequency of cancer diagnoses between pathologists ($p=0.5758$). The re-biopsy rate was lower ($p<0.0001$) for benign (9.7%) than ASAP/PIN (17.6%), but there was no significant difference in rates of re-biopsy cancer ($p=0.5912$), with the positive predictive value of ASAP+/-PIN only 44%.
Conclusion: PIN and ASAP in PBs are subjective and systematically suffer from inter-observer reporter bias. Although non-malignant diagnoses influence re-biopsy rates, ASAP and PIN have little value in predicting malignancy in follow-up biopsies.

PS-18-017

Grading of non-invasive urothelial carcinoma on transurethral resection: a comparison of digital whole slide image vs. glass slide

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Background & objectives: Digital pathology is non-inferior to microscopy for diagnosis, however the evidence-base for grading is limited and is an area of uncertainly as these technologies are adopted. This study aims to compare bladder cancer grading between glass slide and digital reporting.
Methods: 48 consecutive transurethral bladder resections of non-invasive papillary urothelial carcinomas were graded by three specialist uropathologists - initially on a digital screen, followed by glass slide after a two-week washout period. Both WHO 2004 and 1973 systems were compared using linear weighted Cohen's and Fleiss' kappa.
Results: Agreement between all three pathologists on glass was 0.56 (2004) and 0.49 (1973), whereas on digital was 0.61 (2004) and 0.44 (1973). Comparing individual digital vs. glass, agreement for pathologist A was 0.74 (2004) and 0.70 (1973), pathologist B 0.82 (2004) and 0.77 (1973), and pathologist C 0.53 (2004) and 0.77 (1973). Consensus grade digital vs. glass agreement was 0.78 (2004) and 0.82 (1973).
Conclusion: Moderate agreement was demonstrated between pathologists for bladder cancer grading. Agreement for individual pathologists between modalities was actually superior overall than agreement amongst pathologists on glass. These results suggest that grading bladder tumours on digital systems is non-inferior to glass.

PS-18-018

Testicular cancer in Polish men in NHS Lothian: a collaboration between histopathology and public health medicine aiming to improve migrant health

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Background & objectives: Poland has a similar incidence of testicular cancer to the UK but higher mortality. In our practice, we observed cases of testicular cancer in Polish men with a poor outcome.
Methods: This study aimed to retrospectively identify differences in the clinico-pathological features of testicular cancer in Polish men compared to non-Polish controls in Lothian, over a ten-year period.
15 Polish cases and 32 non-Polish controls were identified from a total sample of approximately 260 patients in ten years. We collected clinico-pathological data from our electronic laboratory management and health record systems.
Results: We found no difference in the distribution of seminoma versus non-seminomatous germ cell tumours between the Polish and non-Polish cohorts. However, a different spectrum of NSGCT (possibly enriched for embryonal carcinoma) was seen in the Polish group. We observed a non-significant decrease in pT1 stage (40.0 vs 50.0%), increase in pT3 stage (20.0 v 9.4%), and increase in nodal (26.7 v 9.4%) and visceral (13.3 v 3.1%) metastases in the Polish cohort compared with the control cohort. We found the mortality rate in the case cohort to be higher than both the mortality rate in the control cohort and the overall ten-year mortality in our centre.
Conclusion: Although the findings described are not statistically significant, they are suggestive of poorer outcomes in Polish men with testicular cancer in our region. We recommend that this study is replicated in other centres with large Polish migrant populations.

PS-18-019

MMP-13 and E-cadherin expression in prostate proliferation

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Background & objectives: Studies show that E-cadherin and MMP-13 plasma concentration can be used to predict prognosis and outcome in prostate cancer. The aim of this study is to identify a possible correlation between MMP-13 and E-cadherin tissue expression in prostate proliferation.
Methods: Our study included 45 consecutive patients with ADKP and 45 BPH cases diagnosed on TURP specimens. We generated multi-tissue blocks including representative samples from each case. E-Cadherin and MMP13 stains were performed. The results were also correlated with Gleason score in ADKP.
Results: E-cadherin expression was intensely, continuous membranous, positive in HBP cases, and focal, incomplete or absent in carcinoma. There was no significant difference between MMP-13 stromal expression in ADKP and BPH cases. Gleason score negatively correlates with E-cadherin expression but not with MMP-13 stromal expression.
Conclusion: E-cadherin could be useful in diagnosis and prognosis in prostate cancer but the impact of MMP13 upon prognostic data remains questionable.
Funding: Work partially supported by a Romanian-Ministry-of-Research-and-Innovation grant no.61PCCDI/2018PN-III-P1-1.2-PCCDI-2017-0341.

PS-18-020

Possible implication of HER2 amplification in progression of urothelial carcinoma of the urinary bladder

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Background & objectives: The role of HER-2 in oncogenesis of many malignancies has been well described and drugs targeting HER-2 are currently approved in some cancers. The aim of this study is to evaluate the immunohistochemical expression of HER-2 in bladder urothelial carcinoma.
Methods: Multi-tissue blocks were made from 84 urothelial bladder cancer samples and 12 non-neoplastic bladder samples, removed during transurethral resection. Immunohistochemistry was performed on coresponding slides and the expression of HER-2 was evaluated considering the intensity of expression and the percentage of positive cells. The results were correlated with tumour grade in relation to non-neoplastic urothelium.
Results: Our findings demonstrate that HER-2 expression is statistically significantly higher in patients with urothelial carcinoma of the urinary bladder than in patients without neoplastic lesions. It is also higher in invasive, high-grade tumours in comparison with non-invasive, low-grade tumours.
Conclusion: Higher HER-2 expression in high grade, invasive bladder carcinoma, compared to low grade, non-invasive tumours and to non-tumoral urothelium may suggest an implication of HER-2 amplification in tumour progression. Further studies are needed to determine its role in the pathogenesis and to formulate a targeted therapy strategy in patients with urothelial carcinoma of the urinary bladder.

PS-18-021

PD-L1 expression in penile squamous cell carcinoma: correlation and concordance between two commercially available antibodies

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Background & objectives: The need for new therapeutic options in penile squamous cell carcinoma (PSCC) has led to investigate the immunohistochemical expression of the programmed cell death ligand-1(PD-L1). We have evaluated the correlation and concordance between the two more used available assays.
Methods: Whole-slide sections from 23 PSCC (8 HPV related and 15 non-HPV related) were immunostained for PD-L1 using Ventana SP263 and Agilent 22C3 assays. PD-L1 expression was assessed estimating the percentage of positive tumour cells (TCs) of the total number of TCs. To evaluate correlation and concordance, Spearman coefficient and kappa indexes were calculated.
Results: Expression of PD-L1 was 0-80% with SP263 and 0-60% with 22C3 assays. In 14 cases (60.8%) the staining was less extense with the 22C3 assay. Staining was always heterogeneous in each tumour. Positive cases for different cutoff points comparing SP263/22C3 were: for cut-off=1%, 15 (65.2%) / 9 (39.1%); and for cutoff=5%, 13 (56.5%) / 8 (34.7%). The two antibodies exhibited strong correlation ($r=0.851$; $p<0.001$) mainly in high-percentage-positive cases, but moderate concordance ($k=0.511$; $p=0.005$) in low-percentage-positive and the negative cases. This fact emphasizes the importance of standardization as well as the need to choose carefully the most clinically useful cutoff and assay to evaluate PD-L1.
Conclusion: Expression of PD-L1 in TCs of PSCC is heterogeneous and varies depending on the assay (from 34.7 to 65.2 %). The Ventana SP263 and Agilent 22C3 assays have showed strong correlation mainly in high-

percentage-positive cases, but moderate concordance in low-percentage-positive and the negative cases. It is highly relevant the need of optimal assays with best standardization and choice of a useful cutoff.

PS-18-022

PD-1 and PD-L1 expression in neuroendocrine carcinomas of bladder

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Background & objectives: Neuroendocrine carcinomas of bladder are rare and aggressive tumours. We aimed to search the relationship between PD1 and PDL1 expression and clinicopathologic features.
Methods: Fifteen cases diagnosed between 2009 and 2018 in our institute were selected. Immunohistochemically PD1 and PDL1 were performed to formalline fixed paraffine embedded tissues. The results were compared with clinicopathologic data.
Results: Male/female ratio was 13/2. Mean age was 61.9 (31-79). Histopathologically; seven cases were mixed (urothelial + small cell) carcinoma, six cases pure small cell carcinoma, one large cell neuroendocrine carcinoma, one mixed urachal (mucinous + neuroendocrine) carcinoma. Mean survival was 17.6 (1-60) months. PDL-1 positivity in tumour cells was present in five cases and, in tumour infiltrating lymphocytes in three cases. PD1 positivity was present in tumour infiltrating lymphocytes in seven cases
Conclusion: PD1 and PDL1 positivity in these aggressive tumours may be a good alternative treatment choice in terms of immunotherapy.

PS-18-023

Eosinophilic solid and cystic renal cell carcinoma – an emerging entity

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Background & objectives: Eosinophilic solid and cystic renal cell carcinoma (ESC RCC) is a rare and emerging subtype of renal cell carcinoma. This tumour is known to occur in association with tuberous sclerosis complex but has recently been described in the sporadic setting.
Methods: We present two patients diagnosed with ESC RCC in the Queen Elizabeth University Hospital, Glasgow, in 2018 and 2019.
Results: The patients are both female, aged 58 and 30 years, and found to have small incidental renal tumours. Gross examination showed a solid tan tumour in one specimen and a solid and cystic tan tumour in the other. Microscopic examination demonstrated the characteristic cytological appearance of neoplastic cells with abundant eosinophilic cytoplasm and basophilic stippling, solid and acinar architecture, macro- and microcysts and multinucleate cells. On immunohistochemistry, the tumour cells were positive with PAX-8 and negative with CD117. One tumour had a CK20+/CK7- immunophenotype, whilst the other was CK20+/CK7+, a less common finding. Both patients remain well with no recurrence or metastasis at 13- and 14-months follow-up.
Conclusion: ESC RCC is an important consideration in the differential diagnosis of eosinophilic renal tumours as these cases have been labelled as 'unclassified renal cell carcinoma' or 'unclassified renal neoplasm with oncocytic or eosinophilic morphology' in the past.

PS-18-025

Hypertension and risk of cancer histotypes in the kidney and urinary tract in UK women

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Background & objectives: Hypertension has been associated with increased risk of kidney cancer; evidence for cancers elsewhere in the urinary tract is mixed. We examined associations between hypertension and cancer incidence in the kidney and urinary tract in a cohort of UK women.
Methods: At recruitment in 1996-2001, participants completed a questionnaire on lifestyle and health factors, including hypertension requiring treatment. They were followed for cancer and death via record linkage to national registries. We used Cox regression models to estimate relative risks (RRs) of cancers of the kidney and urinary tract, associated with self-reported hypertension requiring treatment at recruitment, adjusted for potential confounders.
Results: In 1,319,718 women without previous cancer, 211,663 (16%) reported at recruitment that they were currently being treated for hypertension. After 16.9 years' (SD 4.6) mean follow-up, 5391 kidney cancers, including 4248 renal cell carcinomas and 442 urothelial carcinomas, accrued. Hypertension requiring treatment at recruitment was associated with a significantly greater increase in the risk of renal cell carcinomas (RR=1.69, 95% CI: 1.57-1.82) than urothelial carcinomas of the kidney (RR=1.27, 95% CI: 1.00-1.62); heterogeneity by histotype, p=0.02. There were no clear associations between hypertension at recruitment and the risk of urothelial carcinomas elsewhere in the urinary tract (ureter: n=249, RR=0.82, 95% CI: 0.57-1.17; bladder: n=2929, RR=1.00, 95% CI: 0.91-1.11).
Conclusion: Hypertension is strongly associated with an increased risk of kidney cancer, with significant heterogeneity by histotype. The risk of renal cell carcinoma is substantially increased in those with a history of hypertension, but there is little or no association with urothelial carcinomas, either in the kidney or the rest of the urinary tract. These differences by histotype can help inform ongoing debates as to possible underlying biological mechanisms.
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PS-18-026

PD-L1 as a potential biomarker in high grade non muscle invasive bladder cancer

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Background & objectives: PD-L1 is an important immune checkpoint involved in different tumours, including advanced bladder cancer. There are few studies evaluating the expression of PD-L1 in stage Ta and T1 urothelial carcinomas, that constitute a heterogeneous group with different risk of progression.
Methods: Immunohistochemistry was performed on tissue arrays sections corresponding to 129 patients with Ta and T1 high grade urothelial carcinomas. A qualitative immunohistochemical assay anti-PD-L1 clone SP142 (Ventana) was used. PD-L1 status was determined by the proportion of tumour area occupied by PD-L1 expressing tumour-infiltrating immune cells (positivity: >/=5% of any intensity).
Results: 41 (31,8%) cases were categorized as negative 0 (no expression of PD-L1), 15 cases (11,6%) as negative <1% (minimal expression), 45 cases (34,9%) as negative 1-5% (low expression) and 26 cases (20,2%) were positive >5% (intermediate-high expression). In 19 cases (14,7%) membrane staining was found in tumour cells that has not been considered as positivity. Finally two cases (1,6%) were not classifiable for loss of the tissue.

Conclusion: Positivity for PD-L1 (SP142) was found in 20% of Ta and T1 high grade urothelial carcinomas. Aditional studies could be desirable to correlate this result with bladder cancer molecular classification (basal and luminal types, that have a different behaviour), and in future to analyse if these patients could benefit from immunotherapy.

PS-18-027

Prostatic cancer cytokeratin 19 expression across Gleason patterns and its implications for sentinel lymph node examination using RT-PCR

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Background & objectives: Since breast sentinel lymph node examination using Cytokeratin19 (CK19) mRNA detection gained approval, there are ongoing efforts to translate this success to other scenarios, including prostate cancer. We evaluated the protein expression of CK19 in prostate cancer.
Methods: We retrieved 22 consecutive prostate biopsies and prostatectomy specimen as well as a single macrometastatic lymph node from our hospital archives. Immunohistochemistry (IHC) was used to evaluate CK19 expression across different Gleason patterns and normal prostatic glands. Percentage of positive cells as well as stain intensity was recorded. If present, CK19 expression in the intraductal component was also assessed.
Results: There was high heterogeneity of CK19 expression across biopsies and intra-biopsy. Overall CK19 expression ranged from 0 to 100% across samples (Median = 60%, IQR 5%-95%). All Gleason patterns analysed showed great variability in the percentage of cells stained. IQR were 10-100% for Gleason 3, 3-98% for Gleason 4-ill-defined glands, 5-80% for Gleason 4-cribriform pattern and 25-100% for Gleason 5. Of note, only 5% of the neoplastic cells in the lymph node metastasis included in this study showed positivity for CK19 IHC while previous prostate core biopsy showed 95% positivity for CK19.
Conclusion: CK19 expression is highly heterogeneous in prostate cancer and in all Gleason patterns. This heterogeneity makes CK19 evaluation in prostate cancer challenging and implies potential limitations for the application of CK19 mRNA based detection of metastasis in prostate lymph nodes.

PS-18-028

The protein arginine methyltransferases PRMT1 and PRMT4/CARM1 are implicated in the pathogenesis and progression of prostate cancer

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Background & objectives: Arginine methylation is a post-transcriptional protein modification mediated by Protein Arginine Methyltransferases (PRMTs), involved in many cellular functions including epithelial mesenchymal transition (EMT) and transcriptional regulation. However, little is known about their expression during the progression of prostate cancer (PCa).
Methods: The immunohistochemical expression of PRMT1 and PRTMT4/CARM1 was examined in tissue microarrays constructed from 276 prostatectomy specimens of patients with PCa (44 low-grade, 119 high-grade, 63 hormonally treated, 40 castrate-resistant and 10 neuroendocrine carcinomas and 61 lymph node metastasis and 78 non neoplastic peripheral zone tissue samples). In addition, their expression was correlated with the EMT markers, ZEB1 and TWIST.
Results: Both markers were mainly expressed in the nucleus. Cytoplasmic staining was also seen in some cases and was separately evaluated. Nuclear expression of PRMT1 and PRMT4/CARM1 was higher in carcinomas compared to non-neoplastic peripheral zone tissue ($p<0.001$ and $p=0.001$, respectively). Nuclear expression of PRTMT4/CARM1 gradually increased from low grade to high grade ($p<0.001$) and treated ($p=0.022$) carcinomas and was higher in lymph node metastasis than in primary carcinomas ($p<0.001$). Cytoplasmic and nuclear PRMT4/CARM1 were strongly correlated with each other ($p<0.001$, $r=0.504$). Nuclear PRMT1 expression was positively correlated with ZEB1 expression ($p<0.001$, $r=0.478$).
Conclusion: PRMT1 and PRTMT4/CARM1 may be implicated in the initiation of PCa. In addition, CARM1 is gradually increased in the early stages of prostate cancer progression, as a response to androgen ablation and during the development of lymph node metastasis. The correlation of PRMT1 with the EMT marker ZEB1 is of interest and needs further study.
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PS-18-029

Clinical and prognostic evaluation of the histopathological characteristics of adenocarcinoma of the prostate in radical prostatectomy specimens according to WHO 2016 classification

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Background & objectives: Although prostate adenocarcinoma is the most common cancer in men,survival is quite high. With the help of histopathological examination,patient management strategies are developing.We aimed to evaluate the correlation between the histopathological and prognostic features in patients who underwent radical prostatectomy.
Methods: A total of 285 prostate adenocarcinoma cases that underwent radical prostatectomy between January 2009 and December 2017 and followed up for at least 3 months postoperatively in our institution were included in the study.The cases were re-evaluated according to WHO-ISUP 2016 classification and postoperative PSA values,clinical and prognostic findings of the patients were recorded and statistically analysed using SPSS program.
Results: The mean age was 63,4 years. Gleason scores of the cases were as follows: 3+3 144 cases (50,5%), 3+4 81 cases (28,4%), 4+3 28 cases (9,8%), 4+4 7 cases (2,5%), 3+5 6 cases (2,1%), 5+3 2 cases (0,7%) and 4+5 17 cases (6%). There were 198 (69,5%) pT2, 54 (18,9%) pT3a and 33 (11,6%) pT3b cases. The mean follow-up time was 44,1 months and biochemical recurrence was detected in 97 cases (34%).There was a significant correlation between preoperative PSA value, extraprostatic extension, seminal vesicle invasion, surgical margin positivity, tumour volume, pattern 4 percentage, presence of cribriform glands and biochemical recurrence and recurrence free survival in both univariate and multivariate analysis.
Conclusion: Histopathological evaluation is of great importance in predicting biochemical recurrence in prostate adenocarcinoma cases. The Group Grade system seems to be helpful in this regard. More studies should be done to prove the relatively worse prognostic effect of cribriform glands.

PS-18-030

Solid field and comedonecrosis Gleason 5 growth patterns have independent predictive value for post-operative metastasis-free survival in prostate cancer patients

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Background & objectives: Cribriform Gleason pattern 4 prostate cancer is associated with adverse outcome. Our objective was to analyse the occurrence and predictive value of Gleason 5 growth patterns (G5) in a radical prostatectomy (RP) cohort.
Methods: We reviewed 1,064 consecutive RPs and recorded Grade Group (GG), pT-stage, surgical margin status, Gleason 4 and 5 growth patterns. Single cells, strands and/or cords were analysed together as cords. The clinical endpoint was post-operative distant metastasis.
Results: G5 was present in 339 (32%) RPs, as primary (14%), secondary (49%) or tertiary (37%) pattern. Cords were present in 319 (94%) tumours, solid fields in 61 (18%) and comedonecrosis in 32 (9%). Cribriform architecture was present in 568 (53%) tumours and observed in 179/274 (65%) men with cords and 61/61 (100%) men with solid fields (P<0.001). Metastasis occurred more frequently in GG2-5 patients with cribriform and/or solid fields (23%) than in patients with neither (2%, P<0.001). In multivariable analysis, cribriform (HR7.2; 95%CI2.9-18, P<0.001), solid fields (HR1.8; 95%CI1.1-3.1, P=0.03) and comedonecrosis (HR1.9, 95%CI1.1-3.3, P=0.03) were independent predictors for metastasis-free survival in GG2-5 patients, while cords were not (HR1.2; 95%CI0.7-1.8, P=0.55).
Conclusion: In conclusion, solid fields and comedonecrosis are more aggressive growth patterns than single cells, strands and/or cords Gleason pattern 5 prostate cancer, as they have independent predictive value for metastasis-free survival.
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PS-18-031
Cribriform architecture outperforms individual Gleason scores in predicting outcome of grade group 4 prostate cancer patients
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Background & objectives: The Grade Groups (GG) are one of the most important parameters for prostate cancer outcome. GG4 includes Gleason score (GS) 3+5, 4+4 and 5+3 tumours. Our aim was to investigate the clinicopathological characteristics of individual GS and cribriform architecture.
Methods: We reviewed 1,064 consecutive radical prostatectomy specimens for GG, GS, pT-stage, surgical margin status, and Gleason 4 and 5 growth patterns. We identified 140 GG4 prostate cancer patients for analysis. Biochemical recurrence, post-operative distant metastasis and disease-specific death were used as endpoints.
Results: GS3+5 (n=76;54%), 4+4 (n=46;33%) and 5+3 (n=18;13%) tumours had comparable pathological features, although patients with GS5+3 presented with higher PSA levels (P=0.05). Biochemical recurrence, metastasis and disease-specific death were not significantly different for GS3+5 and 5+3 tumours. Biochemical recurrence (63% versus 41%, P=0.02), metastasis (39% versus 18%, P=0.02), and disease-specific death (15% versus 5%, P=0.06) occurred more often in GS4+4 than 3+5 patients. Cribriform architecture was present in 87 (62%) tumours and associated with higher pT-stage (P=0.003). Cribriform architecture was an independent predictive parameter for biochemical recurrence- (HR2.0; 95%CI1.0-3.9, P=0.04) and metastasis-free survival (HR3.5; 95%CI1.0-12.0, P=0.05), whereas different GS were not. No deaths were reported in patients without cribriform architecture.
Conclusion: Cribriform architecture had independent predictive value for biochemical recurrence- and metastasis-free survival in GG4 prostate cancer patients, while individual GS did not.
This research was supported by a grant from the Jaap Schouten Foundation.

PS-18-032
ERG expression in HGPIN is a marker of coexisting adenocarcinoma - a pilot study in totally embedded cystoprostatectomy specimens
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Background & objectives: The prevalence of ERG rearrangement in high grade prostatic intraepithelial neoplasia (HGPIN) without PCa is unknown. We aimed to assess the status of ERG in HGPIN with and without concurrent PCa in radical cystoprostatectomies (RCP) with fully analysed prostates.
Methods: A preliminary series of 31 fully embedded prostates from RCP were included (Parc de Salut Mar-Biobank). All selected cases had HGPIN foci. Cases with prostatic infiltration by bladder carcinoma were excluded. Immunohistochemistry (IHC) for ERG was performed in HGPIN and PCa foci, and maps of these lesions with their respective ERG status were drawn.
Results: There were 16 cases of isolated HGPIN foci (Group 1, G1), and 15 cases with both HGPIN and prostatic adenocarcinoma (Group 2, G2). ERG-positive HGPIN was observed in only 1 of 16 cases (6.25%) in G1. In G2, 8 of 15 PCa (53.3%) were ERG-positive of which 3 cases (37.5%), had ERG-positive HGPIN (p=0.27). The global prevalence of ERG expression was 12.9% for HGPIN (4/31) and 53.3% for PCa (8/15) (p=0.02).
Conclusion: ERG overexpression in HGPIN is associated to ERG+ PCa, with a lower prevalence of ERG+ in isolated PIN. This could indicate that the acquisition of the TMPRSS2-ERG fusion by HGPIN is a crucial step towards the development of PCa. ERG IHC of HGPIN foci should be performed in needle biopsies without PCa, as most of the ERG+ HGPIN cases seem to be associated to a concomitant PCa.
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PS-18-033
CK14 expression identifies a basal/squamous-like type of papillary non-muscle-invasive upper tract urothelial carcinoma
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Background & objectives: CK14 is an important marker of basal/squamous-like (BASQ)-type muscle-invasive bladder carcinoma. However, CK14 expression and its significance in non-muscle-invasive upper tract urothelial carcinoma (NMIUTUC) remain unknown. We investigated the prognostic and transcriptional characteristics associated with CK14 expression in papillary NMIUTUC.
Methods: Immunohistochemical (IHC) staining for CK14 was conducted in 204 papillary NMIUTUC specimens. CK14 positivity was defined as a positive signal in >0% of tumour cells. RNA sequencing data were analysed from 8 papillary high-grade NMIUTUC fresh-frozen specimens consisting of 4 CK14-positive and 4 CK14-negative tumours.
Results: CK14 positivity was significantly associated with poor progression-free survival (p = 0.015). Gene set enrichment analysis demonstrated that the CK14-positive tumours had characteristics reminiscent of the BASQ subtype. In addition, differentially expressed genes between CK14-positive and CK14-negative tumours enriched in positive regulation of cellular proliferation in CK14-positive tumours. Consistent with this, the mean Ki-67 proliferative index was higher in CK14-positive tumours than it was in CK14-negative tumours (p = 0.002).
Conclusion: CK14-positive papillary NMIUTUC is an aggressive subtype with BASQ-like molecular characteristics and dynamic proliferative activity. We propose that CK14 IHC staining can be a useful biomarker of BASQ-type papillary NMIUTUC that can be applied in daily practice with the aim of precision oncology.
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PS-18-034

Morphological characteristics and immunophenotype of renal cell carcinomas with light cytoplasm

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Background & objectives: The heterogeneity of renal cell carcinomas with a light cytoplasm creates certain difficulties in the correct morphological verification of these neoplasms. Objective: to study the morphological and immunophenotypic features of rare variants of renal cell carcinoma with light cytoplasm.
Methods: The study was performed on surgical material obtained from 264 patients with a kidney tumour. Immunohistochemical studies were performed on paraffin sections according to a standard protocol using a wide panel of antibodies against 36 molecular markers.
Results: Based on morphological analysis and immunohistochemical studies, the tumours were divided into 4 groups: cystic kidney tumours with low nuclear gradation (n = 65; 25%); kidney tumours of a solid and / or tubular and papillary structure with low nuclear gradation (n = 98; 37%); kidney tumours with high nuclear gradation (n = 94; 36%); and polyphase renal cell carcinomas (n = 7; 2.7%).
Conclusion: The results obtained suggest that among the morphological forms of clear cell renal cell carcinoma there is a direct relationship between the degree of nuclear gradation and the histological picture of the tumour.

PS-18-035

The relationship between PD-1 and COL6A1 expressions and prognosis in renal cell carcinoma

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Background & objectives: Programmed cell death receptor-1 (PD-1) and Collagen 6 alpha-1 polypeptide subunit (COL6A1) have prognostic significance in clear-cell renal cell carcinoma. In this study, we evaluated the expression of COL6A1 and PD-1 in 4 different renal cell carcinoma (RCC) subtypes.
Methods: A total of 161 RCC cases from five different centres were included in this study. Clinical data of the cases were taken from electronic records of the institutions. Paraffin blocks of cases were re-evaluated by an expert uropathologist. The correlation of COL6A1 and PD-1 expression with sex, age, tumour type, lymphovascular invasion, WHO/ISUP grade and tumour stage (pT) was analysed.
Results: In this study, COL6A1 and PD-1 immunohistochemical staining intensities did not have statistically significant correlations with any of these parameters. When COL6A1 and PD-1 expressions were examined on a case-by-case basis, no statistically significant relationship was found between COL6A1 and PD-1 expressions ($p > 0.05$).
Conclusion: In high-grade renal cell carcinomas, COL6A1 and PD-1 were not associated with other prognostic parameters included in the study, but further studies are needed to elucidate a possible relationship between lymphovascular invasion and COL6A1 immunohistochemical staining intensity because of slight correlation between these parameters.

PS-18-036

KIF11 as a poor prognostic factor in clear cell renal cell carcinoma

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Background & objectives: Broad resistance to systemic therapies remains a major challenge in renal cancer-related research. We investigated associations of KIF11 expression with the clinical course of clear cell renal cell carcinoma (ccRCC) using the tissue microarray (TMA).
Methods: The TMA contained specimens from 88 ccRCC patients, tumour and matched normal adjacent tissue (1 core/case). To assess KIF11 protein expression levels, we performed immunohistochemical staining. The overall survival (OS) was analysed using the Kaplan-Meier method and log-rank statistics. We used Cox proportional hazard models to conduct univariate and multivariate analyses.
Results: Median follow up for the TMA cohort was 7.0 years. Mean cytoplasmic expression of KIF11 in tumour tissues was lower than that in adjacent controls ($p<0.05$). 49 of 88 ccRCC tissues (55.7%) presented high KIF11 cytoplasmic expression. Mean OS of patients with high KIF11 expression was 61.6 months vs 65.5 months in those with low KIF11 expression ($p<0.05$). KIF11 expression positively correlated with tumour grade ($p<0.05$). We found no association between KIF11 expression and stage of the disease.
Conclusion: Elevated KIF11 protein expression served as an independent unfavorable prognostic indicator of survival in ccRCC. This observation, together with the emerging reports, suggest that KIF11 in kidney cancer may contribute to development of the resistance to systemic therapies.
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PS-18-041

Testicular germ cell tumours: p53/MDM2 expression and association with patient outcome

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Background & objectives: p53-MDM2 axis is reported to have a role in the pathobiology of testicular germ cell tumours (TGCTs). However, protein expression of these players has been scarcely explored. We aim to characterize their immunoexpression patterns in a large cohort of TGCTs,
Methods: We performed immunohistochemistry for p53 and MDM2; in order to improve the consistency and reproducibility of our findings, p53 and MDM2 immunoexpression was evaluated using a digital image analysis system (GenASIs™, Israel), which semi-automatically quantified nuclear immunostaining. The H-score for each sample was calculated, corresponding to the sum of the products of each immunostaining score by its proportion.
Results: 230 TGCT chemo-naive primary tumour components were included, together with 12 cisplatin-resistant metastases. There was a significant positive correlation between p53/MDM2 ($r=0.590, p<0.0001$). Non-seminomas showed significantly higher expression of both p53/MDM2 ($p=0.0002, p<0.0001$), especially embryonal carcinoma/choriocarcinoma. MDM2 was significantly overexpressed in chemo-treated metastases compared to chemo-naïve primary tumours ($p<0.0001$). Higher MDM2 expression associated with higher stage and IGCCCG prognosis group and associated with a tendency for poorer relapse-free survival ($p=0.057$).
Conclusion: These data reinforce the suggestion of MDM2 in the acquisition of a more aggressive phenotype, with tendency for recurrence and for becoming resistant to cisplatin. p53-MDM2 interaction inhibitors and MDM2 antagonists may be particularly useful in TGCTs.
Funding: Fundação para a Ciência e Tecnologia (PTDC/MECONC/29043/2017 and SFRH/BD/132751/2017).

PS-18-042

Investigation of biomarkers predictive of relapse in stage I testicular germ cell tumour patients on surveillance

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Background & objectives: Better biomarkers for assessing risk of relapse in stage I testicular germ cell tumour patients are urgently needed, which can complement classical histopathological variables, such as vascular invasion. We aimed to assess the prognostic value of previously suggested biomarkers, related both to proliferation (MIB-1 and TEX19) and to the immune microenvironment (CXCL12, CXCR4, beta-catenin and MECA-79), in a true surveillance cohort of stage I testicular germ cell tumour patients.
Methods: A total of 70 tumour samples (42 non-seminomas and 28 seminomas) were included in the study. Immunohistochemistry for the above-mentioned markers was performed. Impact on relapse-free survival (RFS) was assessed, including multivariable analyses.
Results: Patients with no vascular invasion but with >50%MIB-1 staining showed significantly shorter RFS (p=0.042). TEX19 nuclear immunoexpression was confirmed in spermatogonial cells, but not in tumours. Non-seminoma patients exhibiting vascular invasion and CXCL12-positive stromal/inflammatory cells showed significantly improved RFS (p=0.015). Exclusively nuclear immunoexpression of CXCR4 associated with better RFS (p=0.032), lost after adjusting for vascular invasion. Higher beta-catenin score-patients showed a tendency for poorer RFS (p=0.056). MECA-79 immunoexpression was absent.
Conclusion: The informative protein biomarkers (i.e., MIB-1, CXCL12, beta-catenin, and possibly CXCR4) may prove useful for risk-stratifying patients if validated in larger, multicentric and well-defined studies. Currently, classical histopathological features of testicular germ cell tumours remain key for relapse prediction.
Funding: JL is supported by FCT - Fundação para a Ciência e Tecnologia (POCI-01-0145-FEDER-29043 and SFRH/BD/132751/2017).

PS-18-043

Infertility testicular biopsy. Review from 2004 to 2019 in our institution

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Background & objectives: The male factor as a cause of infertility can account for 50% of reproduction consultations. From the therapeutic point of view, it is important to distinguish whether an azoospermia or oligospermia is obstructive or secretory.
Methods: We conducted a retrospective descriptive study of men who attend infertility consultations, with testicular surgical biopsy, over a period of 16 years (2004-2019) in our institution, with a total of 136 patients. Those who get sperm in surgery are cryopreserved. We describe the basic lesion patterns of testicular biopsy received in the pathology department.
Results: Of the total of 136 patients, 49 samples of testicular pulp are received in the pathology department, resulting in two of them not valuable. The age is between 23 and 48 years, with an average of 33.8 years.
In surgical intervention (n=136)
- Mobile spermatozoa: 77
- Non-mobile spermatozoa: 4
- Non spermatozoa: 55

Histological findings (n=49)
- Obstructive pattern: 7
- Sertoli Cell-Only Syndrome: Madure: 14, Dysgenetic: 9
- Mixed Atrophy: 3
- Maduration Arrest: 8
- Hypospermatogenesis: 4
- Tubular Hyalinization y fibrosis: 2
- Not valuable: 2

Conclusion: The histological examination of the testicular parenchyma is the fundamental diagnostic method to know in depth what is happening inside the testicle, and to inform us of the reversibility or progressivity of the lesions and their causes.

PS-18-044

Fibronectin and galectin- 3 expression in urinary bladder cancer

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Background & objectives: Urothelial carcinoma comprises most cases of urinary bladder cancer. The aim of this research was to determine the expression of fibronectin and galectin-3 in urothelial carcinoma epithelium and stroma and its relation to tumour grade, stage and disease relapse.
Methods: In this study, 110 patients with bladder urothelial carcinoma were grouped according to tumour grade and stage. Tissue was routinely stained for HE and immunohistochemistry performed according to manufacturer protocol. Epithelial and stromal fibronectin and galectin- 3 expression was scored regarding to intensity and percentage of positive cells.
Results: Positive correlation between fibronectin tumour epithelium expression and tumour grade (p=0,044), pT stage (p=0,001) and pN stage (p=0,037) was found. Positive correlation between fibronectin stromal expression and disease relapse (high grade tumours, Ta/T1) (p=0,03) was determined. Negative correlation between fibronectin stromal expression and pT stage was demonstrated (p=0,001). Galectin- 3 in tumour epithelium positively correlated with pT stage (p=0,046) and disease relapse (tumour group with lymph node metastasis T2N1/2) (p=0,00).
Conclusion: Fibronectin and galectin-3 are glycoproteins of extracellular matrix active in cell adhesion, dedifferentiation, profibrotic, proinflammatory changes, growth and apoptosis. Epithelial and stromal component, as well as changes in extracellular matrix protein expression are responsible for tumour progression and formation of protumoral microenvironment. Our research demonstrated that increased expression of fibronectin and galectin-3 in tumour epithelium and decreased fibronectin tumour stromal expression is related to aggressive tumour growth, therefore these markers are possible candidates to indicate aggressive behaviour of this tumour.

PS-18-046

Nephogenic adenoma: clinico-pathological study of 36 cases

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Background & objectives: Nephrogenic adenoma (NA) is an unusual benign lesion of controversial histogenesis, that can be confused with malignant primary and metastatic carcinomas.
We report the morphological variants of NA and the role of inmunohistochemistry in the differential diagnosis
Methods: We studied a retrospective series of 35 patients that were diagnosed of NA in our institution between 2013 and 2019. Demographic characteristics were obtained from clinical records. All the histological preparations were reviewed. Immunohistochemical analysis of P504S, PSA, CD10, EMA, GATA 3, PAX8 and p63 was performed on formalin-fixed and paraffin-embedded 4-mm sections in all cases.
Results: 86% were male patients. Age range was 40-92 years. Two only patients had no history of urinary trauma or neoplasia. The most common symptom was haematuria follow by obstruction.

The most common location was urinary bladder (20 patients), urethra (8), urether, kidney and prostate (2 patients each) and perirenal fat (1).
The most common patter was tubular (51%), mixed (26%), fibromixoid (11%), papillary (9%) and polypoid (3%). Tubulo-papillary was the most frequent mixed pattern (23%).11/36 patients had a concomitant lesion which 17% correspond to urothelial carcinoma
All cases were inmunoreactive for PAX8 and negative for p63. One case was negative for AMARC (prostatic localization) and four cases were positive for GATA 3.
Conclusion: NA displays morphological features that often coexist. Recognition of its characteristic and unusual architectural features is needed to distinguish this lesion from malignant neoplasms.
According to our results the most reliable IHQ stains for NA differential diagnosis is PAX 8 and p63 to rule out a urothelial and prostatic carcinoma.
NA outside the urinary system is quite rare, but when founded is usually associated to previous surgery (specially renal).

PS-18-047
Sinusoidal obstruction syndrome secondary to diffuse intra-sinusoidal liver metastasis of urothelial carcinomas
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Background & objectives: Diffuse intra-sinusoidal (DIS) liver metastasis of urothelial carcinomas is exceptional leading to hepatic failure secondary to sinusoidal obstruction syndrome (SOS).
We report histological and immunhistochemical classification of DIS metastatic urothelial carcinomas, as PD-L1 status in the primary tumour
Methods: Over a period of 2000-2019, we recorded all cases of metastatic liver urothelial carcinomas in our institution, only four showed DIS infiltration pattern. Histochemical and immunohistochemical stains with Masson trichome, reticulin, CK5-6, CK20, P40, P63 and GATA3 were studied.
PD-L1 (SP 142- Ventana) immunohistochemistry status was studied in the primary tumour
Results: Four cases were studied (three males) aged ranged was 53-64 years. Histological subtypes were: Three high grade urothelial carcinomas (one with trophoblastic differentiation and one micropapillary variant) and one undifferentiated urachal carcinoma. All of them presented SOS and three died of fulminant hepatic failure. All cases showed a luminal immunhistochemical profile. PD-L1 status was positive in 1 case.
Conclusion: DIS liver metastasis of urothelial carcinomas with secondary SOS is exceptional. SOS is related to sinusidal-endothelial damage that conditions a prothrombotic state that is lethal in 90% of severe cases. PD-L1 status could represent a new alternative treatment in disseminated tumours.

PS-18-048
PD-L1 expression in urothelial carcinomas - concordance among 2 commercially available antibodies and correlation with CD8 T lymphocyte count
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Background & objectives: Immunotherapy has transformed the management of advanced urothelial carcinoma (UC) of the urinary tract. Programmed death ligand1 (PD-L1) immunohistochemistry serve as a predictor biomarker of anti-PD-L1/PD1 therapy. Different PD-L1 antibody assays have been approved for specific immune checkpoint blockade.
Methods: We characterized PD- L1 expression in 60 urothelial carcinomas using 2 commonly used and commercially available PD-L1 antibodies [clones 22C3(cutoff 10) and SP142(cutoff 5%)]. PD-L1 expression on tumour cells (TC) and tumour-infiltrating immune cells (IC) were assessed and tumours were defined as high density with the presence of ≥50 CD8+ intraepithelial lymphocytes per high power field in a given spot.
Results: Our series was composed of 58 high grade infiltrating UC and 2 squamous cell carcinomas. Cases of high grade G2/G3 infiltrating urothelial carcinomas showed higher PD-L1 score results for clone 22C3 than SP142 (41.5%>36.6% and 64.7%>58.6%, respectively).
Concordance of both PD-L1 expression status was present in 57/60 cases (95%). CD8 T-cells density did not correlate with PD-L1 expression. Urothelial carcinomas of higher grade were more frequently associated with high density intraepithelial T lymphocytes (G2:24.4% and G3:47.1%). Squamous cell carcinoma showed expression for both PD-L1 clones, in one case.
Conclusion: The correct assessment for PD-L1 expression is essential for immunotherapy decision, improving the outcomes of patients. Higher grade was associated with higher PD-L1 expression and high density of intraepithelial T lymphocytes. We observed high concordance between both PD-L1 clones used.

PS-18-049
Characteristics of metastatic renal cell carcinomas, observed in a 5-year period
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Background & objectives: The purpose of this study was to highlight the metastatic potential of renal cell carcinomas (RCC), investigating the predilection of those tumours for certain anatomical sites. We also wanted to evaluate the ratio between primary RCC and metastatic RCC cases.
Methods: From the database of our pathology department, we evaluated all the cases diagnosed as renal cell carcinomas from 2015 to 2019, selecting the metastatic RCC tumours.
Results: We included in this study 32 cases of secondary RCC (6 women and 26 men). The median age at diagnosis was 62.6 years for females, and 63.8 years for males. Anatomical sites involved: brain (40.6 %), bones (21.8 %), skin (6.25%), periosseous soft tissue (6.25%), distant lymph nodes - axillary and supraclavicular (6.25%), duodenum, ovary and adrenal gland (3.12 % each); a case presented subcutaneous and peritoneal involvement. Histologic types: clear cell (90.6%) and chromophobe (3.12%); the histologic type could not be specified in 6.25% of the metastasis. In 46.8 % of the cases, the secondary tumour was diagnosed prior to the renal neoplasm. The primary RCC/metastatic RCC ratio was 9.4.
Conclusion: The brain was the main organ involved, the overwhelming majority of the cases being clear cell RCC. An effective screening tool for RCC is needed to detect renal neoplasms in early stages, for a better therapeutic management of the patients.

PS-18-050
Immune profiling of prostate cancer using multiplex immunofluorescence and gene expression panels
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Background & objectives: Prostate cancer is known for its biological and clinical heterogeneity. The aim of this study was to investigate the in-situ phenotype of tumour infiltrating immune cells in order to determine whether they correlate with metastasis to regional lymph nodes.

Methods: We applied multiplex immunofluorescence to characterise the immune microenvironment of tissue samples obtained from radical prostatectomy. Patients with pathologically confirmed regional lymph node metastases were matched with patients without nodal metastases. The identified immune signature of nodal metastasis was validated in a comparable independent patient cohort. The functional orientation of immune cells was explored using a targeted gene expression panel.
Results: Patients with nodal metastasis had significantly decreased stromal effector CD4 cells (p=0.0003). This CD4 immune cell density was a significant predictor of lymph node spread in multivariate analysis. An independent cohort of 184 patients was also stained with the same panels and the CD4 cell density remained a predictor of nodal spread. The targeted gene expression analysis revealed increased extracellular matrix components expressed within primary prostate cancers with nodal spread.
Conclusion: Together, these findings suggest differences in the immune infiltrate (particularly CD4 effector T cells) between prostate cancer patients with vs without lymph node metastasis. This suggests that prospective clinical studies could test its value in the diagnostic setting in order to improve patient stratification for regional lymph node dissection. Also, gene expression analysis suggested increased extracellular matrix components in tumours with nodal spread and although this requires further mechanistic exploration it highlights the potential for stroma-modifying treatments in those patients.
Funding: CRUK

PS-18-051
Histomorphological characteristics and distribution of prostate carcinoma foci using multiple site-specific labelled core biopsies
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Background & objectives: Evolving prostatic biopsy sampling techniques aimed at improving diagnostic accuracy, prognostication and localization of prostate cancer assist to dictate treatment options. This study analysed the Histomorphology, spatial distribution and prognostic implications of site-specific core biopsies of the prostate gland.
Methods: Double-sextant prostate biopsy cores were microscopically examined prospectively over an 18-month period representing the medial and lateral aspects of the left and right apices, mid-gland and bases of the glands. These were obtained by transrectal ultrasound guidance. H&E-stained slides were examined for the presence, volume, Gleason score and ISUP grade-group of cancer. Frequency statistics was utilized to evaluate the data.
Results: A total of 91 patients aged 48 to 88 years with a median age of 70 years were seen. Entire sextant regions showed cancer in 68.1% of cases whilst cancer was restricted to one sextant region in 8.8% and to two regions in 7.7% of cases. The apical, mid-gland and basal regions were positive for cancer in 35.6%, 33.8%, and 30.6% of the time respectively. Tumour was restricted to apices and mid-gland in 9.9% of the cases whilst it was restricted to bases in 2.2% of the cases. ISUP grade group 5 was most frequently seen with grade group 2 least frequent. Carcinoma volume was lowest in basally located cancers.
Conclusion: Prostatic carcinomas in this environment have poor prognostic indicators of poor differentiation and high tumour volume and multifocal occurrence of tumours. Site-specific labelling of biopsies enabled determination of spatial distribution of prostate cancers and involving all sextants ensures clear assessment.

PS-18-052
Prognostic impact of rhabdoid differentiation incorporated in a novel two-tiered grading system for chromophobe renal cell carcinoma
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Background & objectives: A histological grading system of chromophobe renal cell carcinoma (chRCC) is highly desirable to identify 5–10% of tumours at risk for progression. In this study, we evaluated the prognostic value of rhabdoid differentiation in chRCC.
Methods: Vimentin immunohistochemistry was done to detect rhabdoid differentiation in chRCC. Log-rank test and Cox proportional-hazard model for time to progression (TTP) (i.e. cancer-specific death or recurrence after surgery) were used for survival analysis. 11 of 142 (7.7%) Japanese chRCCs exhibited rhabdoid differentiation.
Results: Presence of rhabdoid differentiation was significantly associated with shorter TTP (P<0.001, log rank test). When rhabdoid differentiation was incorporated together to previously reported grading scheme, 2-tiered grading system based on three components including necrosis and/or sarcomatoid differentiation and/or rhabdoid differentiation were significantly associated with shorter TTP (P=0.003) and gave stronger prognostic power than previous system based on two components with sarcomatoid differentiation and/or necrosis (P=0.005).
Conclusion: These findings support the grading system recommendation incorporating presence of rhabdoid differentiation. Further validation on the interobserver variability has to be tested.
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PS-18-053
Synoptic versus narrative reporting of prostate biopsies at a tertiary healthcare institution challenges, successes, and expectations
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Background & objectives: Cancer pathology reports are expected to contain all information required for patient management and disease surveillance. Moreover, reports for patients with prostate cancer have become increasingly complex with the addition of more pathological details. This study aimed to compare narrative and synoptic prostate cancer reports for core needle biopsies received at a tertiary hospital in Nigeria in order to determine which form was most complete according to international standards.
Methods: All malignant prostate cancer histopathology reports received from 2010 to 2015 were analysed for the presence of important clinicopathological parameters, including the numbers of cores taken and those involved by the tumour, percentage of tumour involvement, Gleason score and the presence of high-grade prostatic intraepithelial neoplasms (HGPINs) and perineural and lymphovascular invasion.
Results: There were 27 narrative and 56 synoptic reports. The documentation in narrative reports was significantly incomplete compared to synoptic reports as follows: number of cores (33.3% versus 96.4%), number of cores involved by the tumour (11.1% versus 94.6%), percentage of cores involved by the tumour (3.7% versus 100.0%) and the presence of HGPINs (7.4% versus 100.0%) and perineural (59.3% versus 98.2%) and lymphovascular (48.1% versus 100.0%) invasion (P <0.001 each).
Conclusion: Synoptic reports of malignant prostate cancer biopsies received at the Lagos University Teaching Hospital were found to contain more complete information than narrative reports. Highlighting significant parameters may contribute to management decisions, thereby improving the quality of patient care.

PS-18-054
Can BCL-2 be a potential prognostic marker for clear cell renal cell carcinoma?
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Background & objectives: Renal cell tumours are among the common tumours in adults. The most common type is clear cell renal cell carcinoma. Although the formation mechanism of the tumour is largely resolved,

an immunohistochemical marker that determines the prognosis has not been detected yet

Methods: 84 cases of clear cell renal cell carcinoma diagnosed between 2008-2015 in our institution were re-evaluated by two pathologists who were blind to outcome. One representative block from of all tumours was selected to perform Bcl2 immunhistochemistry. The immunoreactivity was evaluated semi-quantitatively based on the percentage of positively stained cells (proportion) and also staining intensity.

Results: Our follow-up range was 4-141 months. Statistical analysis revealed that there was an inverse relationship between bcl 2 expression and clinical course. The decreased levels of bcl2 were statistically related with metastasis, shorter disease free survival and shorter overall survival on both univariate and multivariate analysis (univariate analysis p=0.019, p=0.05, p=0.009 respectively, multivariate analysis OR=2.136, 95% CI=0.222–0.625, p= 0.012, HR=1.856, 95% CI=0.034–0.725, p= 0.018, OR=1.552, 95% CI=0.703–0.645, p= 0.06) Kaplan-Meier survival curves revealed statistical significance (p< 0.05) between decreased expression levels and strong and moderate levels.

Conclusion: The role of apoptotic mechanisms in both programmed cell death and tumour formation have not been fully elucidated. There may be compensatory relations that we do not yet know among these complex chain of events.

However, our study may constitute a base for further research in the field of prognostic estimation, as bcl-2 expression is statistically significant with metastasis, recurrence, and overall survival.

PS-18-055

Low-grade oncocytic tumour: retrospective reappraisal of previous diagnosis

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Background & objectives: In 2019, new renal entities were described that include an oncocytic tumour that is CD117 negative and diffusely CK7 and e-cadherin positive, with specific morphologic features. Our aim was to retrieve cases that could fit this new entity.

Methods: We analysed 47 resections and 8 needle core biopsies of renal cell tumours from January/2018 to January/2020. We excluded 7 biopsies and 45 resections based on the incompatible morphology or immunohistochemistry required for this diagnosis. Immunohistochemical panel of CK7, CD117 and e-cadherin was performed, when missing. Clinical history and outcome was examined, when provided.

Results: In the last 2 years, in our institution, we found 3 oncocytic renal cell tumours with inconclusive sub-classification that fit the description for this new entity: Low-grade oncocytic tumour. The 3 selected cases belonged to men between 69 and 72 years old, were unifocal with sizes ranging from 15mm to 60mm, grossly well delimited, with yellow and brown areas. All patients are currently alive and well, one still awaiting surgery. All cases have round to oval nuclei, low Fuhrman grade (1-2), solid/tubular growth pattern, diffuse positivity for CK7 and e-cadherin, and were negative for CD117.

Conclusion: Renal cell oncocytic tumours sometimes show non-specific morphology and immunophenotype leading to inconclusive sub-classifications between multiple renal cell tumours with oncocytic change. This optimization in classification can help reduce diagnostic observer variability and discover potential therapeutic targets or outcome predictors.

PS-18-056

Intraluminal inclusions cause apoptosis in prostate cancer tissue

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Background & objectives: Intraluminal inclusions (IIn) in prostate cancer (PCa) causes the development of inflammation, tumour progression and metastasis. However, their effect on apoptosis remains unstudied.

Objective: To study the influence of intraluminal inclusions on apoptosis of prostate cancer cells.

Methods: 60 PCa samples (group within 30 samples of PCa with IIn (prostatic calculi and corpora amylacea) and group of 30 samples without IIn) were used for study. All samples were examined by hematoxylin-eosin staining and by immunohistochemistry (p53, Bax and Casp3). All data were analysed by Shapiro-Wilk test, Mann-Whitney's U-test and Student's t-test.

Results: We have indicated no significant difference in expression of p53 protein between groups. However, the localization of p53-positive cells was associated with IIn. PCa with IIn had a significant higher expression of Bax (p<0.001) and Casp3 (p<0.001). It may indicate a stimulation of apoptosis by IIn. The intensity of immunostaining was also higher in PCa tissue with IIn.

Conclusion: IIn promote cell injury of PCa cells and modification of cell live cycle. It results in higher level of apoptosis in tumour tissue. This may indicate a adverse effect of IIn on the course and progression of PCa.

PS-18-057

Correlations between different tumour architecture compounds assessed through fractal analysis and tumour cells specific features in prostate adenocarcinoma

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Background & objectives: The authors' aim is to assess the correlations between the main tumour constitutive elements evaluated using the fractal dimension (FD) and three main features of tumour cells in prostate adenocarcinoma (PC).

Methods: 269 fields with different PC architectural patterns were selected then classically and immunohistochemically stained.

Images were binarized. The FD (<1.5="linear-like"-LLD and >1.5="area-like"-ALD distributions) was computed for each binary image. Immunohistochemical stain intensities were assessed through a proprietary computational algorithm.

Tumour cells architecture-GO, tumour stroma architecture-TC, vascular network-VN, the capacity to degrade extracellular matrix-ECMD, intercellular adhesion-ICA and aggressiveness degree-AgD were assessed.

Results: MMP9 intensity trend was smoothly descending as GO evolved towards ALD and ascending as TC evolved towards ALD distribution. PTEN intensity, instead smoothly increased as GO evolved towards ALD and decreased as TC evolved towards ALD.

MMP2 intensity trend was descending as both GO and TC evolved towards ALD.

E-CAD intensity trend was ascending as both GO and TC evolved towards ALD.

MMP9 and E-CAD intensities had no correlation with VN while MMP2 and PTEN had both a smoothly descending trend as VN evolved towards ALD.

Conclusion: Tumour cell behaviour (ECMD, ICA, AgD) is different according to architectural distribution of tumour cells architecture, tumour stroma architecture and vascular network, suggesting a dynamic interrelation between the heterogeneous tumour cell population and tumour microenvironment.

PS-18-058

Correlations between different tumour architecture compounds assessed through fractal analysis and different grading systems in prostate adenocarcinoma

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Background & objectives: The aim of the study is to assess the correlation of the main tumour architecture constitutive elements evaluated using the fractal dimension (FD) with three different grading systems of prostate adenocarcinoma (PC).
Methods: Gleason modified system-GS with GS2, GS3A, GS3B, GS3C, GS4-Fused, GS4-Cribriform, GS5A and GS5B patterns, Srigley system-SS with SS1, SS2, SS3, SS4 and authors' system-PS with Necrotising-N and Solid-S groups were used.
Tumour cells architecture-GO, stroma architecture-TC, vascular network-VN were assessed on binarized images from 420 fields with PC patterns by computing fractal dimensions-FD (<1.5="linear-like"-LLD and >1.5="area-like"-ALD distributions) for each image.
Results: GO FD value classes (VCs) showed an obvious ALD trend, irrespective the used grading system. Conversely, VN FD value classes showed an obvious LLD trend. TC FD value classes showed a trend in between LLD and ALD.
GO FD VCs were better grouped by the SS and also by the PS.
TC FD VCs showed almost the same distribution irrespective the used grading system.
VN FD VCs showed an increased LLD in most poorly differentiated groups of all grading systems.
GO and VN FD VCs strongly correlated with all tested grading systems (c2 test p values<0.05).
TC FD VCs proved instead no correlation with any of the three grading systems.
Conclusion: The results suggest that tumour cell architecture proved the strongest relationship with the degree of differentiation irrespective the used grading system. Srigley's and our systems proved to be more accurate in defining the degree of differentiation than Gleason system.

PS-18-059

Correlation between PD-L1 (22c3) immunoexpression and panel next generation sequencing (pngs) analysis in innusual high grade urothelial carcinoma (hguc) subtypes

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Background & objectives: The PD-L1 immunoexpression has been a suboptimum predictive response biomarker, often being negative in aggressive and infrequent UC subtypes such us micropapillary or nested.
New assays seem to be promising in predicting sensitivity to ICIs, such as pNGS, among others.
Methods: Immunohistochemical studies (IHQ) with PD-L1 (22C3, Agilent) have been done on 25 samples of paraffin-embedded tumour tissue from 23 patients.
They correspond to HGUC mixed with variant pattern. We have studied the correlation between PD-L1 IHQ and these phenotypes, and performed a pNGS (Oncomine comprehensive assays v3) on each of the samples
Results: Combined Positive Socre (CPS) of each case and each different variant subtypes has been calculated, and they were positive: 2/4 squamous; 1/2 lipid-rich; 1/2 poorly differentiated; 2/4 sarcomatoid and the only one plasmocytoid differentiation.
In pNGS study, molecular alterations related to ARID1A, TSC1, ERCC2, PIK3CA and TP53 stand out. Several of these alterations´ve been linked in the literature to a greatly accelerated rate of tumour growth and clinical deterioration after ICIs.
To this end, we highlight one of the case which is positive because of the squamous areas, although micropapillary areas were negative. And its corresponding pNGS showed genomic alteration in 2 alleles of PIK3CA, RB1, ERCC2, TP53 and ARID1A.
Conclusion: We should give special interest to cases that combine several histological subtypes with divergent PD-L1 expression, since a global positive score could be obtained in a case wich could have PD-L1 negative unusual areas that result in a hyper-progressive patient.

PS-18-060

The neurosafe proof feasibility study: a report of the concordance between intraoperative frozen-section assessment of margin status and subsequent paraffin-embedded sections

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Background & objectives: Intra-operative neurovascular structure-adjacent frozen-section examination (NeuroSAFE technique) aims to guide safe preservation of neurovascular bundles (NVB) during radical prostatectomy (RP) regarding margin status to increase rates of nerve sparing. We report the findings of the NeuroSAFE PROOF feasibility study (NCT:03317990).
Methods: Forty-nine men at two regional uro-oncology centres underwent robot-assisted radical prostatectomy (RARP) between May 2018 and March 2019. 25 men underwent NeuroSAFE RARP (intervention) as per random allocation. Intra-operative frozen-section margin was compared with subsequent paraffin-embedded margin assessment for each section (NVB).
Results: 50 NVBs were analysed in the NeuroSAFE arm with a total of 250 individual frozen-sections; mean 10 sections per patient, 5 sections per NVB. On an NVB basis (n=50), diagnostic accuracy was 94%, sensitivity was 100%, specificity 92.7% and kappa's coefficient for agreement was 0.831 (p=<0.0001). Slightly lower specificity was on account of 3 positive margins on frozen section that were changed to narrowly clear on final paraffin section diagnosis. On an individual frozen-section to paraffin-section basis (n=250), diagnostic accuracy was 97.2%, sensitivity 100%, specificity 99.2%. Kappa's coefficient for concordance was 0.914 (p<0.0001). There were no false negatives.
Conclusion: We note excellent concordance between frozen-section margin and final histological margin diagnosis that shows good pathological conduct of the NeuroSAFE technique in the feasibility study. The full NeuroSAFE PROOF RCT is currently underway at 4 NHS centres.
Funding: JP Moulton Charitable Foundation NHS NIHR UCL Hospitals Charitable Foundation Rosetrees trust

PS-18-061

The significance of the NOTCH3 expression in the urothelial bladder cancer patients' follow-up

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Background & objectives: Angiogenesis is the hallmark of the urothelial bladder cancer (UBC) and NOTCH3 is a very important receptor in this process. The aim was to determine the association between NOTCH3 expression and the long-term clinical outcome in UBC patients.
Methods: The present research included 614 UBC samples incorporated in paraffin tissue microarrays, analysed for immunohistochemical NOTCH3 expression. The majority of the UBC samples were NOTCH3 positive (over 90%). We semi-quantified the membranous expression (0-3), and the mean degree was 1.81±0.94.
Results: The median follow-up in the study group was 45.0 (24.0-64.0) months. During this period, the mortality rate was 42.5%, cancer specific in most of the cases (69.7%). There was a weak negative correlation between

NOTCH3 expression and overall-survival (p<0.001) and cancer-specific mortality (p<0.05). Each higher degree of positivity was associated with 1.3 higher risk of mortality (p<0.001), and 1.4 higher risk of cancer-specific mortality (p<0.001). Even though we identified NOTCH3 as a possible predictor, it was not shown to be an independent predictor of cancer-specific mortality. Recurrences occurred in 230 (37.5%) patients, mostly one time (58.7%). In this study NOTCH3 expression was not a statistically significant predictor of recurrence-free survival.
Conclusion: NOTCH3 could be used as a predictor of cancer related mortality and for selecting the UBC patients that require an intensive follow-up, especially if they are elder and presented with high grade and high stage disease.
This work was supported by Grant no. 175092 from the Ministry of Education and Science of Serbia.

PS-18-062
Investigation of the role of tumour cell immune escape by PD-1 / PD-L1 interaction and microsatellite instability on the failure of BCG therapy in high grade urothelial carcinomas
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Background & objectives: The aim of this study was to investigate the role of PD-1/PD-L1 interaction on BCG failure and the relation between MSI status and BCG response to evaluate the option of immune checkpoint inhibitors on treatment of BCG resistant urothelial carcinomas.
Methods: Expressions of PD-L1(SP263), MSH2,MSH6, PMS2, MLH1 were evaluated immunohistochemically on TUR materials of 29 BCG-refractory and 30 BCG-responsive high grade urothelial carcinomas(Ta,T1). PD-L1 expression on tumour cells and tumour associated immune cells were categorized as Negative/Low and High expression. DNA MMR protein expression were classified as "reduced (≤30%)" and "preserved(>30%)". Microsatellite analysis was performed by PCR using 5 mononucleotide markers.
Results: PD-L1 expression did not show any difference between neither the pre- and post-treatment biopsies in the BCG refractory group, nor the BCG refractory and the BCG responsive groups. Most of the carcinomas (70.8%) with reduced expression of DNA MMR proteins were in the BCG responsive group (p=0.022). All the carcinomas were microsatellite stable (MSS).
Conclusion: Immune escape mechanism by PD-1/PD-L1 interaction seems to have no role on BCG failure of urothelial carcinomas. It can be suggested that reduced DNA MMR protein expression may lead to predict cases that will respond to BCG therapy, but this should be supported by larger case series. Finally, according to our results the presence of immunexpressions of DNA MMR proteins, even focal, seems to be enough to determine MSS cases.
Funding: The Scientific And Technological Research Council Of Turkey (TUBITAK) and Scientific Research Projects Coordinator of Ankara University.

PS-18-063
Inter-observer variability in Gleason grading of prostate cancer biopsies
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Background & objectives: Prostate cancer is frequently diagnosed malignancy and Gleason scoring is an important parameter for therapeutic decision of prostate cancer patients. The aim is to determine inter-observer variability in the reporting of Gleason scoring in tissue biopsies.
Methods: A total of 30 cases reported at the Royal Oldham Hospital were reviewed by three local pathologists with a special interest in urological pathology and the results also compared with a central Specialist Urology MDT (SMDT) review to ascertain the degree of agreement in Gleason scoring and the Grade Group.
Results: Within the 3 local pathologists, there was complete agreement for Gleason pattern in 15 cases (50%). These were most with 3+3 (10 cases), 3+4 (1 case), 4+4 (3 cases) and 4+5 (1 case). Including the SMDT opinion, the complete agreement with regard to Gleason pattern drops from 50% to 30% (9 cases). With regard to Grade Group, exact agreement within the 3 local pathologists was 63% (19 cases) and when the SMDT opinion included, this drops to 43% (13 cases). Only 2 cases showed complete agreement in Gleason score 7 between the 4 pathologists (including SMDT review). One case had a complete agreement as 3+4.
Conclusion: Inter-observer agreement in Gleason score differs between studies as some literature reporting up to 71% exact agreement. In our review, total agreement was demonstrated in only 50% of cases which indicate a low degree of concordance between the pathologists.

PS-18-064
Granulomatous prostatitis: clinicopathological and histomorphologic study
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Background & objectives: Granulomatous prostatitis clinically mimics prostate cancer by causing PSA elevation and giving low signal intensity on T2 MRI. The aim of this study was to evaluate the aetiology of granulomatous prostatitis and its association with prostate adenocarcinoma.
Methods: A retrospective analysis of 3250 prostatic specimens received in the pathology department was done over a period of 16 years (2004 to 2020). We identified 15 cases of granulomatous prostatitis (GP) diagnosed in our hospital. Clinical data were collected retrospectively from the medical records and the histological slides were reviewed. Additional stainings (Ziehl Neelsen, Gram, PAS+ and Groccot) were performed.
Results: Samples were obtained from 15 males with a median age of 64.0yrs with a median follow-up period of 21.5 months. The incidence of GP was very low (0.46%). Histological examination showed poorly formed granulomas with negative stains for microbiological agents. Two patients had a previous history of BCG treatment because of the papillary urothelial cell carcinomas (2/15). None of the patients had previous transurethral prostate resection or systemic granulomatous disease. Six patients (6/15; 40%) had a concurrent prostate adenocarcinoma. Three patients had Grade Group 1 adenocarcinoma (Gleason score 3+3), one patient had a Grade group 2 (Gleason score 3+4), and another two patients Grade group 3 (Gleason score 4+3) adenocarcinoma.
Conclusion: Granulomatous prostatitis was a rare disease and the majority of cases showed nonspecific granulomatous prostatitis in our population. A concurrent prostate adenocarcinoma can be seen in a subset of cases, hence a close follow-up and possibly re-biopsy can be considered.

PS-18-065
Prognostic value of CD36 expression in urothelial bladder carcinoma
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Background & objectives: CD36 has been related to tumour invasion and metastases in several cancer types. We aim to study CD36 expression in urothelial bladder carcinoma (UBC) devoid of distant metastases and explore its correlation with tumour stage and progression-free survival, among others.

Methods: Eight tissue microarrays containing samples from 208 cystectomy specimens were studied. No neoadjuvant therapy had been administered to patients. CD36 immunostaining (HPA2018, Sigma-Aldrich, 1:100) was performed and the percentage of neoplastic cells with positive membrane and cytoplasmic expression was assessed. Cases showing CD36 immunoreactivity in at least 1% of neoplastic cells were considered to be CD36-positive.
Results: Thirty cases (15.3%) were immunoreactive for CD36. Positive cases showed higher pT stage (pT3b-pT4) than negative ones (pT1-pT3a) (p=0.007). In addition, the median 12-month progression-free survival was shorter (6.505 months) in the CD36-positive group than in the negative group (8.44 months) (p=0.034). Although tumours with regional lymph node metastases tended to be CD36-immunoreactive (66% of them were CD36-positive), the trend did not reach statistical significance.
Conclusion: Our results indicate that CD36 expression could constitute a negative prognostic factor in UBC, similarly to what has been described in other tumour types such as melanoma and lung, ovary and breast carcinomas. Further studies, with more cases and different clinical scenarios, are needed to evaluate CD36 as an independent prognostic factor, its relation to the metastatic process, and its possible role as a predictive factor of chemotherapy in UBC.

PS-18-067
Incidence of involvement of pre-prostatic fat samples in robotic prostatectomy specimens
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Background & objectives: In our institution, separate samples of pre-prostatic fat are usually taken at robotic prostatectomy surgery. This study aims to determine how often these specimens are involved by tumour, and the associated laboratory costs.
Methods: Pathology reports for robotic prostatectomy surgery (n=669) were analysed. 144 were excluded due to pre-prostatic fat not being submitted or not being reported. Within the remaining 525 cases, the presence of tumour and/or benign or malignant nodes was recorded. An estimate was made of the laboratory costs of processing the tissue (two blocks with a single H&E slide from each).
Results: 50 (9.5%) specimens had ≥1 benign node present, and 2 (0.38%) had malignant nodes.
The 2 cases with malignant nodes also had pelvic nodal dissections yielding malignant nodes. Therefore, regardless of the positive pre-prostatic nodes, the nodal staging was N1. Within 3.5 years of data analysed, we were unable to find a single case where analysis of pre-prostatic fat changed the stage. Technical costs were approximately £5360 over the period.
Conclusion: In our experience, pathological analysis of pre-prostatic fat samples does not change the staging of prostatic carcinoma following robotic prostatectomy but does have a financial cost. We consider the analysis of pre-prostatic fat specimens to be of doubtful clinical value and that it should not be carried out routinely following robotic prostatectomy.

PS-18-068
An immunohistohemical study of transforming growth factor beta-1 expression in urothelial bladder cancer and its prognostic significance
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Background & objectives: Deregulation of transforming growth factor-beta (TGF-β) signalling pathways plays important roles in tumour development and progression. This study aimed to analyse the profile of immunohistochemical expression of3 TGF-β1 in urothelial bladder cancer (UBC) and to evaluate its prognostic impact.
Methods: Immunohistochemical analysis of TGF-β1 expression was performed on 647 UBC samples, obtained by transurethral resection, incorporated in tissue microarrays. Expression status was correlated with clinicopathological and follow-up data. The median follow-up was 61 months.
Results: High TGF-β1 expression was observed in 66.5% of tumours and was significantly associated with high tumour grade, and advanced pathologic stage (p<0.001, respectively). There was no significant association with tumour recurrence (p=0.387). TGF-β1 was directly linked to cancer-specific mortality (p=0.001). Survival analysis showed that high TGF-β1 was associated with shorter overall survival of the patients (p=0.005). In multivariate regression analysis, TGF-β1 manifested as an independent predictor of poor outcome (p<0.001).
Conclusion: This study recognized the expression of TGF-β1 as an important prognostic factor in UBC, where high TGF-β1 expression in tumour cells indicates shorter survival and poor prognosis. Assessment of TGF-β1 status in UBC patients may provide useful predictive information and identify patients that could have the most benefit from therapy targeting TGF-β signalling cascade.

PS-18-069
CD10 and carbonic anhydrase 9 expression in sarcomatoid transformation in renal cell carcinomas
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Background & objectives: Renal sarcomatoid carcinomas are a pathway of dedifferentiation, present in all subtypes of renal cell carcinomas (RCC). Their prognosis is poor. Although uncommon, underlying RCC subtype may not be detected. We hypothesize CD10 and carbonic anhydrase 9 (CAIX) may help.
Methods: We retrieved renal carcinoma cases from our archives between 2009 and 2019. We looked for those cases of any RCC with either sarcomatoid transformation (ST) or rhabdoid transformation (RT). We recorded subtype of renal carcinoma; percentage of ST and RT. Later, we performed CD10 and CAIX staining.
Results: Out of 677 cases of renal carcinomas, 13 showed ST with or without RT and 5 exclusively presented RT. Prevalence was 2%. Percentage of ST ranged between 5% and 100% (mean: 43.92%), and RT ranged between 0% and 85%. RCC subtype most frequently associated with was clear cell RCC (8 /13). CD10 showed positive staining in 88% and, 33% presented CAIX expression in the ST. RT showed a similar immunoexpression.
Conclusion: The uncommon presence of ST encountered in our study is concordant with literature. CD10 may be more useful than CAIX identifying ST regardless of underlying RCC subtype, meanwhile, CAIX appears to be closely associated with ST of clear cell RCC.

PS-18-070
Prognostic significance of P16 expression in high-grade prostate adenocarcinoma
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Background & objectives: Management of advanced hormone-naïve prostate cancer is a critical public health issue. Useful prognostic markers are needed to select patients who will benefit from chemotherapies. This study is aimed to determine whether p16 expression would be an adverse prognostic marker.
Methods: Patients diagnosed with adenocarcinoma with Gleason score ≥8 by needle biopsy from 2010 to 2013 at Aichi Medical University were enrolled (n=79). p16 staining was considered positive when nuclear and/or cytoplasmic staining was observed in regions where > 50% cells were stained.

Results: The median patient age was 73 (range, 52–87) years. The median follow-up was 62 months (range, 2-98). Fourteen patients had p16-positive samples. Fifteen patients died from prostate cancer, 10 of whom were in the p16-positive group. p16 positivity was associated with clinical T stage (P<0.001), presence of IDC-P (P<0.001), distant metastasis (P<0.001) and lymph node metastasis (P<0.001). p16-positive patients had significantly worse prognoses for CSS and PFS (P<0.001, P<0.001, respectively).
Conclusion: Our results indicate that p16 expression is associated with adverse prognostic factor of prostate cancer and suggest that p16 expression may provide useful information for treatment planning and identifying suitable candidates for upfront chemotherapy or androgen receptor axis-targeted therapy.

PS-18-071
Clear cell renal cell carcinoma - the real deal?
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Background & objectives: Renal cell carcinoma (RCC) accounts for more than 90% of adult kidney cancers, occurring more frequently in males and histology is dominated by clear cell RCC. The goal of this study is to highlight the necessity of routinely genetic assays.
Methods: We included in our study a total of 155 adult patients with RCC excised by radical nephrectomy between 2016-2018 with focus on identifying incidence, social aspects, histologic subtypes (correlated with WHO 2016 guidelines), nuclear grade, immunohistochemical features and all relevant prognostic factors. Only a few patients benefit of genetic tests and results were compared with morphology and molecular phenotype.
Results: Males were affected more commonly than females with a ratio of 1,44:1 and mean age was 61 years ± 12,6. The majority of RCC were unifocal, confined to the kidney and with nuclear grade 2. Histology revealed that most of clear cell RCC had classical acinar pattern admixed with papillary, cystic, tubular or sarcomatoid features. Although clear cell RCC is still the most common subtype of adult kidney cancers, the incidence of this subtype has slightly decreased over these years, from 72% to 68% in our study. Even with adequate sampling and nearly correct fixation time, immunostains expression is variable, being not very helpful for positive diagnosis.
Conclusion: Clear cell RCC is probably over-diagnosed due to its multiple histologic patterns and it is likely to lose this kind of supremacy in future pathology reports.
Molecular and genetical subtyping needs to be included in an accurate RCC diagnose.

PS-18-072
HOXB13 – future opportunities in sporadic prostate cancer profiling
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Background & objectives: HOXB13 plays a key role in normal prostate development, regulating cellular response to androgens. Tissular overexpression of HOXB13 has been studied, particularly in hereditary prostate cancer. We focus on establishing HOXB13 as a potential prognostic biomarker, in non-inherited prostate cancer.
Methods: The immunohistochemical expression of HOXB13 was assessed on a preliminary lot of 25 prostatectomy specimens with sporadic prostate cancer. Results were correlated with ERG and SPINK1 molecular subtypes and histopathological variants. For estimating the potential prognostic value, HOXB13 expression was correlated, using chi square and Fisher tests, with age of onset, Gleason Grade, Gleason Score, predominant pattern, staging, PSA levels.
Results: All 25 cases, were ERG IHC positive and, thus SPINK1 negative, and only 60% of these showed moderate and strong IHC expression of HOXB13, suggesting a positive link between ETS rearrangements and HOXB13. Also, tumours with Gleason Score ≥ 7, overexpressed nuclear HOXB13 in 73% of the cases, with moderate and strong staining observed in dominant histopathological variant ≥ G4. All tumours staged pT3 or pT4 (16%) showed moderate to strong HOXB13 nuclear signal. HOXB13 expression was not statistically correlated with PSA levels (p value of 0.18423), and also with the age of onset, Gleason Score or Gleason grade, mainly due to the small size of the lot.
Conclusion: In pursuit of novel prostatic biomarkers, for detecting indolent and aggressive forms of disease, and for refining the therapeutic management, HOXB13 appears to be a potential candidate, apparently combined with other consistent markers, but validation on bigger populations is required.

PS-18-073
Histopathology of cryptorchidism. Review of ten undescended testicles from 2012 to 2019
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Background & objectives: Cryptorchidism refers to an absence of at least one testicle in the scrotal sac. Testicles develop in the abdomen, scrotal migration is usually completed around 35 weeks' gestation. About 3% of full-term/30% of premature infants are born with undescended testicles.
Methods: Undescended testicles are associated with decreased fertility, increased germ cell tumours (more commonly seminomas), torsion and inguinal hernias. Orchidopexy is the preferred mode of management in case of viable testes, recommended before 1 year of age.
We will review 10 cases of cryptorchidism diagnosed in Hospital Universitario Marqués de Valdecilla from 2012 to 2019, detailing their clinical and histologic features.
Results: Our cohort was aged from 3-month old to 48-year-old patients (mean age: 17.8-year-old). Location was inguinal in 8 patients and intraabdominal in 2 patients. 9 cases were left-sided and 1 case was bilateral. Every testicle was age-adjusted atrophic, with volumes ranging from 0.3 cm3 to 7.5 cm3 (mean volume: 2.8 cm3), except for a 21.9 cm3 testicle with gonadal dysgenesis (GD) syndrome.
Conclusion: Histologic features included atrophic seminiferous tubules, hypospermatogenesis, Leydig cells hyperplasia, Pick adenomas, intratubular microlithiasis, fibrous parenchyma with interspersed presence of Fallopian tube, ovarian cortex and endometrial tissue in the GD patient, and parenchymal haemorrhage in two patients with testicular torsion.
Understanding the spectrum of features associated with undescended testicles is essential in order to be able to detect suspicious lesions.

PS-18-075
Mismatch repair protein status and GATA3 expression in bladder urothelial carcinoma
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Background & objectives: Mismatch repair genes and GATA3 are important in preserving genetic stability and cell proliferation. Although GATA3 is used as a marker for urothelial differentiation, there are few reports regarding MMR status or its correlation with GATA3 in bladder urothelial carcinoma.

Methods: 66 patients who underwent transurethral resection of bladder tumour were selected. Multi-tissue blocks were made and slides were stained for GATA3, MLH1, PMS2, MSH2 and MSH6. We evaluated MMR status and GATA3 expression in muscle invasive high-grade (MIBC - 36 cases) and non-invasive low grade (NMIBC - 30 cases) bladder urothelial carcinoma and correlated them with pathological parameters
Results: Four cases express loss of MMR protein (three for PMS2; one for MSH6). Three of them were MIBC with extensive necrosis or squamous differentiation. Only one NMIBC showed loss of PMS2 and it was associated with early onset and papillary features We found a statistically significant correlation between GATA3 expression and invasion status (p<0,001) and tumour extent (p<0,05). There was an inverse relationship between GATA3 expression and perineural/perivascular invasion or tumour necrosis but it was not statistically significant (p=0,173). Although GATA3 presumably interacts with MSI through TGBβ pathway we found no correlation between these two in our study.
Conclusion: MMR loss is rare in bladder carcinoma and the most frequent mutation is for PMS2. GATA3 expression was significantly lower in high versus low grade tumours and it correlates with tumour extent.

PS-19 Cardiovascular Pathology

PS-19-001
Aortic medial degeneration: a clinicopathologic study of 269 cases in a cardiovascular centre

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Background & objectives: This study aimed to apply the Consensus Statement on surgical pathology of the aorta from the Society for Cardiovascular Pathology and Association for European Cardiovascular Pathology on Noninflammatory Degenerative Diseases – Nomenclature and Diagnostic Criteria in a Philippine cardiovascular centre.
Methods: This retrospective cross-sectional study involved archival cases from institutional and surgical pathology files from the Division of Laboratory Medicine from patients who underwent aortic surgery between January 2009 to December 2016. Slides were reviewed to evaluate histologic abnormalities. Standardized reporting is applied based on the Consensus Statement from the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology.
Results: A total of 269 cases were included in the study [male = 183 (68%), female = 86 (32%), range of 12-82 years, mean age of 53.27 years]. Majority of surgical indications (97%) were aortic aneurysm and/or dissection. Concomitant surgery was performed on 163 patients (61%), mostly aortic valve replacement (41%). Overall, 184 patients (61%) had one or more forms of acquired cardiovascular disease including systemic hypertension in 65%. Mucoid extracellular matrix accumulation was the predominant component of medial degeneration (82%) and 48% of cases were moderate medial degeneration. There were 35 deaths among 269 patients, 24 (69%) of which died as a result of aortic dissection or rupture.
Conclusion: We identified the clinicopathologic features of patients with aortic medial degeneration using the consensus grading system which provides a standardized and unified method for surgical pathology reporting of noninflammatory degenerative aortic pathology.

PS-19-002
The spectrum of rheumatic valvular heart disease in a cardiovascular centre in the Philippines spanning 40 years

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Background & objectives: High incidence of rheumatic heart disease (RHD) is still reported in underdeveloped nations. In this study, we described the socioeconomic, demographic, clinical pattern, and histopathology of patients with RHD in a cardiovascular centre in the Philippines from 1977 to 2016.
Methods: This retrospective cross-sectional study involved archival cases from institutional and surgical pathology files from the Philippine Heart Center from patients with RHD who underwent valvular replacement surgery, repair, and redo, and in whom clinical history and histopathologic data were concordant, from January 1977 to December 2016. Medical charts and/or hospital information system records were reviewed and corresponding data were recorded.
Results: The study group of 4,455 patients consists of predominantly female (54%), with interquartile mean age of 16 (paediatric) and interquartile mean age of 31 (adult). Patients from low-income households consists of 51.20%, most of which hail from Central Luzon (21.80%). Associated comorbidities include pulmonary hypertension (15.98%), congestive heart failure (11.31%), and cerebrovascular accident (2.96%). The mitral valve is mostly implicated in chronicity, severity, and rheumatic activity (53.74%).
Conclusion: The spectrum of RHD comprises low socioeconomic status from dense populated regions, female gender, and early adult age at presentation. There still exists a significant number of cases of RHD in the Philippines. Updated screening tools should be explored, and preventive practices from developed countries with declining incidences should be modelled upon. Early detection, community education, and efficient diagnostics are instrumental for appropriate antibiotic coverage to thwart development of acute rheumatic fever and to cull the rise of RHD.

PS-19-003
New strategy for investigations bioelectrical signals during embryogenesis

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Background & objectives: The Looping of the human primitive cardiac tube transforms the straight tube in a helical Loop by complex atrioventricular (AV) rotations and cells migrations which may lead to the most complex congenital heart diseases (CHD).
Cell polarity and electrotaxis play an important role in the embryogenetic process.
We present a new device focusing on endogenous bioelectric field in chick embryo model comparable to the human and on the effects of applied electrical DC tensions that implements morphologic patterning.
Methods: We assumed the Maxwell's equations in a biological system, the Coulomb law and the Lorentz's forze concept expressed as vector at a given embryogenetic point.
We designed a passive two terminal condenser storing a uniform 800 mV/mm electric field (EF) between two aluminium plates 13.5x25 cm each other faraway 6 cm connected to the poles of 48/V battery.
Inside the EF is positioned a two wood shelfs container with 6 orizontal fertilized eggs almost simultaneously led with their long axis perpendicular to the plates so the EF forces will act perpendicular to the embryo's primitive streak, from 18 till 40 hours of incubation (gastrulation looping septation periods). Inverting the poles in other 6 eggs we reverse the polarity of the EF and therefore of the embryos. The chicks at birth are sacrificed, stored in liquid nitrogen -196 and the heart is micro-examined.
Results: The experiments are ongoing. We present the preliminary results.
Conclusion: We believe that reversing the embryonic polarity may deeply influence the AV rotation therefore the incidence of complex CHD.

PS-19-004

Congenital heart diseases: linking embryology to clinical practice

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Background & objectives: The classical paediatric cardiac surgery in severe Congenital Heart Diseases (CHD) still carries high mortality and poor results: operative mortality in Fontan 1.2%; Glenn/Emi-Fontan 2.5%; Arterial Switch-VSD 5.3%; Truncus Arteriosus 9.4%; Norwood procedure 15.7%. Can we do better? On the light of the current molecular biology, a very early diagnosis and not invasive treatment during pregnancy would strongly affect the medical and surgical history of these severe malformations.
Methods: We reconsidered:
- The embryogenesis and the morphology of the most severe CHD focusing on the right ventricle and the trabecula septomarginalis (TSM) anatomy in malformed cardiac phenotypes from dextroposition of the aorta to tetralogy of Fallot, double outlet or single outlet ventricles, transpositions of great arteries, univentricular hearts reviewing the related literature.
- The last advances of molecular biology on cardiac lateralization, cell polarity, cells migration and exosome characterization.
Results: Findings.
- The TSM rotates and follows the development of the right ventricle,
- The abnormal connections recapitulate an abnormal embryogenesis at Horizon X-XI (somite number 4-20) secondary to a pathological Looping and Lateralization of the primary cardiac tube
Conclusion: - NGS targeted sequences of selected genes panel known or suspected associated with a specific phenotype during the first month after conception can detect specific maternal cardiac exonic variants linked to an abnormal Looping (Lateralization),
- Stem-cells or CRISPR-Cas9 based techniques have the potential to interfer with the TSM rotation process leading up to less severe or normal cardiac phenotypes.

PS-19-005

Plasma cell infiltrate in the carotid plaque

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Background & objectives: Atherosclerosis is a chronic inflammatory disease that mainly involves T lymphocytes and monocytes. B lymphocytes and plasma cells have occasionally been detected. The aim of this study is to assess plasma cells frequency in a series of carotid plaques.
Methods: We evaluated retrospectively 50 carotid endartherectomies analysed at the Pathology Department of the University of Cagliari between January and May of 2018 and March and July of 2019. The histological assessment was confirmed with CD38 immunostain.
Results: Groups of at least 5 plasma cells were observed in 28% of cases: 18% were distributed in clusters (5-10 plasma cells) and 10% in sheets (more than 10 plasma cells). In almost half of cases (24 out of 50 cases) scattered plasma cells were revealed. No plasma cells were observed in 12 cases out of 50 cases analysed (24%).
Conclusion: Our preliminary data evidence that plasma cell infiltrates characterise more than a half of the carotid atherosclerotic plaques. Moreover, clusters or sheets of plasma cells are present in almost one third of cases. Further studies will highlight the clinical significance of the "plasma cell" subgroup of atherosclerotic plaques.

PS-19-007

Sudden arrhythmic death syndrome specialist referral centre: results from a national biobank

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Background & objectives: Rarely sudden cardiac death in the community is due to underlying genetic disease. In Ireland 10,000people carry mutations for inherited cardiac conditions (ICC). A biobank created in 2015 facilitates testing from autopsies, including a referral service for cases requiring expert pathology.
Methods: We retrospectively reviewed all referred cases between May 2015-Jan 2020 from those who have had tissue samples taken for genetic testing at the time of autopsy. Patient age, sex, weight, height, heart weight, thickness of left and right ventricles, toxicology results and diagnosis were recorded together with results from molecular analysis.
Results: 187 cases were bio-collected, including 121males and 66females, age range 5weeks-79years. 32% of the hearts were structurally normal. 34.7% were cardiomyopathies. Genetic studies were performed on 21 probands. 19 had a full 380 inherited gene panel and 2 had targeted cardiomyopathy 173-gene panel. 9 (43%) showed genetic variants: 4 were American College of Medical Genetics Class IV/V pathogenic mutations, and 5 were class III variants of uncertain significance (VUS). Follow-on familial screening detected 3 positive genotypes in 9 first-degree relatives. Screening of relatives of probands who displayed a VUS showed 5 ICC diagnoses in 19 first-degree relatives. Despite negative gene testing in 12cases, 9.5% of relatives were given an ICC diagnosis.
Conclusion: This study demonstrates the unique potential our biobank has to offer in terms of identifying those most at risk. Increased awareness of the current screening pathway is pivotal to diagnose these potentially lethal cardiac conditions and prevent further deaths.

PS-19-008

Cardiac tumours – a 20 year-long experience in a tertiary Portuguese institution

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Background & objectives: Heart tumours(HT) are known to be very rare, occurring in <1% of the population, supported by autopsy and clinical data-they showed that primary tumours(PT) have a lower prevalence than secondary tumours(ST). We present our expertise through a 20 year-long series.
Methods: Retrospective data pertaining to the period 2000-2019, including biopsy and excision specimens, were evaluated for the following criteria: diagnosis, age and sex.
Results: A total of 125 cases were assessed, 53%(n=66) were biopsies and 47%(n=59) were excision specimens; 64%(n=80) corresponding to women, 36%(n=45) to men; the mean age was 64,5 years, (maximum:86; minimum:18). From all, 95%(n=119) were diagnosed with PT and about 5%(n=6) with ST. Regarding PT, two-thirds (n=76) were diagnosed in women; from these 96%(n=114) were benign and 4%(n=5) were malignant. In the benign group, 85%(n=97) were cardiac myxomas, followed by papillary fibroelastomas, haemangiomas, lipoma, paraganglioma and inflammatory myofibroblastic tumour. In the malignant group, there were lymphomas, leiomyosarcomas and one myxofibrosarcoma. Concerning the ST group, carcinomas prevailed (67%) followed by melanoma, direct extension of thymoma and a peculiar case of intravenous leiomyomatosis.
Conclusion: HT are rare, mainly benign, occurring in women on the seventh decade, being predominantly myxomas, as described in the literature. The obtained data showed a higher frequency of PT once our sample did not include autopsy data.

PS-19-009

Inborn errors of energy metabolism are an infrequent cause of heart failure in adults undergoing cardiac transplant

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Background & objectives: Aim of the study was to assess the prevalence and phenotype of cardiomyopathy due to inborn errors of energy metabolism in adult patients undergoing cardiac transplant (CT).
Methods: A total of 110 hearts, consecutively explanted at the Department of Cardiac Surgery of San Camillo Hospital of Rome over an 8-years period, were retrospectively reviewed. The population consisted of 82 males and 28 females, mean age 50 years (range 19-73).
Results: Cardiomyopathy due to disorders of energy metabolism was observed in 4 out of 110 patients (3,63%), 2 males, mean age 25 years (range 20-45).
In three patients, skeletal muscle biopsy, performed before cardiac transplant, guided the diagnosis. Diagnoses were confirmed by genetic analysis.
Gross cardiac examination showed symmetric, biventricular hypertrophy (n=3) and biventricular dilation with multiple foci of myocardial scarring (n=1). Histologic examination showed extensive vacuolation of cardiac myocytes (n=4). Immunohistochemistry for lysosomal-associated membrane protein 2 (LAMP2) allowed diagnosis of Danon disease in one patient. Combined cytochrome c oxidase/succinate dehydrogenase stain demonstrated mitochondrial dysfunction in two patients. Ultrastructural analysis revealed glycogen accumulation (n=1), massive mitochondrial proliferation (n=2), autophagic vacuoles (n=1).
Conclusion: Cardiomyopathy due to inborn errors of energy metabolism are a rare cause of CT in adult. Pathologists may play a role in unravelling the aetiology, provided that a detailed diagnostic flowchart, including histology and ancillary technique is followed.

PS-19-010

Amitosenescence cells in aging heart

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Background & objectives: Human aging occurs both at the body level and at the cell level. Postmitotic cells may develop senescence and are called amitosenescence cells. The goal was to investigate amitosenescence cells in aging heart.
Methods: 42 biopsies of the heart and 48 autopsy cases (38 women and 62 men) were taken: 1 group - 80 patients (average age 72.9 ± 13.3 years) and 2 group - 20 patients, (average age 42.9 ± 13.3 years). Serial paraffin sections were stained with hematoxylin and eosin, picrofuchsin; p16ink, Apocas, CD68 and CD 45 were detected by immunohistochemistry (DakoCytomation).
Results: Amitosenescence cells were found in in myocardium of 77 aging patients and 2 young patients (premature aging?). Amitosenescence cells were characterized by prominent degenerative changes, that results of distuebances in intracellular regeneration, accumulation of lipofuscin in perinuclear zone of cytoplasm - which is the marker of mitochondria disfunction and increased lipid peroxidation. Reduction and sclerosis of capillary bad caused ischimia, cell degeneration and apotosis. Stroma of aging heart was lightly infiltrated with CD68+ macrophages and CD45+ lymphocytes. The latter may result from proinflammatory activity of amitosenescence cells.
Conclusion: Aging heart has increased number of amitosenescence cells that are characterized by disturbances in intracellular regeneration and protein metabolism, mitochondria dysfunction, genome alteration and proinflammatory response that may result in deterioration of heart diseases in aging patients.

PS-19-011

Tissue expression of ligand to programmed death receptor 1 (PD-L1) in endomyocardial biopsies of patients after heart transplantation - association with allograft rejection

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Background & objectives: Data suggest that PDL1 expression in donor tissue can down-regulate recipient alloreactive T cell responses by interaction with the PD-1 receptor expressed on alloreactive T cells, thus limiting the local inflammation leading to rejection and vasculopathy. The aim of the study was to assess the relation between PDL-1 expression in endomyocardial biopsies (EMBs) of adult patients after heart transplantation and allograft rejection.
Methods: The study included 15 patients with diagnosed antibody-mediated rejection (AMR), 12 patients with diagnosed grade 2 R acute cellular rejection (ACR), and 16 patients with no rejection. PDL-1 and C4d immunohistochemical stainings were performed in all EMBs. Graft rejection was evaluated according to ISHLT criteria. The non-parametric tStudent test was used to compare the results.
Results: 6 patients were diagnosed with AMR 1 (I), 4AMR 1 (H) and 5 AMR 2. Among all 15 patients with AMR, 5 additionally had grade 1R ACR features. The difference in PDL-1 expression within the groups was very different from the rest (patients with simultaneous AMR and ACR had a higher percentage of marker tissue expression), while the individual groups did not differ statistically from each other.
Conclusion: It seems that higher tissue expression of PDL-1 may be associated with a faster graft rejection resolution, however, it is not related to the type of rejection.
Funding: Internal grant of The Children's Memorial Health Institute for the development of young scientists no M36/18.

PS-19-012

Microvascular shift in dilated cardiomyopathy

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Background & objectives: Dilated cardiomyopathy (DCM) is a myocardial structural disease with reserved prognosis and "malignant behaviour". Our goal is to create a model of microvascular alteration and highlight a pattern that can be included in these new regenerating therapies.
Methods: From a total of 211 corpses, we randomly selected 35 cases with DCM related deaths and used automated immunostudies (CD34, CD31, Vimentin and Desmin). We compared our results with a control group of 7 patients (who died without cardiac causes) in purpose of quantifying fibrosis and correlate it with clinical evolution.
Results: In areas with advance fibrosis, endothelial expression (CD31 and CD34) was scarce combined with severe structural alteration (Desmin). These immunomarkers helped us revealing vascular channels near myocardial fibres. In 4 patients who died from malignant heart rhythm disorders, histology revealed subendocardial muscle nodules with central fibrous scar. These findings can be promising in the new regenerating therapies because it can show the quality of myocardial interstitial tissue.
Conclusion: Damage of cardiac microcirculation stands almost alone at the base of myocardial destruction, scarring and development of pump dysfunction.
Using gene recombining techniques (transferring 4 transcription factors), we can transform fibroblasts directly into endothelial cells stopping myocardial death and eventually, fibrillogenesis.
When applied in endomyocardial biopsies, advanced stage of fibrosis, severe structural changes can lead to inadequate response to new therapies.

Unfortunately, the affecting myocardium is patchy and can mislead us in grading structural lesions depicted in small biopsies.

PS-19-013

Modification of alcoholic cardiomyopathy by changing circadian rhythms (CR) in wistar rats in modelling of chronic alcohol intoxication

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Background & objectives: Alcohol abuse is a serious problem for modern society. The biological processes occurring in the eukaryotic organism undergo cyclic fluctuations associated with a change in the time of the day, the study of the chronotoxicity of ethanol seems relevant.
Methods: The study was conducted on 72 six-month-old male rats, divided into 2 groups, over 3 weeks. The first group (n=36) was kept under the fixed mode "light-darkness" (14 hours / 10 hours) and the second group (n = 36)-under constant lighting. Animals received a 15% solution of ethanol ad libitum. The material was examined histologically, histochemically and by electron microscope.
Results: In the first group of rats, the heart cavities did not expand. 19.4% of rats shows a moderate fatty degeneration of cardiomyocytes, small foci of cardiosclerosis and plasma impregnation of the walls of the arterioles. At ultrastructural level, a slight swelling of the mitochondria, single accumulations of lipofuscin were found. In the second group of rats, moderate hypertrophy of the heart was shown. The cavities of the heart, especially the left ventricle, were dilated. The myocardium in the section had a pale appearance. Fatty degeneration of cardiomyocytes, focal or diffuse cardiosclerosis were determined in all individuals. Electron microscopy revealed single Mallory bodies in the myocardium.
Conclusion: The results of the study suggest that changes in the CR lead to increased toxic effects of ethanol on the myocardium and the appearance of morphological markers of ethanol abuse (Mallory bodies).

PS-19-015

A qualitative and quantitative study of cardiac innervation in the myocardium of the normal human heart

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Background & objectives: Sudden cardiac death (SCD), mediated by ventricular arrhythmia (VA), is the most common cause of death worldwide. Recent studies have highlighted the importance of the autonomic nervous system (ANS) as a trigger and predisposing factor for VA. We aim to provide detailed topography and quantification of general, sympathetic and parasympathetic cardiac innervation in the normal heart.
Methods: Panel reviewed normal heart control cases had a non-cardiac cause of death. From ten cases, six sections of right ventricle and three of left ventricle were stained with PGP9.5, tyrosine hydroxylase (TH) and the choline transporter (CT). Slides were scanned using a Hamamatsu Nanozoomer 2.0RS and analysed using Visiopharm software.
Results: Within the epicardial fat there are large nerve fascicles and ganglia, most prominent around coronary arteries. These extend into the myocardium associated with blood vessels arborizing and becoming fibres and fibrils extending between and lying in close contact to myocytes. Very thin fibrils are seen in the subendocardium. No ganglia are seen in the myocardium.TH is predominantly distributed in the epicardial nerve fibres whereas CT is predominantly distributed in the small fibrils within the myocardium. We extrapolate that sympathetic nerves exert their effect through the epicardial ganglia whereas parasympathetic nerves act directly through cell to cell contact.
Conclusion: Defining the normal cardiac innervation, alongside potential mechanistic mediators that cause innervation alterations in the ANS within SCD victims with cardiomyopathy will identify novel targeted neuromodulatory techniques and therapeutic strategies. Specific innervation profiles will be established, enabling improved diagnostic characterisation and risk factors for SCD.
Funding: Cardiac Risk in the Young Pathological Society British Division of the International Academy of Pathology

PS-20 Cytopathology

PS-20-001

CINtec plus dual stain immunoassay and cobas HPV DNA test for triaging women with a history of LSIL referred to colposcopy

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Background & objectives: We assessed the clinical application of CINtec PLUS to serve as an adjunct test in comparison with cobas HPV DNA assay (Roche Diagnostics) for triaging women referred to colposcopy with LSIL cytology history.
Methods: Patients with LSIL history seen at the colposcopy clinic, Juravinski Hospital, Hamilton, Canada were prospectively enrolled with informed consent. Residuals of cervical specimens collected in PreservCyt at enrolment were tested with CINtec PLUS and HPV tests once at baseline. Biopsy confirmed cervical intraepithelial neoplasia 2 or worse (CIN2+) served as the clinical endpoint.
Results: Among all ages, there were 266 (44.3%) patients testing CINtec PLUS positive, and 331(55.2%) HPV positive ($p < 0.05$). For those >30 years, these figures were 41.2% and 50.8%, respectively. There was a significant difference between CINtec PLUS positivity and age groups: 50% in <30 years vs 41.2% in >30 years. These figures were 63.1% and 50.8%, respectively, for HPV positivity. Overall, 79.3% of CINtec PLUS positive cases were associated with HPV infection. In total, there were 54 (26%) cases of CIN2+ among 226 having biopsy. Sensitivity to detect CIN2+ was 81.5% for CINtec PLUS vs. 94.4% for HPV testing; specificities were, 52.4% and 44.1%, respectively.
Conclusion: CINtec PLUS assay or HPV DNA test is suitable for triaging women referred to colposcopy with a history of LSIL cytology and could serve as a predictor of CIN2+ with high sensitivity. Either test can significantly reduce the proportion of LSIL referral population requiring further colposcopy clinic visits, investigations and follow up, especially women >30 years. A greater reduction is achievable with cobas HPV testing through genotype 16/18-specific risk threshold.

PS-20-002

Lower resection rate and higher risk of malignancy in Asian series alter predicted outputs of the Bethesda system for reporting thyroid cytopathology

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Background & objectives: There is a growing evidence to suggest that clinicians employ different management approach while using The Bethesda System for Reporting Thyroid Cytopathology (TBS). We aimed to study the difference between Western (USA, Europe) and Asian series of thyroid nodules.
Methods: PubMed engine was queried from January 2010 to January 2019. Meta-analysis of proportion and their 95% confidence intervals

(CIs) were calculated using the random-effect model. We used independent samples t-test to compare frequencies, RRs, and ROMs between Western and Asian practices.
Results: A total of 38 studies with 145,066 nodules were analysed. Compared to Asian series, Western cohorts had a significantly lower ROM in most of TBS categories while the RR was not statistically different. Focusing on indeterminate nodules, RR in Western series was significantly higher (51.3% vs. 37.6%, p = 0.048) while ROM was significantly lower (25.4% vs. 41.9%, p = 0.002) in comparison to those in Asian series.
Conclusion: This study demonstrated a difference in Western and Asian thyroid cytology practice, especially regarding the indeterminate categories. Lower RR and higher ROM suggest that Asian clinicians conducted more conservative approach while immediate diagnostic surgery was favoured in Western practice for indeterminate nodules. The addition of Asian series into meta-analysis of TBS increased ROM for most of the diagnostic categories compared to the original TBS outputs, which should be considered in the future revisions of TBS.

PS-20-003
Audit on success rate of molecular testing in neoplastic lung cytological material in an Irish lung cancer centre
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Background & objectives: Lung carcinomas are often diagnosed via cytological specimens and tissue is often not available. Molecular methods have been adapted for cytological material. This audit assesses molecular testing success rates on cytological material obtained from lung cancers St Vincent's University Hospital.
Methods: All neoplastic lung cytological specimen reports between January 2016 and September 2019 in SVUH were reviewed. Sample types included EBUS-FNAs, pleural fluid, and bronchial washing/brushings. Data collected included tumour type, tumour content, molecular testing status, and whether molecular testing was performed on prior/concurrent tissue.
Results: 473 cytology reports were included, representing 432 unique patients. Molecular testing was conducted on 81 specimens (cell blocks, single gene/Oncomine lung panel), with 89 patients investigated on prior/concurrent tissue. Testing was successful in 68 cases (84%), with a mean tumour yield of 47% (median 50%, range 10%-90%). Failed tests mean tumour yield was 19% (median 10%, range 5%-80%). Tumour yield was significantly correlated to success rate (p=0.015). There was no statistical difference in the success rates between different sampling methods included.
Conclusion: Our success with molecular testing on cytological material indicate that this is a viable technique, particularly when tissue is limited. Further, success rates in our department are similar to other institution's reported rates. This audit also highlights the importance of high tumour yield, however, high yields still produced failed exams. We propose DNA yield be also reported and used to assess specimen quality in order to limit failed tests.

PS-20-004
Introducing the Milan system for reporting salivary gland cytopathology in the UK - how does it help?
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Background & objectives: The latest WHO Head&Neck Pathology edition includes 45 salivary glands tumours which, in combination with their rarity makes histological assessment difficult. The challenges are greater when reporting cytology specimens (FNA). Here we suggest the Milan System as a helpful tool.
Methods: To overcome some of these difficulties the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) was created to provide more standardized reporting and, mostly, a new category of Risk of Malignancy (ROM). ROM can guide cytological diagnosis, avoid medico-legal challenges of false positive/negative results, improve patient management. The MSRSGC is being successfully tested in several countries including the UK.
Results: Preliminary observations at the Royal Surrey Hospital -UK indicate: the introduction of ROM in cytopathology reports is clinically relevant to a) help cyto-pathologists to group salivary glands lesions into clinically meaningful categories, b) useful guide for treating clinicians to decide if further management according to the ROM category is required, c) meet turn-around time targets set for cancer treatment d)promote discussion of cytology reports in multidisciplinary Team (MDT) meetings.
Conclusion: The Milan System for Reporting Salivary Gland Cytopathology in the UK is a helpful tool in routine reporting of FNA specimens from salivary glands. A group of histo- and cyto-pathologists has been created to widen knowledge of MSRSGC & to implement application in routine practice in the UK. Given the shortage of cytopathologists in the UK MSRSGC can provide clinical guidance even in cytopathologists' absence at MDTs. Further work is recommended to create awareness of the MSRSGC in the NHS.

PS-20-006
Diagnostic value of fine-needle cervical lymph nodes cytology and needle washout thyroglobulin measurement for preoperative diagnosis and staging of papillary thyroid carcinoma
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Background & objectives: In this study we aimed to evaluate the diagnostic value of fine-needle cervical lymph node aspiration cytology (FNAC-LN) and needle washout thyroglobulin measurement (FNA-Tg) for preoperative diagnosis and staging of papillary thyroid carcinoma (PTC).
Methods: Twenty-eight patients with PTC with cervical lymph node metastasis (LNM) (n=23) and no LNM (n=5) on histology were included. Preoperative neck US, US-guided thyroid nodule FNAC and US-guided FNAC-LN with FNA-Tg measurement were performed. All the cases underwent surgery and histological examination. The sensitivity, specificity and accuracy of FNAC-LN and FNA-Tg for preoperative detection of LNM were calculated.
Results: The cyto-histological verification showed that in the group of cases with PTC and LNM, FNAC-LN was non-diagnostic in 4 cases (17%), benign – in 1 case (4%), suspicious for LNM –in 4 cases (17%) and positive for LNM in 14 cases (61%). In 21 patients with LNM (91%) FNA-Tg was positive (mean 158.20±115.39 ng/ml, 10.1-371.0 ng/ml) and in the remaining 2 cases (9%) –FNA-Tg was negative. In all PTC cases without LNM, FNAC-LN was benign and FNA-Tg was negative. The sensitivity, specificity and accuracy of FNAC-LN and FNA-Tg were 78.3%, 100% and 82.1% and were 91.3%, 100% and 92.9%, respectively.
Conclusion: Combined use of FNAC-LN and FNA-Tg showed improved sensitivity and accuracy in the preoperative diagnosis of metastatic PTC in cervical lymph nodes.

PS-20-008
Celldetect® results of a novel diagnostic staining method for detecting urothelial neoplasms
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Background & objectives: Urothelial cell carcinoma is the most common malignancy in the urinary system. Urine cytology has low sensitivity

for detecting low-grade urothelial neoplasms. Our objective is to evaluate the results of a new biomarker (CellDetect®) that promise improvement of diagnostic sensitivity.
Methods: Voided urine was collected from 78 patients undergoing follow-up for urothelial carcinoma or presented haematuria. Each sample was processed by ThinPrep® into two smears, one stained with Papanicolaou method and the other with CellDetect® technique. Results were compared with cystoscopy reports and patients' history.
Results: The Papanicolaou slides were classified according to the Paris reporting system. 78 were enrolled in the study. 26 were negative, 22 low grade urothelial neoplasms (LGUN), 10 high grade urothelial carcinoma (HGUC) and 20 atypical.
Interpretation of CellDetect® results is based on the combination of cell colour and morphology. CellDetect® was positive in all LGUN and HGUC as well as in 14/20 atypical cases. Nuclear staining of the neoplastic cells was red-purple, clearly distinguishable from the green shade of nonneoplastic cells.
Conclusion: Our findings show that CellDetect® is a promising novel staining technology that improves diagnostic sensitivity and can lead to the reduction of unnecessary cystoscopy. Additional research is required for establishing a minimum cell number for a positive CellDetect® result.

PS-20-010
Atypical breast cytology: a one-year experience
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Background & objectives: Atypical breast cytology poses significant diagnostic and management problems. The aim of the study was to review our experience with atypical breast cytology samples (C3 according to NCI criteria) and to correlate them with subsequent histological examination and/or radiological follow-up.
Methods: A total of 3504 breast cytology samples comprising fine needle aspiration biopsies and discharge smears were analysed in the year 2016. Among them, 270 cases (7.7%) were reported as atypical (C3). Follow-up was available for 173 cases (64%).
Results: Out of 173 cases with atypical cytology, subsequent histological examination was performed in 65 cases (37.6%), while the radiological follow-up only was provided in 108 cases (62,4%). None of the cases with radiological follow-up only was suspicious for malignancy. Histological examination was negative for malignancy in 44 cases (67.7%), and malignant in 21 cases (32,3%) . The overall malignancy rate was 12.1% (21 out of 173 cases).
Conclusion: Due to the relatively high percentage of histologically confirmed malignancy in atypical breast cytology samples (roughly 12% in our series), radiological follow-up should be mandatory for these patients, eventually supplemented by histological examination in cases with atypical/suspicious radiological features.

PS-20-011
The use of P16/ki67 double-stain immunocytochemistry in liquid-based exfoliative cytology specimens to screen for precursor lesions of the anal canal cancer in patients infected with HIV
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Background & objectives: Considering the role of p16 and Ki67 co-expression in high-grade cervical intraepithelial neoplasia, we hypothesized that CINtec PLUS®, an immunostain test that shows the simultaneous staining for p16/Ki67, has the same performance in detecting high-grade anal intraepithelial neoplasia anal.
Methods: Liquid-based cytology and biopsy of anal samples from 33 men and women infected by the Human Immunodeficiency Virus (HIV), with no visible lesions detected on external examination, were evaluated by immunocytochemistry using a morphology independent interpretation of the double-stain for p16/Ki67 and by the PapilloCheck® test for HPV detection.
Results: positive samples were observed in 77.77% of those with cytological abnormalities and in 42.85% of the negative samples. Concomitant positive expression of p16/Ki67 (p16/Ki67+) was observed in 33.33% of samples with cytological abnormalities. P16/Ki67+ cytology samples showed double-stained cell clusters and most positive cells were atypical cells. In biopsy with high-grade squamous intraepithelial lesion (HSIL), double-stained cells were observed in full thickness of the epithelium.
P16/Ki67 expression was observed in the only sample diagnosed as HSIL by biopsy, but only one of the seven samples diagnosed as low grade squamous intraepithelial lesion (LSIL) was p16/Ki67+.
Conclusion: The results suggest that p16/Ki67 immunostaining is a method that may be useful for improving cytology specificity in detecting high-grade anal squamous intraepithelial lesions.

PS-20-012
The accuracy of liquid based cytology in the diagnosis of salivary gland lesions
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Background & objectives: Fine needle aspiration (FNA) is widely used to investigate salivary gland lesions (SGLs), traditionally by conventional smear but increasingly by liquid based cytology (LBC). Our aim was to assess accuracy of LBC in the diagnosis of SGLs.
Methods: FNA was performed freehand or under ultrasound guidance (USG), collected into PreservCyt and Papanicolou-stained ThinPrep slide prepared. Specimens were classified as non-diagnostic or diagnostic (subclassified as specific or indeterminate - descriptive or differential diagnosis). Compared to histology, they were classified as non-concordant or concordant (subclassified as complete - correct specific diagnosis, or satisfactory - correctly classified as benign or malignant).
Results: Over 3 years, 84 FNAs were received with 45 (53.6%) diagnostic and 39 (46.4%) non-diagnostic. The percentage of non-diagnostic specimens is slightly higher than that reported in the limited literature (up to 40%). Using freehand sampling, 50.9% were non-diagnostic, while 38.7% of USG specimens were non-diagnostic. The specific diagnosis with USG FNAs was 41.9%, more than double that of freehand (18.9%). 18/27 lesions which underwent a histological assessment had an initial FNA classified as diagnostic. 17/18 (94.4%) were concordant, with 6/18 complete and 11/18 satisfactory. The overall concordance at 94.4% is slightly higher compared to that previously published (75.5-91.1%).
Conclusion: In most cases LBC is sufficient for correct classification of SGLs as benign or malignant, appropriately directing further management. However, a specific diagnosis could be provided in more cases with greater use of USG.
Funding: Hayley Morris is an NHS Education for Scotland funded Clinical Lecturer in Pathology.

PS-20-015
Comparison between cytology and biopsy in the diagnosis of lung nodules using the Papanicolaou Society of Cytopathology system for reporting respiratory cytology
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Background & objectives: To compare the results of respiratory cytology and corresponding biopsy specimens in the diagnosis of lung nodules

using the Papanicolaou Society of Cytopathology System for Reporting Respiratory Cytology, published in 2019.
Methods: 68 patients (42 male and 26 female) with suspected lung lesions by imaging studies underwent a CT-guided biopsy between August 2019 and January 2020. Cytologies were reported according to the proposed by the Papanicolaou Society of Cytopathology in its most recent publication and subsequently compared with their respective biopsy specimens. The results were obtained through statistical analysis.
Results: The average age of patients included in this study was 63.5 years old. The comparison resulted in 41 true-positive cases, 3 false-positive cases, 7 false-negative cases and 17 true-negative cases. Statistical analysis leaded to a sensitivity of 85.4%, specificity of 85.0%, positive predictive value of 93.2%, negative predictive value of 70.8% and accuracy of 85.3%.
Conclusion: The recent system for reporting respiratory cytology is very useful, with high rates of accuracy, sensitivity and specificity. This fact highlights the importance of the incessant search for the improvement of the standardization of cytological reports, aiming at making a more accurate examination. In addition to better results for patients, these standards facilitate the communication and understanding of pathologists and cytopathologists from all over the world.

PS-20-016

Fine needle aspiration biopsy of atypia of undetermined significance (AUS) with predominant Hurthle cells of the thyroid

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Background & objectives: Thyroid nodules with Hurthle cells(HC) comprise different pathologic entities; Hashimoto Thyroiditis, HC adenoma-carcinoma and oncocytic type papillary carcinoma(PC).Various diagnostic cytological criteria have been proposed in FNAs containing HCs to distinguish nonneoplastic from neoplastic lesions but there is limited agreement between the investigators.
Methods: FNAs of thyroid nodules, were diagnosed as being atypia of undetermined significance (AUS) with predominant HCs (>%50), between 2015-2019, were included in the study. All patients underwent surgical resection at our institution. FNAs were retrospectively reviewed for the presence of cytomorphologic features; cellularity, cytoarchitecture, percentage of HCs and dyscohesive HCs, presence of multinucleated cells, nuclear pleomorphism, nucleolar prominence.
Results: We also evaluated small cell dysplasia, large cell dysplasia, background colloid, chronic inflammation, cystic change, papillary nuclear features (glassy nucleus, elongation, nuclear irregularity, groove, overlapping and intracytoplasmic inclusion).The results were estimated by using SPSS analysis. A total of 20 FNA samples (5 nonneoplastic, 9 oncocytic type PC,3 classic type PC,2 follicular type PC,1 HC carcinoma) from 16 females and 4 males with a median age of 42.5, were reviewed. All cases were divided into two categories on the basis of the diagnosis; benign HC lesion(BHCL)(n=5) and malignant HC neoplasia (MHCN)(n=15).Presence of multinucleated giant cells was evaluated statistically significant(p=0.014) in predicting BHCL cases; nucleolar prominence (p=0.033)and small cell dysplasia(p=0.014) were significant in malignant cases.
Conclusion: The cytologic distinction between HC lesions can be diagnostically challenging. More comprehensive studies are needed in this regard.

PS-20-017

Non 16/18 hrHPV genotyping – results from the Northern-Portuguese cervical cancer screening program

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Background & objectives: The Northern-Portuguese Cervical Cancer Screening Program is primarily based on Human Papillomavirus detection of 14 high-risk(hr) genotypes.
Aims:To determine (1) the prevalence of hrHPVs, particularly non-16/18 hrHPVs; and (2) the prevalence of persistent infection with non-16/18 hrHPV 1-year after detection.
Methods: Retrospective cohort study at IPO-Porto with (1) 88,890 women screened from May 2017 to April 2018; and (2) 461 non-16/18 hrHPV-positive women screened in May2017 and without cytological abnormalities, who were retested for hrHPV after 1-year.
Clinicopathological information was collected from electronical clinical files (age, hrHPV subtype and cytological classification according to Bethesda 2015).
Results: A total of 10,246/88,890(12%) women, mean age of 44years(range:24-66), tested positive for hrHPV. Distribution of hrHPV genotypes was as follows HPV16(15%)|-18(5%)|-31(16%)|-33(4%)|-35(5%)|-39(15%)|-45(4%)|-51(12%)|-52(12%)|-56(10%)|-58(9%)|-59(7%)|-66(10%)|-68(15%). Co-infections (2-8 genotypes) were observed in 2878(28%). Of the 10,246 hrHPV-positive cases, 8484(83%) underwent cytological evaluation: NILM(60%)|ASC-US(23%)|ASC-H(3%)|LSIL(11%)|HSIL(2%)|SCC(<0.1%)|AGC(<0.1%)|AIS(<0.1%)|-Unsatisfactory(2%). Of the 8102 women with exclusive non-16/18 hrHPV infections, 3075(38%) had abnormal cytologies [abnormal results for single-HPV infections ranging from 26%(HPV45)-44%(HPV51)]. Co-infections were associated with higher percentages of abnormal results (68%vs32%;p<0.001).
Of the 461 women with non-16/18 hrHPV-positive cytology retested after 1-year, 47% maintained hrHPV-positivity, including 184(84%) with persistent infections and 34(16%) with new hrHPV infections (29/34 non-16/18). Excluding HPV16/18 infections, cytologic abnormalities were tendentially more frequent in women with persistent infection (38%vs21%,p=0.097).
Conclusion: In conclusion, genotyping of non16/18 hrHPV, including determination of the presence of co-infection and accurate definition of viral persistence, provides valuable information from an epidemiological and clinical perspective.

PS-20-018

Significant clinico-radiological factors affecting risk of malignancy in atypical diagnostic category by the Yokohama system for reporting breast fine needle aspiration cytopathology

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Background & objectives: Atypical diagnostic category by the Yokohama system for breast fine-needle aspiration (FNA) reveals risk of malignancy (ROM) from 13 to 25%. Selecting cases for further management may reduce invasive procedures. We aim to determine significant clinico-radiological factors that affect ROM
Methods: All breast FNAs with atypical diagnostic category at Chiang Mai University Hospital between 2015 – 2019 were selected. Surgical follow-ups were compared for calculated ROM. The clinical and radiological findings were analysed to find the significant factors which were associated with increased ROM, using multivariable logistic regression.
Results: There were 240 aspirates from patients aged between 15-77 years old. The tumour size ranged from 0.2 to 9.5 cm. The breast imaging showed 42 cystic lesions, 187 solid lesions, 19 architectural distortion, 32 intra-tumoral calcification. Histology were available in 218 cases. The ROM was 27.52%. The significant clinico-radiological factors were age; 40-60 years (p-value 0.033); >60 years (p-value <0.001), size; >1 cm (p-value <0.001); intra-tumoral calcification (p-value < 0.001).
Conclusion: Atypical diagnostic category revealed a variety from benign to malignant in histological diagnoses. However, most cases in this category were benign (ROM 27.52%). For these reasons, this category was

difficult to make clinical decisions. This study showed the significant clinico-radiological factors that increased malignant behaviour, including age (>40 years), tumour size (>1 cm), and intra-tumoral calcification. Selecting cases with these findings for further management may reduce invasive procedures and improve cost-effectiveness.

PS-20-019

The relevance of rapid onsite evaluation in endoscopic ultrasound-guided fine-needle aspiration to improve the diagnosis of autoimmune pancreatitis

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Background & objectives: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) and biopsy (EUS-FNB) represent important tools in the evaluation of pancreatic masses, having high sensitivity and specificity rates. The diagnosis has a great impact on surgical approach and the management of the patient.
Methods: We present three cases of male patients with solid pancreatic masses, one of them with suspicion of autoimmune pancreatitis. All patients underwent EUS-FNA and two of them underwent EUS-FNB using SharkCore needle with a rapid onsite evaluation (ROSE) by a cytopathologist.
Results: The smears showed a haemorrhagic background with abundant cellularity represented by large stromal fragments with embedded chronic inflammatory infiltrate, including neutrophils and eosinophils.
These findings raised the suspicion for an autoimmune process. Since autoimmune pancreatitis has diagnostic criteria that cannot be evaluated in a smear, a EUS-FNB was performed.
The cell block material revealed cylindrical fragments consisting of normal pancreatic tissue and fragments of pancreatic tissue substituted by abundant fibrosis with a storiform pattern around the ducts, associated with lymphoplasmacytic inflammatory infiltrate with few neutrophils and eosinophils.
Conclusion: According to the International Consensus Diagnostic Criteria (ICDC) EUS-FNA is not considered to be a good method for cytopathological diagnosis of autoimmune pancreatitis.
ROSE allows an immediate assessment and feedback about the adequacy of the material which leads to the improvement of the diagnosis and reduces the number of FNA passes. At the same time, it allows to evaluate the need for a FNB sample.

PS-20-020

Role of repeat fine needle aspiration in diagnosis of tuberculous lymphadenopathy

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Background & objectives: Tuberculous lymphadenopathy due to its protracted course associated with variable morphological findings, may at times cause difficulty in its diagnosis.
This study aims to find how a repeat aspiration study was beneficial in the diagnosis of Tuberculous lymphadenopathy.
Methods: The study included a total of 23 cases in which aspiration studies on the lymph node was performed and was earlier reported as reactive lymphadenitis. Repeat aspiration was performed on these same cases due to the persistence of lymph node enlargement from January 2019 to January 2020.
Results: A total of twenty-three (23) cases of cervical lymphadenopathy; twenty-one (21) of which were diagnosed initially as Reactive lymphadenitis and two (2) were diagnosed as suppurative lymphadenitis underwent repeat fine needle cytology aspiration procedure. The duration between the two procedures was 10-22 days. The result of the second procedure revealed marked differences in the cytomorphological features. Seventeen (17) cases showed frank caseous necrosis with positive Ziehl Nelsen stain for acid-fast bacilli. Remaining six (6)cases showed granulomas, giant cells, and caseous necrosis.
Conclusion: Repeat aspiration studies can be very helpful in cases of Tuberculosis lymphadenopathy. A proper patient counselling and communication with the clinician helps the patient to undergo repeat aspiration procedure thereby sparing the clinician from diagnostic uncertainty.

PS-21 Digestive Diseases Pathology - GI

PS-21-001

The prognostic impact of CD73 and a2a adenosine receptor (a2ar) immunohistochemical expression in colorectal cancer

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Background & objectives: In immune cells, CD73 degrades adenosine triphosphate into adenosine, which binds the A2A adenosine receptor (A2AR). This interaction potently inhibits immune responses against cancer. However, the expression of these two markers has never been studied in colorectal cancer (CRC) simultaneously.
Methods: We evaluated the immunohistochemical expression of CD73 and A2AR in tumour cells and stromal lymphocytes in tissue microarrays collecting tumour and adjacent non-tumour tissue specimens of 103 patients with CRC. Each of CD73 and A2Ar staining was evaluated by H-score.
Results: H-score values of CD73 and A2AR in tumour tissues were significantly higher compared to matched adjacent non-tumour tissues. Higher H-score values of both CD73 and A2AR in tumour cells were significantly correlated with advanced stage, poor overall survival and short recurrence free survival. However, High CD73 stromal expression was significantly correlated with better overall survival. Multivariate analysis further confirmed that both markers were independent prognostic markers for CRC patients.
Conclusion: CRC cases harbouring high levels of CD73 and A2AR are more liable for tumour progression. Therefore, these markers could be used as predictors for high risk patients, thus, to optimize individualized treatment for this group.
Funding: British Division of International Academy of Pathology, educational fellowship

PS-21-002

Colonic polyps in Nigerians; are adenomatous polyps on the rise?

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Background & objectives: The increasing access to colonoscopy services in sub-Saharan Africa has led to a rise in the number of adenomatous polyps seen, suggesting that they may well play an important role in the increased incidence of colorectal carcinomas in this region
Methods: This was a retrospective review of all colonic polyp specimens received at the Department of Pathology in our hospital between 2010 and 2018(9 years) utilizing the histopathology request cards and the Haematoxylin and Eosin stained slides. The specimens included both endoscopic biopsies and surgical resection specimens. Histologic diagnosis was confirmed and adenomatous polyps were subtyped and graded for dysplasia.
Results: 125 cases were reviewed in the study period. 60 cases(48%) were adenomatous polyps, 52 (42%) were inflammatory polyps while the remaining 10% included 9 hyperplastic polyps, 3 juvenile polyps and 1

harmatomatous polyp. The age of patients ranged from 5 to 86 years with a mean age of 55 years. The Male to female ratio was 1.75:1. Amongst the adenomatous polyps, 56 were tubular adenomas(93%), 3 were villous adenomas(15%) and 1 was a tubulovillous adenoma(2%). 16 of the adenomatous polyps showed high grade dysplasia (27%) while 44 only showed low grade dysplasia(73%). 2 of the adenomatous polyps were associated with colonic carcinoma in other parts of the colon.
Conclusion: Adenomatous polyps are increasingly being seen amongst Africans in the Sub-Sahara region and perhaps they aren't as rare as it was once thought. They may yet play a more important role in the pathogenesis of colorectal carcinomas in Africans.

PS-21-003
Pancreatic heterotopy: an unusual finding in cholecystectomy specimens - report of three cases
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Background & objectives: Heterotopic pancreatic tissue can be located in various regions of the digestive system with the least reported location being in the gallbladder. Gallbladder pancreatic heterotopia can be either an incidental finding or diagnosed in association with cholecystitis.
Methods: We report three cases of heterotopic pancreatic tissue in the gallbladder. One patient was a 24-year old male who presented with acute pancreatitis symptoms and an ultrasonographic mass in the gallbladder which proved to be heterotopic pancreatic tissue. The other two cases were female patients aged 24 and 32 respectively incidentally diagnosed on histopathological examination.
Results: A 24-year old man presented to the hospital with a intense upper abdominal pain radiating to the back. Ultrasonography revealed a mass initially believed to be an enlarged Mascagni lymph node and therefore laparoscopic cholecystectomy was performed. After the surgical removal, the tissue fragments were sent for processing and examination to our Department of Pathology. Gross examination revealed a white-yellowish pseudo tumoral mass, slightly lobulated. Microscopic examination showed a well-circumscribed fully developed heterotopic pancreatic tissue in the muscularis layer and extending to the subserosal adipose connective tissue. The findings were consistent with type 1 pancreatic heterotopia according to the Hindrich classification. In the other two patients, ectopic pancreatic tissue was incidentally discovered.
Conclusion: Despite being a exceptional encounter, gallbladder pancreatic heterotopia should be considered as a potential diagnosis in cases of cholecystitis and as an explanation for unusual ultrasonographic findings. In any case, the definitive diagnosis is only by histopathological examination.

PS-21-005
Gallbladders – a "grumble" for patients and pathology departments – a model for potential savings?
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Background & objectives: As numbers of specimen requests increase so do workload pressures in Histopathology. Over 60,000 UK patients undergo cholecystectomies/year. We determined diagnostic yield and processing costs based on block numbers per gallbladder. We propose resource savings through reduction in block numbers.
Methods: Numbers of gallbladders and block numbers were determined for the years 2012-19 from the pathology database of Greater Glasgow & Clyde NHS trust with SNOMED codes for chronic inflammation, dysplasia and adenocarcinoma for disease patterns. Workload and cost details were determined for a 12-month period in 2017/18. Complex resections and referrals were excluded.
Results: Annual gallbladder block numbers varied between 5555 and 7694 with requests static at approximately 2200 per annum. Mean number of blocks per gallbladder was 2.2. Approximately 72.5% of gallbladders show chronic inflammation. Significant pathology, including dysplasia (0.2%) and adenocarcinoma (0.1%) are rare. Processing costs for one block approximate £8.84, two blocks £11.29. Reducing the number of tissue blocks processed by one would save ~ £5000 per annum.
Conclusion: Reduction in the number of tissue blocks may improve turnaround times and reduce block storage costs. There is little good evidence for the cost-effectiveness of different tissue sampling strategies in Histopathology. Such evidence would allow more effective use of finite resources.

PS-21-006
A tale of two cities: a comparison of current practice in two district general hospitals looking at the impact of routine elastin staining to detect venous invasion in colorectal cancer resections
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Background & objectives: Venous invasion (VI) is a well-established independent prognostic indicator in colorectal carcinoma.
Elastin is a useful adjunct for detecting VI.
We compared VI reporting between Harrogate District Hospital (elastin as standard) and York Teaching Hospital (not using elastin as standard).
Methods: The reporting of venous invasion in all colorectal cancer resections was retrospectively audited at Harrogate District Hospital and York Teaching Hospital over a 1-year period (October 2018 – October 2019). The results were compared to the RCPath recommended standards and analysed for any significant impact in the routine use of elastin staining in Harrogate on the detection rate.
Results: 89 colorectal cancer resections from Harrogate and 210 cases from York were included for analysis.
Venous invasion was identified in 95 colorectal resections in York. Elastin staining was requested in 1 case and confirmed the presence of extramural venous invasion detected on Haematoxylin and Eosin.
There is a significantly higher detection rate of venous invasion in Harrogate where elastin is used as standard compared to York ($p = 0.037$).

	York Teaching Hospital [n=210] (%)	Harrogate District Hospital [n=89] (%)	P value
Cases with Identified Venous Invasion	95 (45)	52 (59)	0.037
Cases without Identified Venous Invasion	115 (55)	37 (41)	

Conclusion: Both trusts are exceeding the recommended RCPath reporting standards for detecting venous invasion in a minimum of 30% colorectal cancer resections.
Our comparison demonstrates a significantly higher detection rate of venous invasion in Harrogate where elastin is used as standard.

PS-21-007
Clinicopathological and molecular characteristics of poorly differentiated adenocarcinoma of the stomach
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Background & objectives: Adenocarcinoma with little glandular formation is classified as poorly differentiated adenocarcinoma (PDA) including signet-ring cell carcinoma (SRCC), non-solid type PDA and solid-type PDA. The present study aimed to clarify the relationship among clinicopathological and molecular features of gastric PDAs.
Methods: We randomly collected 154 PDAs (75 solid-type PDAs, 52 nonsolid-type PDAs, and 27 SRCC) from 154 patients. According to the method by Gonzalez et al., PDAs were classified into 4 groups using immunohistochemistry and in situ hybridization: EBV-associated GCs (EBV), microsatellite-unstable GCs (MSI), chromosomal-unstable GCs (CIN), and genomically stable GCs (GS). These clinicopathological variables were analysed statistically.
Results: Solid-type PDA showed significantly higher proportion (44%) of MSI in comparison with those (4% and 7%) of non-solid-type PDA and SRCC, respectively. Although most of non-solid type PDA and SRCC showed CIN and GS, proportion (85%) of GS in SRCC was significantly higher than that (48%) in non-solid-type PDA. In addition, SRCC preferred to occur in the middle third (70%) whereas non-solid type PDA developed in both middle third (35%) and lower third (35%).
Conclusion: These results suggest that solid-type PDA is different tumour from non-solid type PDA and SRCC. Moreover, although non-solid type PDA and SRCC shared several features, it is possible that SRCC which maintains signet-ring morphology is different from tumour which can transfer to non-solid type PDA.
Funding by: Governmental grants

PS-21-008
Topical application of high dose mesna prevents adhesion formation: an experimental animal study
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Background & objectives: Adhesions are common complications of abdominal surgeries. Mesna is a drug used in surgical field to facilitate tissue dissection. The aim of this experimental animal study was to investigate the effect of mesna on prevention of intraabdominal adhesion in rats.
Methods: 28 Wistar albino rats were used in the study. Cecum was abraded to create abdominal adhesion. No surgeries were performed other than adhesion in Group 1. 0.9% saline administered to Group 2, 40 mg/kg mesna for Group 3 and 400 mg/kg mesna for Group 4. Rats were sacrificed on postoperative 21st day. Histopathological and macroscopic evaluations of adhesion were performed.
Results: There were statistically significant differences in median severity, quantity, and total adhesion scores, but there were no statistically significant differences in median degree of adhesion scores. Group 4 had lower median quantity score than Group 1 ($p<0.038$) and 2 ($p=0.049$). Group 4 rats had lower median severity score ($p=0.042$) and median total score ($p=0.038$) than Group 2. Although there were no statistically significant differences in median degree of adhesion scores, Group 4 rats had lowest median degree of adhesion score than others. There were significant differences in median histopathological grading scores between the groups. Group 4 had lower median adhesion grading score than Group 1 ($p<0.001$) and Group 2 ($p=0.003$).
Conclusion: This is the first study for mesna on prevention of abdominal adhesion in rats. We concluded that dose-dependent reduction of adhesion was achieved by mesna which may indicate it as a potential adhesion-preventing agent for abdominal surgeries in the future.

PS-21-009
Histopathologic assessment of appendectomy specimens in elderly patients
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Background & objectives: The aim of our study is to determine the histopathological findings of appendectomy specimens in elderly patients who were over the age of 60.
Methods: Histopathological records of 130 appendectomy specimen submitted to the pathology Department at Baskent University in Ankara between 2011-2020 were reviewed retrospectively. The demographic data of 130 patients (59 males, 71 females; age range, 61-96 years) were noted. Histopathological diagnosis, acute appendicitis, gangrene and perforation rate, negative appendicectomy rate, and unusual findings on histology were recorded.
Results: Out of the 130 cases, acute appendicitis were detected in 104 (80%) specimens. Perforation rate was %38, gangrene rate was 18% and negative appendectomy rate was 1%. There was no statistically significant difference between males and females in the rate of perforation and gangrene. Low grade appendiceal mucinous neoplasm (n=8), carcinoid tumour (n=2), adenocarcinoma (n=1), diverticular disease (n=4), serrated polyp (n=3), hyperplastic polyp (n=13) and adenomatous polyps (n=14) were observed.
Conclusion: The findings suggest that acute appendicitis is the main histopathological findings in elderly population. In spite of the fact that the rate of acute appendicitis is high, precursor lesions and neoplasia were detected in 31.5% of specimens. Therefore, appendectomy specimens should be subjected to careful histologic examination in this age group.

PS-21-010
Comparative analysis of PD-L1 as prognostic factor in stage II and III colonic adenocarcinomas with the expression of mismatch repair proteins
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Background & objectives: Results of PD-L1 expression in colon carcinoma are heterogeneous, due partly to antibody selection and expression assessment, rendering its prognostic value unclear. We aim to study the prevalence and disease-free survival of PD-L1 expression and its relationship with MMR proteins.
Methods: Tissue microarrays (TMA) of 144 paraffin embedded tissue samples from early stage colon carcinoma patients were constructed. TMAs included four samples of central and infiltrative areas of each patient and were automatically stained for PDL-1 (SP142) and MMR proteins (MLH1/PMS2, MSH2/MSH6). PDL-1 expression was assessed in the tumour- stroma interface.
Results: Prevalence of deficit MMR proteins was (12.5%) and (20.1%) for PDL-1. The latter was significantly more expressed in deficient MMR tumours ($p<0.001$), right-sided localization and providing a better relapse-free survival p(log-rank) = 0.012. Additionally, the lack of PDL-1 presented a HR (95% CI) of 2.15 (0.91, 5.04) consistent with previous results. In the infiltrating zone, tumour-associated immune cells were more intense and frequent in PDL-1 expression compared to tumour cells.
Conclusion: The presence of PDL-1 in microsatellite stable tumours seems protective for both OS and RFS, while lack of expression confers a worse prognosis. Pathological assessment of PDL-1 is determinant, outstandingly if any trace of PDL-1 expression is considered positive "PDL-1 Sensitive", it reaches statistical significance for OS and DFS

and an overall risk reduction in the multivariate analysis of HR=0.52 (0.27, 0.98). The value of PDL-1 and MMR as a predictive maker for anti PD-1 therapy remains to be studied.
Funding: Project funded by European Development Fund.

PS-21-011

In search of an immunohistochemical classification of early stage colon adenocarcinomas, results of a tertiary hospital

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Background & objectives: Through transcriptomics, four Consensus Molecular Subtypes were delineated to classify colorectal cancer patients, however remains unviable to most hospitals. The aim is to emulate the concordant immunohistochemical panel proposed by Trinh et.al and Mismatch-Repair proteins and validate its prognostic utility.
Methods: For a cohort of 160 colon cancer stage II and III patients, four samples of each paraffin-embedded tissue sample (2 central and 2 infiltrating areas) were automatically stained for MMR proteins and CDX2, FRMD6, HTR2B and ZEB1 using tissue microarrays (TMAs). TMA slides were then digitalized and assessed. Score classifier was retrieved from the published online tool (crcclassifier.shinyapps.io/appTesting/).
Results: Subtype prevalence was CMS1=12.5%, CMS2/3=80.6% and CMS4=6.3%. Disease-free survival curves for the three groups were statistically significant (p=0.012), where CMS4 presented the worst prognosis. Right-sided localization related to CMS1 (p=0.003) who also presented a lower lymph node ratio and better prognosis. Pathological parameters as vascular or perineural invasion were also bad prognostic factors.
Conclusion: Our results correlate to those presented by Trihn et.al, particularly of CMS4 with known poor prognosis factors, which are also consistent with published literature and with clinical impact. Subtype prevalence seems diminished compared to Trinh, most likely due to early stage tumours of our cohort. Strikingly, more than 50% of patients were classified very near the proposed cut-off value. The sub-classification of CMS2 and CMS3 remains the biggest challenge.
Project funded by European Development Fund.

PS-21-013

Molecular characterisation of an adenoid cystic carcinoma (ACC) of the ooesophagus: case report and literature review

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Background & objectives: Adenoid cystic carcinoma is commonly associated with salivary glands but has been reported in other sites such as skin, breast and rarely, oesophagus. ACC has a distinctive biphasic morphology and is associated with specific molecular changes, namely the MYB-NFIB fusion.
Methods: We assessed a case of ACC of the oesophagus in a 74-year-old male for the presence of MYB-NFIB fusion. We also assayed for the presence of mutations in a Next Generation Sequencing panel of known cancer-associated genes. Finally, we present a review of the literature of ACC of the oesophagus.
Results: Our case of oesophageal ACC does not possess the MYB-NFIB fusion gene; however, sequencing of a panel of cancer genes revealed the presence of a mutation in TP53 (c.737T>G; M246R), which is a common mutation in salivary gland ACC. Reviewing recent literature cases of ACC of the oesophagus, we identified a tendency to misdiagnose oesophageal ACC.
Conclusion: This is, to our knowledge, the first description of the genomic analysis of ACC of the oesophagus. These results suggest an alternate genetic aetiology for ACC of the oesophagus compared to the majority of salivary gland ACC, and a similar lack of actionable mutations. Finally, we recommend a high index of suspicion for ACC in morphologically atypical squamoid malignancies in the oesophagus, and a low threshold for requesting appropriate immunohistochemical stains to rule it out.

PS-21-014

Duodenal gangliocytic paraganglioma

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Background & objectives: Gangliocytic paraganglioma in duodenum is exceedingly rare entity. Most gangliocytic paragangliomas are benign but metastases to regional lymph nodes are described in 10% of cases. Tumour size and invasion depth are considered as risk factors of lymph node metastases.
Methods: We present a case of a 72-year-old man who underwent upper gastrointestinal endoscopy as a part of normocytic anaemia workup. Endoscopy revealed a small duodenal subepithelial lesion adjacent to papillary orifice. Endoscopic ultrasound was subsequently performed, which demonstrated a 7 mm hypoechoic lesion localized in the submucosal layer, with no direct attachment to the muscle layer.
Results: Underwater endoscopic mucosal resection was performed. Microscopic examination of the resected specimen revealed a well-circumscribed submucosal tumour with characteristic triphasic, organoid growth pattern composed of three cell types: epithelioid carcinoid-like cells, Schwann-cell like spindle cells and ganglion type cells. Immunohistochemical reaction was positive for S100 in spindle cells, synaptophysin in epithelioid cells and calretinin in ganglion type cells. The resection margin was tumour free.
Conclusion: These findings are consistent with gangliocytic paraganglioma. Gangliocytic paraganglioma is extremely rare in duodenum but it should be included in the differential diagnosis when dealing with duodenal tumours. Tumour size and the depth of bowel wall involvement should be stated in the pathology report. Underwater endoscopic mucosal resection can be safe and effective technique for these subepithelial lesions.

PS-21-015

Gastric intestinal metaplasia: prevalence and distribution of Helicobacter pylori infection, dysplasia and carcinoma in its subtypes

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Background & objectives: Gastric intestinal metaplasia is considered as a precursor lesion for gastric adenocarcinoma. The aim of this study was to evaluate the prevalence of gastric intestinal metaplasia and distribution of Helicobacter pylori infection, dysplasia and carcinoma in its subtypes.
Methods: This prospective study was conducted at Kathmandu Medical College Teaching Hospital between December 2018 to December 2019. The endoscopic biopsies were evaluated for intestinal metaplasia and its subtyping was done with the help of periodic acid- Schiff/Alcian Blue and High Iron Diamine- Alcian Blue stain at pH 2.5. The biopsies were assessed for Helicobacter pylori, dysplasia and carcinoma.
Results: Intestinal metaplasia was observed in 182 (13.5%) out of 1350 biopsies. Type III intestinal metaplasia was the most frequent subtype found in 48.3% of cases. Helicobacter pylori was positive in 74(40.6%) cases most commonly observed in type I subtype (69.2%) whereas dysplasia (2.7%) and carcinoma (13.7%) were commonly seen in type III subtype.
Conclusion: Intestinal metaplasia is the common finding in endoscopic biopsies. Subtyping and long term follow-up studies is necessary with or

without eradication of helicobacter pylori to clarify the natural history of intestinal metaplasia and also to define the value of type III intestinal metaplasia as a precursor lesion for gastric carcinoma.

PS-21-017

Colorectal adenomas with high-grade dysplasia and pT1 adenocarcinoma arising on adenomas – significant morphologic prognosis factors

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Background & objectives: Colorectal adenomas can harbour high-grade dysplasia. Malignant polyps are defined by the invasion of adenocarcinoma, limited to the submucosa (pT1). This study compares the morphological features of these two entities to see how they affect the management of patients.
Methods: We conducted a retrospective, comparative study including 90 cases of colorectal adenomas (30 cases with high-grade intraepithelial neoplasia, 30 cases with intramucosal adenocarcinoma and 30 cases of pT1 adenocarcinoma arising on adenomas), recording age, gender, localization, size, tumour budding, angiogenesis, inflammatory response, necrosis, stromal reaction, vascular invasion, involvement of lamina propria, muscularis mucosa or submucosa and resection margins.
Results: The study included 50 males (55.55%) with ages between 36-81 and 40 females (44.44%) with ages between 35-87 years. 67 (74.4%) of the lesions were localized on the left colon. The size of the tumour correlated with the percentage of high-grade dysplasia (p=6,97E-08), with tumour budding grade (p=0.0002), with stromal reaction (p=0.001) and with the rate of angiogenesis (p= 0,00004). Vascular invasion was detected in 5 cases with pT1 (16.66%) and in a case of intramucosal adenocarcinoma (3,33%). In 15 cases the resection margins were positive and this correlated with the degree of recurrence and progression. 27 (30%) patients had more than one lesion in the colon.
Conclusion: Adenomas with high-grade dysplasia and pT1 adenocarcinoma arising on adenomas are more frequent in men and in the left colon. Tumour budding, angiogenesis, stromal reaction, vascular invasion and complete resection are the most important prognostic factors.

PS-21-018

Prognostic significiance of poorly differentiated clusters in mucinous colorectal adenocarcinoma

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Background & objectives: Mucinous adenocarcinoma (MAC) of the colon has >50% extracellular mucin within the tumour area. Currently there are no established histopathological parameters to accurately predict prognosis. Our aim is to evaluate prognostic value of poorly differentiated clusters (PDC) in MACs.
Methods: A total of 70 mucinous colorectal adenocarcinomas (MACs) with curative resections were included in the study. Tumours were graded according to the glandular differentiation (WHO; low&high grade) and on the count of poorly differentiated tumour clusters (PDC). The amount of extracellular mucin was classified into two categories as low (51-90%) and high mucin (>|90%).
Results: The median age was 56 years (min24-max85) with a M:F ratio of 43/27. Overall 42% of cases were stage 2, 48% were stage 3 and 10% were stage 4. According to the PDC; 50 (71.4%) of cases were PDC-grade1, 8 (11%) PDC-grade2, and 12 (17%) PDC-grade3. Based on glandular differentiation, 51 (73%) of cases were low grade and 19 (27%) high-grade. The proportion of extracellular mucin was low in 39 (56%) and high in 31(44%). tumours. Follow-up data was available for 44 patients and ranged between 5 to 135 months (median 34 months). 35% patients had recurrence and 30% of the patients died of disease.
Conclusion: PDC-grading, glandular differentiation and amount of mucin did not show prognostic significance in MACs. Our result is in conflict with previous limited-data on PDC-grading which found PDC to be a promising prognostic indicator in MACs. Further studies are required to establish PDC as a prognostic factor.

PS-21-019

Role of lymph node ratio in resected gastric cancer: a comparison with traditional N-staging

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Background & objectives: Gastric cancer (GC) shows high incidence and mortality rates. AJCC TNM classification system is the main tool for GC staging, and it determines patient prognosis and management. Lymph-node ratio (LNR) is a recently studied feature which could improve patient stratification.
Methods: Retrospective study of 198 cases of GC surgically resected in a tertiary hospital (Spain, 2000-2017). Clinicopathological features were collected, statistical analyses were performed and Kaplan-Meier curves were plotted and compared. LNR was categorized into 5 groups for survival analysis: score 0 (0%), 1 (>0%-<25%), 2 (25%-<50%), 3 (50%-<75%) and 4 (≥75%).
Results: 68% of patients were N+ (mean LNR:0.22). N-stage and LNR were significantly associated with vascular invasion, perineural infiltration, recurrences, and tumour death. Overall survival Kaplan-Meier curves depending on LNR showed good stratification, and three risk groups could be differentiated (scores 0+1,2+3, 4). N-stage curves were more overlapped and showed an inconsistent better survival for N2 patients in the first months. In cases with ≥15 LN resected, LNR showed an excellent stratification into 5 groups. N stage curves improved, but still showed overlapping. In cases with <15 LN resected, LNR curves were non-informative (p=0.692). Regarding disease-free survival, both LNR and N-stage showed good stratification but LNR curves were more evenly spaced.
Conclusion: LNR seems to stratify patients better than N-stage for GC recurrence and survival. LNR could be used as an adjunct to the traditional TNM classification. Unlike some previous studies, we have found that the retrieval of less than 15 LN could affect LNR prognostic significance, and LNR may not be used as an alternative to N-staging in this context. More studies are needed to confirm LNR prognostic role in GC.

PS-21-020

Prognostic role of TBK1 expression in resected gastric cancer

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Background & objectives: TANK-binding kinase 1 (TBK1) belongs to the non-canonical nuclear factor-kappa B (NF-KB) pathway. It is involved in cell proliferation, survival, metabolism, immune response, and autophagy. However, its role as oncogene or tumour suppressor depending on tumour origin is unclear.
Methods: Our aim is to evaluate the prognostic role of TBK1 immunohistochemical (IHC) expression in gastric cancer (GC). Retrospective study of 77 cases of GC surgically resected in a tertiary hospital (Spain). Tissue microarrays were constructed, TBK1 IHC expression was assessed and statistical analysis were performed.

Results: Most patients were T3 stage (61.6%) and N+ (77.5%). 50.7% of patients recurred and 36.2% died due to GC. TBK1 was positive in 64.4% of cases. TBK1 expression was associated with tumour desmoplasia and systemic symptoms, and inversely correlated to tumour stage. The association with Laurén subtype and tumour stage tended to significance. Disease-free survival curves successfully stratified patients into two significant risk groups, according to TBK1 expression (p=0.006). Survival analysis using Kaplan-Meier curves tended to significance (p=0.065). Patients with negative TBK1 tumours showed poorer prognosis than TBK1-positive patients. Multivariate analysis showed that TBK1 expression was independently associated with tumour recurrence.
Conclusion: Although nearly all previous studies recognize TBK1 as an oncogene, our results support the study published by Lee et al., in which TBK1 expression in GC was associated with better prognosis. Careful should be taken when extrapolating TBK1 prognostic role to other tumour types. Further research in larger sample sizes is needed to clarify the prognostic impact of TBK1 in different stages of GC.

PS-21-021
Prognostic role of YAP and P53 expression in gastric cancer
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Background & objectives: Yes-associated protein (YAP) is the nuclear effector of the Hippo-signalling pathway, which regulates cell proliferation and apoptosis. YAP overexpression has been identified in many cancers, but its role as oncogene or tumour suppressor gene is controversial.
Methods: Our aim is to investigate the clinical significance of YAP immunohistochemical (IHC) expression in gastric cancer (GC), and its relationship with p53 IHC expression. Retrospective study of 206 cases of GC surgically resected in a tertiary hospital (Spain, 2000-2017). Clinicopathological features were collected and tissue microarrays were constructed. YAP and p53 IHC expression were assessed and statistical analysis were performed.
Results: Both high YAP expression and complete loss of YAP expression were considered abnormal YAP staining. 83.4% and 16.6% of cases showed abnormal and "wild-type" YAP staining, respectively. Abnormal YAP staining was significantly correlated with lymphovascular invasion and tumour death. Stratification by YAP expression was significantly associated with overall survival. Multivariate analysis identified YAP expression as an independent prognostic factor. Kaplan-Meier curves were plotted, and patients with "wild-type" YAP expression showed significantly better survival rates. We further classified our patients into three groups: YAPabnormal+p53high, YAPabnormal+p53"not high" and YAPwild-type. This classification was also significantly and independently related to patient survival, and Kaplan Meier curves showed three groups with significantly different survival rates.
Conclusion: Abnormal YAP expression may be associated with GC prognosis, and p53 accumulation could enhance its prognostic impact. More studies are needed to clarify the role of YAP expression, its interaction with p53, and its effect on chemotherapy and immunotherapy.

PS-21-022
Differential expression of cytokine-coding genes BMP8B, LEFTY1 and INSL5 in ulcerative colitis and crohn's disease
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Background & objectives: Ulcerative colitis (UC) and Crohn's disease (CD) are characterized by imbalance between pro-inflammatory and anti-inflammatory cytokines, interfering with resolution of inflammation. New insights into their profiles would help to improve understanding of pathogenesis and enable development of new treatment modalities.
Methods: We analysed cytokine expression profiles of UC and CD, revealing 201 statistically significant differentially expressed cytokine-coding genes in UC and 36 in CD tissue samples. From 10 genes with inverse expression, BMP8B, LEFTY1 and INSL5 were selected for experimental validation with qPCR on endoscopic biopsies from 31 patients with UC, 25 patients with CD and 22 samples of normal mucosa.
Results: BMP8B was down-regulated in both diseases, but more in UC, followed by CD in the colon and the least in CD in the ileum. LEFTY1 was up-regulated in CD in the colon and down-regulated in the ileum, and less down-regulated in UC in the colon. INSL5 was down-regulated in CD in the colon and less in UC, while it was not expressed in the ileum.
Conclusion: Using bioinformatics approach, followed by an experimental validation, we found differences in expression profiles between UC and CD for INSL5, LEFTY1 and BMP8B. These three genes seem promising as potential diagnostic and therapeutic targets in CD and UC.
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PS-21-023
Tumour budding in colorectal carcinoma: results of TCGA dataset
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Background & objectives: Tumour budding (TB) is an independent adverse prognostic factor in colorectal carcinomas(CRC) and morphological representation of epithelial-mesenchymal transitions. However, its extensive correlation with genomic features is still missing. Here, we sought to perform genotype-phenotype correlations in the Cancer Genome Atlas (TCGA) data.
Methods: TB was evaluated and graded on the digital H&Es slides of CRC from TCGA (n=631) according to the guideline by two pathologists. TB defined as single cells or small clusters (<5 cells) at the peritumoral invasive front (pTB) and within the main tumour body (iTB). Association with molecular features was performed from the TCGA matched data.
Results: In the preliminary analysis reported here %34 (217/631) of TCGA colorectal carcinoma samples' H&E slides were evaluated. The level of agreement between observers was very high. We found high correlation between grade 1 pTP and low grade pTP. Higher grade of tumour buds, both iTB and pTB, were found significantly correlated with metastatic disease ($p<0.01$, both). High pTB and iTB showed significant correlation with microsatellite stable ($p<0.05$, $p<0.01$, respectively) and cancer molecular subtype 4 mesenchymal type ($p<0.01$, iTB)
Conclusion: Tumour bud is a worse prognostic parameter on colorectal carcinoma with particular genomic signature which reflects its position on EMT. Additionally, intratumoral tumour buds convey similar prognostic and characteristic information from tumours and they are big candidates on treatment decisions by endoscopic biopsies in the future.

PS-21-024
The feasibility of tissue microarray in immunohistochemical assessment of mismatch repair proteins in colorectal cancer – preliminary results
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Background & objectives: Tissue Microarray (TMA) enables allocating dozens of specimens to a single paraffin block. This is cost-effective for

expensive tests like Mismatch Repair (MMR) in colorectal cancer (CRC). This study demonstrates the accuracy of TMA in testing MMR mutations in CRC.
Methods: 864 2mm-TMA tissue cores were obtained from paraffin tissue blocks of 11 CRC patients who underwent previous immunohistochemical analysis of tumoral MMR status. 52 cores were incorporated into each TMA block and stained with specific antibodies for 4 MMR proteins (MSH2, MLH1, MSH6, PMS2). TMA-MMR staining was compared to the original results of each patient.
Results: The sensitivity rates for each MMR protein were 100%, with lower 95% confidence interval (95%CI) of 85%. The specificity of MSH2 and PMS2 were also 100% with lower 95%CI of 98.6%. The specificity of MLH1 and MSH6 were 96% with 95%CI: 94.3%-100%; and 98% with 95%CI: 96.6%-100%, respectively. Over-fixation seems to inhibit PMS2 staining (46.6% of the cores did not stain), whereas the rest had negligible unstaining rates (0%-0.93%).
Conclusion: Our results show remarkable per core sensitivity and specificity of TMA tissue samples. These results suggest that TMA may be considered an option for CRC MMR testing. Further studies which will estimate sensitivity and specificity per patient should be considered.

PS-21-025
Mast cells in colorectal cancer: potential prognostic marker?
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Background & objectives: The aim of the study is to assess the role of Mast cells (MC) in the morphogenesis of colon cancer and to identify the relationship between the prevalence of MC and the prognosis of the disease.
Methods: Two groups (n=30 each) of patients: death within the first year and patients who have lived more than 5 years since diagnosis. MC was identified by histochemical method (Giemsa staining). Quantitative evaluation of MC was performed in the stroma of the tumour and in invasive margin.
Results: MC were distributed unevenly the largest number was found in the invasive margin of the tumour. No significant difference was found between patients with different survival rates. However, in the group with early death without regional metastases, the number of MC in the invasive region was more than 2 times higher than the number of cells in individuals with metastases (4.5±0.4 and 2.1±0.3, respectively). All groups showed an increase in the number of MC in the invasive margin with decreasing degree of differentiation: in the group with early death: 2,1±0,2 (G1), 3,5±0,3 (G2), 11.4±0,4 (G3); in the group with five-year survival 1,6±0,2 (G1), 2,4±0,2 (G2), 3,6±0,4 (G3), respectively.
Conclusion: Quantitative indicators of MC were most different in groups with different degrees of tumour differentiation. MC can be used to assess tumour progression (the degree of differentiation in dynamic biopsy studies).

PS-21-026
Evaluation of toll-like receptors 9 expression in colon cancer
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Background & objectives: The role of TLR9 in the cancer process is ambiguous: they are involved in antitumour immunity and contribute to the evasion of tumour from the immune response. The aim is evaluation of the expression of TLR9 receptor in colon cancer.
Methods: Two groups (n=30 each) of patients: death within the first year and patients who have lived more than 5 years since diagnosis. Identification of TLR9 was performed using an immunohistochemical method.
Results: TLR9 expression in the centre of the tumour was observed in all the studied groups. Expression in the invasive region was found in 35% of patients with early death and in 80% of patients who lived 5 years or more. In the invasive margin, the average number of TLR9 positive cells in the first group was 0.6±0.3, and in the second group 1.2±0.3. The expression of TLR9 varies in the studied groups. In patients with a survival rate of more than 5 years, TLR9 expression is more pronounced. Increased expression at the edge of the invasion can be used as a criterion for predicting survival in patients with cancer.
Conclusion: The study of TLRs allows us to evaluate the activity of immune processes in the tumour microenvironment and the dependence of the clinical course of the tumour on these indicators.

PS-21-027
Low-grade appendiceal mucinous neoplasm (LAMN), an incidental finding?
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Background & objectives: LAMN are rare and account for 1% of the gastrointestinal neoplasms. They can determine a variable clinical behaviour. In case of rupture, the mucin spreads to the adjacent peritoneum, leading to pseudomyxoma peritonei, associated with poor prognosis.
Methods: We present three cases of LAMN: an incidental finding in a 81-year-old female patient who underwent surgery for ascending colon cancer, a 32-year-old female patient who underwent caesarean section at 38 weeks and appendicectomy and a 78-year-old female patient with non-specific symptoms, who performed a CT scan that revealed an enlarged appendix, with fluid content and calcifications of the wall.
Results: On gross examination, the appendix was dilated in all cases, up to 4 cm in diameter, with abundant luminal mucin and smooth serosa. Microscopic examination revealed predominantly a flat proliferation of the mucinous epithelium, with focally villous/papillary pattern, mild atypia of the epithelium, marked atrophy of the lymphoid tissue, fibrosis of the appendiceal wall and calcifications. A pushing pattern of invasion was identified in one of the cases. The dysplastic epithelial cells were positive for CK20, CDX2 and MUC2.
Conclusion: Frequently, LAMN are found incidentally. In one of our cases, the association between LAMN and ascending colon cancer raises the question if they might share the same mutation. Even if the prognosis is excellent for tumours limited to the appendix, radiological and clinical surveillance is required to prevent the risk of tumour recurrence.

PS-21-029
Predicting the patterns of response to neoadjuvant chemoradiotherapy in patients with locally advanced rectal cancer
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Background & objectives: To consider organ-preserving approaches for rectal cancer, favourable pathological response is needed. Since response is diverse, the goal of this project is to identify genetic predisposing factors and immune tumour microenvironment markers that could predict tumour response to therapy.
Methods: A cohort composed of 15 patients with complete tumour regression (TRG 0) and 15 patients with poor-or-no regression (TRG 3/4) was collected. Materials were formalin-fixed-paraffin-embedded biopsies and post-chemoradiotherapy resections. Next-generation sequencing was performed using a targeted gene panel. Histological tumour patterns of regression were determined. Immunofluorescence-multiplex was

performed for several immune markers, as well as an LC3-II stain for autophagy.
Results: Biopsies of bad responders tended to have higher intra-tumoral autophagy values compared to good responders. In tumour resections with response, intra-tumoral autophagy was higher in cases with a fragmented pattern compared to shrinkage pattern (p-value = 0.03). No clear difference in mutation patterns were observed. Results of the multiplex immunofluorescence stain of lymphocytes associated with the tumour will follow.
Conclusion: We showed a biological correlation between autophagy and tumour response pattern. The beneficial pattern of shrinkage is associated with low intra-tumoral autophagy. In advanced cancer cases, autophagy is considered a tumour growth promoter and is associated with tumour fragmentation.
Funding by: Alpe d'HuZes/KWF grant (Dutch Cancer Society).

PS-21-030
Redefining patterns of tumour response to chemoradiotherapy in oesophageal cancer with the aid of ai
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Background & objectives: Tumour response has been categorized in many ways within-and-between tumour types. In order for tailored treatment decisions to be made, there is a need for a reproducible, objective and standardized assessment of response which combines histological patterns and downstaging.
Methods: Our cohort was composed of 100 patients with oesophageal adenocarcinoma (cT2-T3) and treated with chemoradiotherapy. Three H&E slides per patient were analysed by a panel of pathologists and run through an algorithm to determine tumour cell percentage, size and distance between tumour fragments. Clinical data was used to determine correlations to survival and recurrence.
Results: Four histological patterns of regression were distinguished; fragmented (clustered or scattered), shrinkage and no-response. Tumour cell percentage was found to be significantly higher in clustered fragmentation subtype compared to scattered subtype in the mucosa (p=0.04) and tended to be higher in submucosa (p=0.08), muscularis (p=0.15) and subserosa (p=0.32). Recognition of these patterns of response and correlation with clinical outcome could provide a useful prognostic marker for further treatment. Preliminary results were obtained with only 70 patients, which we hope to raise to 100.
Conclusion: By using trained algorithms it is possible to accurately determine subtypes of patterns of response in an unbiased approach which might form the basis of predictive biomarker research. Moreover, our algorithms might be transferable to other cancer types.
Funding by: Alpe d'HuZes/KWF grant (Dutch Cancer Society)

PS-21-031
Gene hypermethylation of surrogate genes in subtypes of colorectal cancer
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Background & objectives: Colorectal cancer is one of the leading causes of cancer-related death. Our objective was to evaluate aberrant gene methylation of a recent panel of surrogate markers (CDX2, FRMD6, HTR2B and ZEB1) used to identify Consensus Molecular Subtypes with different clinical background
Methods: Methylation status of CDX2, FRMD6, HTR2B and ZEB1 genes was analysed in paraffin-embedded DNA by PCR and pyrosequencing in a series of 150 CRC patients and normal tissues. The presence of methylation of these genes was correlated with pathological and clinical variables by Kaplan-Meier curves and Cox regression model.
Results: - Gene hypermethylation was higher in right colon compared to left colon, being remarkable in the case of ZEB1 hypermethylation (p=0.002).
- CDX2 and ZEB1 hypermethylation were more frequent in cases without progression (p=0.053, p=0.047, respectively).
Conclusion: - Aberrant methylation is present in surrogate genes that help to distinguish between molecular subtypes.
- CDX2 and ZEB1 hypermethylation could be clinical indicators of good prognosis.

PS-21-032
Immunoprofile of tumour cells, in wild-type- versus mutant TP53 gastric carcinomas
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Background & objectives: The aim of this paper was to highlight the immunoprofile of gastric carcinoma (GC) cells, in correlation with the TP53 gene profile.
Methods: In 266 consecutive cases of GCs, mutations in exons 4 to 11 of the TP53 gene were checked and correlated with the immunohistochemical expression of HER-2, p53 and one of the p53-target gene, being known as Maspin protein.
Results: The mutation rate was 33.83% (90/266 cases), all of the mutations being identified in exons 4-8 and 10-11. Longer survival was proved for wild-type cases, compared with the mutant TP53, even in locally advanced tumours (p=0.01). From the 266 cases, 21 (7.89%) did not expressed Maspin; all of these cases showed lymph node metastases and risk for distant metastases and were TP53 mutant GCs, with mutations in exon 7. The p53 negativity was identified in 40 cases (15.04%), without correlation with p53 protein immunoexpression or HER-2 status. The Dukes-MAC-like staging system was proved to exert the most significant independent prognostic value (p=0.0006).
Conclusion: Despite the intention of including new prognostic biomarkers, the pTN stage remains the strongest predictors of outcome of patients with GC. The p53-target gene Maspin might be downregulated in patients with TP53 gene mutations in exon 7. These data are firstly reported in literature. The paper is prepared for publication in extenso.
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PS-21-033
Colorectal gastrointestinal stromal tumour: clinicopathological study of nine cases
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Background & objectives: Colorectal Gastrointestinal Stromal Tumour (GIST) is a rare tumour. This tumour is mainly observed in the transverse and descending colon.
Our aim is to study the clinicopathological characteristics of colorectal GISTs and their prognosis.
Methods: It is a retrospective study including nine cases of colorectal GISTs identified over a period of 17 years, between 2000 and 2017, in the Department of Pathology of Farhat Hached University Hospital of Sousse (Tunisia).
Results: Five men and four women with a mean age of 55.14 years presented with rectal bleeding, followed by abdominal pain and an

occlusive syndrome. The tumour was rectal in 3 cases and ileocecal in 3 other cases. The tumour's mean size was 10.5cm. Mitosis was greater than 5/50 CFG in 83% of the cases. The surgical margins were positive in 22.2% of cases. Immunohistochemistry showed an expression of CD117 in 75% and DOG1 in all cases. The risk of recurrence was high in 77.8% of cases.
One patient who had a rectal tumour developed liver metastases after 1 year. A second patient had a tumour recurrence after 2 months.
Conclusion: Colorectal GISTs are rare. Although their mode of revelation is similar to that of conventional adenocarcinomas, a precise diagnosis of these tumours is imperative because their prognosis and their therapeutic management are different.

PS-21-034
Assessment of HER2 status in appendiceal mucinous neoplasm
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Background & objectives: Appendiceal mucinous neoplasms are rare and heterogeneous mucinous epithelial proliferation, divided into low and high grade tumours (LAMN; HAMN). Therapeutical significance of HER2 status is currently evaluated in tumours of the gastrointestinal tract.
Methods: We conducted a retrospective study, including 8 cases: 5-LAMN and 3-HAMN. Two of HAMN cases displayed pseudomyxoma peritonei. We analysed tumours' expression of HER2 and Ki67 and we correlated the results with clinicopathological data.
Results: Membrane positivity for HER2 was detected in 2/5 cases of LAMN (40%) and 2/3 cases of HAMN (66.66%). HER2 medium levels of expression were found similar in both types of appendiceal tumours (11%-LAMN; 11.66%-HAMN). Media of Ki67 index resulted 2 times higher in HAMN as opposed to LAMN neoplasms (19.2%-LAMN; 33.66%-HAMN). Both pseudomyxoma peritonei cases were positive for HER2.
Conclusion: HER2 expression in appendiceal mucinous neoplasms exhibits low levels regardless of the tumour type. These findings indicate the need to initiate larger studies in order to search for patterns in the marker expression of this particular malignancy of the appendix.

PS-21-035
Late stage diagnosis of oesophageal cancer - facts from a developing country
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Background & objectives: Oesophageal cancer is one of the most aggressive malignancy. Most cases are initially diagnosed in either stage 3 or 4. Our study aimed to determine the frequency of Oesophageal Carcinoma in different ethnic groups of Karachi and to identify factors responsible for late stage diagnosis.
Methods: A multi-institutional prospective cross-sectional study was conducted at Oncology ward, JPMC & AEMC Karachi. Non-probability convenient sampling technique was implemented. Chi square/Fisher Exact was applied to observe any association between ethnic groups, grade, stage and risk factors of delayed diagnosis.
Results: Out of 93 patients, Squamous cell carcinoma (ESCC) was the most common (80.6%) type. Lower 1/3 was the most frequent site (53.8%). Sindhi ethnicity was most commonly effected (33.3%). Moderately differentiated grade was seen in good number of cases (67.7%). First visit to a general physician (GP) was within a month in 54.8% patients. A delayed referral was advised in 21.5% patients. Biopsy was delayed in 19.4% cases. Significant association was noted between late stage diagnosis & factors including late referral (P 0.003), non-availability of laboratory (P 0.018), site of tumour (P 0.000), age of the patient and size of tumour (P 0.001).
Conclusion: Initial diagnosis of most of the patients was made in late stage. Important contributing factors of late diagnosis were inadequate knowledge of patients, delayed initial investigations, poor socioeconomic status and late referrals to oncologist by GP. Sindhi ethnicity was frequently affected however, no significant association was observed between ethnicity and EC grading or staging.

PS-21-037
Role of epithelial-mesenchymal transition in serosal invasion of colon carcinoma
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Background & objectives: Serosal invasion is a well-recognized adverse prognostic feature in colon cancer (CC). Our aim was to investigate the involvement of epithelial-mesenchymal transition (EMT) in serosal invasion by analysing the expression of the miR-200 family and their target genes in CC.
Methods: We analysed the expression of miR-200 family and their target genes CDKN1B, ONECUT2, PTPN13, RND3, SOX2, TGFB2 and ZEB2 using qPCR. Thirty-three cases of formalin-fixed paraffin-embedded tissue were included (20 CC without and 13 CC with serosal invasion). Microscopically normal colon mucosa from surgical margins was used as control.
Results: Association analysis showed a gradual increase of expression of ONECUT2 from normal mucosa to pT2/pT3 and pT4 CC (Rho=0.621, p=0.001). We observed statistically significant change in expression for miR-429 in CC pT2 (p=0.031), for ONECUT2 in CC pT3 (p=0.035) and ONECUT2 (p=0.006), ZEB2 (p=0.017) and SOX2 (p=0.025) in CC pT4a compared to normal mucosa. In addition, there was statistically significant difference in expression of PTPN13 (p=0.037) and ZEB2 (p=0.017) between CC without (pT2/pT3) and CC with serosal invasion (pT4a).
Conclusion: Our results provide further evidence that EMT is involved in the progression of CC, including serosal invasion. Decreased PTPN13 expression in advanced CC suggests a potential tumour suppressor role of PTPN13, at least regarding serosal invasion.
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PS-21-038
Agreement in the assessment of depth of invasion in pT1 colorectal adenocarcinoma
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Background & objectives: One of the strongest independent factors for predicting lymph node metastasis in pT1 colorectal adenocarcinoma is depth of invasion. The aim of this study was to determine the agreement between pathologists to assess this measurement.
Methods: Forty pT1 CRC cases previously diagnosed (20 pedunculated, 20 sessile) were selected. Three pathologists (one GI experienced pathologist, one general experienced pathologist and one non-experienced pathologist) evaluated the depth infiltration level by measuring it in millimetres. Haggitt level was also assessed in pedunculated polyps. Statistical analysis was performed to calculate paired and global interobserver agreement (SPSS version 24).
Results: Fair global agreement was found in sessile polyps (CCI=0,42) with excellent value between experts (CCI=0,99), and moderate in pedunculated ones (CCI=0,72). Nonetheless, poor global agreement was shown for Haggitt level (weighted kappa=0,11), improved by one paired

observation (moderate agreement). Best concordance values were achieved by the 2 experienced observers.
Conclusion: Interobserver agreement in the classification of level of invasion has shown consistency between experienced pathologists in our study, especially for sessile polyps. Measurement with Haggitt level has shown, however, significant limitations. The quantitative value of invasion as recommended, should be the method of choice to evaluate this risk factor. Reviewing by an experienced operator or consultation between pathologists within the multidisciplinary team must always be considered.

PS-21-039
Mixed tumours of the colon and rectum
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Background & objectives: Mixed tumours of the gastrointestinal tract are rare biclonal neoplasms composed of mixed epithelial-neuroendocrine elements of benign and malignant potential that are difficult to diagnose. This project is dedicated to study mixed tumours of the colon and rectum.
Methods: The Laboratory Information System [LIS] computer was searched with terms "adenocarcinoma and/or adenoma, neuroendocrine" for the past 20-years [2000-2019] . The pathological slides were reviewed to confirm the diagnosis with confirmation of the neuroendocrine component by immunohistochemical stains in all cases. Detailed clinicopathological review including age, sex, tumour location, histological type, lymph node status and management outcomes was undertaken.
Results: Twenty-one cases of mixed tumours of the colon and rectum were identified in ages 32-87 years with majority in 7th-8th decade with male predominance-13 cases. Dominant right colon lesions-10, rectosigmoid-5, left colon-4 and rectum-2. Epithelial component was adenocarcinoma-20 and tubulovillous adenoma-1. Neuroendocrine component: low-grade-NET-G1 [5], G2 [4], high grade-NETG3 [2] and neuroendocrine carcinoma [NEC10]. Node positivity seen in 15 cases. Overall disease survival was poor in the tumours with NEC in comparison to NET1-2 lesions
Conclusion: Mixed tumours of the colon/rectum are rare and remain poorly understood entities associated with highly malignant potential and poor prognosis. We propose that any poorly differentiated histology should be investigated with immunohistochemical stains for neuroendocrine differentiation and be reported regardless of its percentage volume as the degree of component differentiation influences the prognosis more than volume. Accurate histological identification of these tumours is vital to determine appropriate treatment strategies.

PS-21-040
Hyperganglionosis in pneumatosis coli –cause or effect- chicken or the egg –a case series
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Background & objectives: Pneumatosis-coli[PC], a rare entity is not an isolated diagnosis but a finding that suggests an underlying process whose pathogenesis is not well understood. In this pilot case series, we explore a novel histopathological finding of hyperganglionosis in PCC as cause-vs-effect.
Methods: An index case of PC with hyperganglionosis led to a twenty-year search of the Laboratory Information Service [LIS] that identified a total of fifteen cases with reported finding of PC. All histopathological slides were reviewed to confirm the PCC. One representative block was subjected to immunohistochemical staining with antibodies to S100, Calretinin and CD68 for further evaluation with clinical correlation.
Results: This pilot study reports on four cases of pneumatosis coli that have been studied in detail with their additional stains. All cases upon review confirmed the presence of the multiple non-communicating cysts of PC. Additionally, prominent, enlarged hypertrophic ganglion associated with hypertrophic nerve fibres were seen in the mucosa/submucosa that were highlighted by S100 and Calretinin. CD68 stained slides outlined the histiocytes and giant cells surrounding the cyst of PC
Conclusion: The exact pathogenesis of non-communicating air-filled cysts within the bowel wall remains poorly understood including mechanical theory of mucosal injury, bacterial theory of gas production, counterperfusion-saturation theory and pulmonary gas theory. We propose "Neuronal theory" of dysgenetic ganglion cells with abnormal peristalsis resulting in 'reversal airflow' with intramural accumulation of intraluminal air or maybe they are the effect of forced mucosal expansion of cysts; thus reminiscent of the chicken-egg scenario

PS-21-041
Expression and prognostic relevance of RIPK3 and MLKL in human colon cancer
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Background & objectives: Receptor-interacting protein kinase 3 (RIPK3) and mixed lineage kinase domain-like (MLKL) might yield therapeutic potential in cancer. The aim of this study was to investigate the protein expression of RIPK3 and MLKL and its prognostic relevance in human colon cancer.
Methods: 375 primarily resected tumours were analysed. Cytoplasmic expression of tumoral RIPK3 and MLKL was determined by immunohistochemical staining of tissue micro arrays of formalin fixated paraffin embedded tissue. Level of protein expression was determined by calculation of immune reactive score (IRS). Expression levels were correlated with histopathological parameters (pT, pN, M, G) and overall survival (OS).
Results: High RIPK3 expression was detected in 25,4% (95/373) of the tumours. 64,9% (242/373) showed low expression and 9,7% (36/373) were negative. MLKL was highly expressed in 24% (90/375), 53,1% (199/375) showed low MLKL expression and 22,9% (86/375) were negative. Positive staining of RIPK3 was significantly associated with positive MLKL staining ($p<0.001$). However, in 18% of the tumours (67/373) we observed the combination of positive RIPK3/negative MLKL and in 4,8% (18/373) negative RIPK3/positive MLKL. Positive RIPK3/negative MLKL expression pattern was significantly associated with peritoneal metastasis ($p=0,009$). High RIPK3 tended towards higher pN status ($p=0,089$). However, no significant association of RIPK3 and MLKL expression with pT, G and OS was found.
Conclusion: Our data does not provide evidence of RIPK3 and MLKL protein expression being independent prognostic factors for OS in human colon cancer. However, we identified cases with exclusive expression of either RIPK3 or MLKL (18% and 4,8% respectively) proposing two distinct biological sub-groups in colon cancer. RIPK3 in the absence of MLKL might be promotive of peritoneal metastasis in colon cancer.
Funding: Else Kröner-Fresenius Foundation

PS-21-042
Oesophageal squamous cell carcinoma in Hargeisa/Somaliland: a study of 90 cases
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Background & objectives: Presenting demographic view and data of oesophageal squamous cell carcinoma in Hargeisa/Somaliland, in 30 month, from August 1st 2017 to Jan 1st 2020.

Methods: Retrospective study in our centre in Hargeisa city, Somaliland, of oesophageal SCC diagnosed in endoscopic biopsies received in our lab, within a period of 30 month, between August 1st 2017 to January 1st 2020, in the city of Hargeisa/Somaliland. All cases diagnosed by routine H&E stained sections. IHC is not available in the country.
Results: We had 90 cases, (28 female and 62 males), age range between 26 to 85 yr (mean age 51 yr), two cases involved patients under age of 30 yr. 13 cases were of keratinizing SCC, and the remaining (77) cases were of non-keratinizing type; with one case of well differentiated SCC, 8 cases of poorly differentiated SCC, one case of sarcomatoid SCC, and one case of pleomorphic giant cell SCC.
Conclusion: Oesophageal squamous cells carcinoma is a serious fatal health condition, with remarkable incidence rate compared to the population count in Hargeisa, capital city of Somaliland, that need more attention and further study.

PS-21-043
Investigative and management pathways, histopathology reporting and clinical outcomes in patients with biopsy features suspicious of eosinophilic oesophagitis
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Background & objectives: The diagnosis and management of eosinophilic oesophagitis (EO) remains a challenge due to differing definitions, clinico-pathological similarities with gastro-oesophageal reflux and a paucity of evidence. We aim to elucidate the current clinical pathways and outcomes of patients with suspected EO.
Methods: A retrospective cohort review was performed on all consecutive patients with oesophageal biopsies which had histopathological features suggestive of EO over a year's period within a single health-board with a catchment population of 1.2 million people. We reviewed diagnostic sampling practices, histopathological reporting, management pathways and clinical outcomes in these patients after a minimum of 1 year's follow-up.
Results: A total of 107 patients had EO-suspicious biopsies. Of this, 38.3% had potentially non-diagnostic single-site or undifferentiated multiple-site biopsies. Eosinophilic densities were not reported in 34.5% of biopsies.
Patients were managed with a wide variety of regiments incorporating proton-pump-inhibitors (PPIs), steroids, dietary exclusion, or combinations thereof.
Only 37.5%, 44.4% and 43.8% of patients with documented therapeutic responses had a good response to PPIs, steroids, and PPI-steroids combination therapy, respectively.
Conclusion: This study suggests wide variability and inconsistencies exists in current endoscopic sampling, histopathological reporting, management, and outcomes of EO. Therefore, there remains an unmet need for EO patients with its associated high morbidity due to recurrent issues of food bolus and chronic oesophageal strictures. Standardised protocol-based diagnostic and treatment pathways would reduce the need for repeat sampling, assist with earlier detection and establish patients on appropriate treatment sooner.

PS-21-044
A model for predicting risk of distant metastasis in stage II colorectal cancer
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Background & objectives: Non-metastatic colorectal cancer can recur as a distant metastasis. It is important to identify a subgroup of patients with the highest risk of relapse. This study aimed to identify the pathomorphological prognostic factors for the selection of this subgroup.
Methods: A retrospective cohort lymph node-negative colorectal cancer with complete surgical resection was studied included 48 and 52 patients, with and without distant metastasis respectively. The mean follow-up period was 5 years. A twenty-one histopathological characteristics of both the cancer cells and tumour microenvironment have been evaluated. Variables that have shown $p<0.05$ were incorporated into model.
Results: In univariate and multivariate analyses, the following factors had significant correlation with metastasis $p<0.05$ or less: high-grade budding, lymphovascular invasion, feeble stromal inflammatory infiltration, low ratio macrophages type 1 to type 2, low number of intraepithelial lymphocytes, nuclear expression of beta-catenin, low pericyte coverage of the tumour vasculature. The colon cancer recurrence nomogram predicted distant metastasis have been proposed.
Conclusion: Proposed model based on tumour parenchyma and microenvironment features interconnection seems to be better personalized prognostication system by identifying patients both the high- and low-risk of relapse within stage II colorectal cancer.

PS-21-045
Fluorescence application for stomach cancer metastasis verification
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Background & objectives: One of the methods of spectroscopic analysis is the method of the luminescence recording, that is fluorimetry.
Objective: to compare spectra of luminescence of stomach adenocarcinomas (SAC) and their metastasis to different organs.
Methods: We examined 20 cases of SAC with their metastasis to lymph nodes, liver, lungs and omentum (42 specimens).To study the structure of the substance we registered luminescence of unstained de-waxed histological sections to detect tissue composition using hardware and software complex "Fluorat-02-Panorama". The luminescence and synchronous scanning spectra were obtained (roughly approximate spectrum of excitation of the luminescence) and compared.
Results: Metastasis in lungs have more angular curves and less noticeable peak in the region of long waves, while the study of the of lymph nodes metastasis spectra showed the presence of a greater number of peaks in the area of long waves, and their peaks are also higher and steeper than similar peaks from the other organs.
Conclusion: It was noticed that the spectra of SACs are qualitatively similar to their metastasis: they have the same number of peaks and maxima at approximately the same excitation wavelengths (280-290 nm and 336-340 nm). Metastasis in omentum and liver have the maximum similarity with the main tumour of synchronous scanning. But also, there are some differences reflecting the impact of the tissue accepting metastasis in spectra. This method of spectral analysis can be used to verify metastasis of stomach cancer.

PS-21-047
Y chromosome loss is a frequent event in Barrett's adenocarcinoma and associated with poor outcome
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Background & objectives: The loss of the Y chromosome (LoY) in frequently described in various malignancies. There is no reliable information on the frequency, significance for tumour progression including prognostic significance, type of Y chromosome loss or homogeneity in oesophageal adenocarcinoma (EAC).

Methods: We analysed a large tumour collective of more than 650 EAC with fluorescence in-situ hybridization (FISH) using tissue micro arrays (TMA) and statistically considering further molecular tumour alterations and clinical aspects with follow-up data. Commercially available FISH probes were validated in oesophageal cell lines of known Y chromosome status.
Results: The median follow-up for the entire cohort was 57.7 months with a 5-year survival rate of 26.6%. LoY of one chromosome arm was present in 3.4%, complete LoY in 55.7%. LoY was not affected by administration of neoadjuvant treatment. LoY was strongly associated with shortened overall-survival (OS) in the entire patients' cohort with an OS of 19.4 months (95%CI 14.8 - 24.0 months, $p < 0.001$). Patients with presence of Y chromosome showed a median OS of 58.8 months (95%CI 33.1 - 83.2 months). In multivariate analysis, LoY is an independent prognostic marker with a hazard ratio of 0.558.
Conclusion: Taken together, LoY is a frequent event in EAC and associated with a poor outcome. Furthermore, the phenomenon of male dominance of up to 9:1 in EAC is still unclear. However, the literature and the study results here provide an informative basis for a biologically and functionally relevant role of LoY in EAC. Also, there might be a direct influence of Y deficiency on the tumour immune microenvironment

PS-21-048
Incidental findings neoplasm in appendectomy specimens with acute appendicitis, during routine histopathological examination
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Background & objectives: Acute appendicitis remains the most common surgical emergency encountered by the general surgeon, diseases and tumours of the appendix are very rare. This study aimed to show the presence of appendicular tumours in patients with acute appendicitis.
Methods: A retrospective study between January-2009-December-2019. The pathology reports of 5628 cases with acute appendicitis and cases with an appendix neoplasm were retrieved to determine the incidence of concomitant appendicular tumours, identify the risk factors associated the incidental appendectomies, or presurgical diagnosis of injury, were excluded. The statistical analysis of the data was compared using quartiles, $\chi 2$test and student's t test.
Results: Appendiceal neoplasms were found in 118 out of 5628 acute appendicitis, the overall incidence was 2.09%. 70 females and 48 males from 11 to 86 years old. The unusual histopathological findings include: Neuroendocrine tumour (n=49,41.5%), Low-grade mucinous neoplasia (n=40,33.8%), Adenocarcinoma (n=11,9.3%), Adenomatous polyp (n=18,15.2%). None of these patients with subsequent diagnosis of tumour were suspected prior to the appendectomy.
Conclusion: The incidence of appendicular malignancies may be underreported; proper histopathological evaluation and being aware of these unusual diseases, allows an adequate treatment. Tumour prevalence in acute appendicitis was low. Younger patients may be at a higher risk of occult appendiceal neuroendocrine neoplasms than other age group. Tumour risk was significantly higher in complicated acute appendicitis compared with uncomplicated acute appendicitis.

PS-21-049
Clinicopathological study of tumours of the gastrointestinal stroma tumour (GIST) in a reference centre in Bogotá, Colombia
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Background & objectives: GIST is the most common mesenchymal neoplasm of the gastrointestinal tract (GIT); little information has been described in third world countries. We Describe pathologic characteristics of 205 patients in the University Hospital FSFB in Bogotá, Colombia, between 2001-2019.
Methods: A cross-sectional observational study using non-probabilistic sampling for convenience of patients with diagnosis of GIST referred to the Pathology Department was performed. Variables as age of diagnosis, institution, sex, immunohistochemically expression of C-Kit, CD34, DOG 1, PDGFR 1, desmin, S-100, tumour location, pattern, symptoms, treatment and classification according to the four risk categories according to Fletcher modified scale were analysed.
Results: The clinicopathological and epidemiological profiles has few differences to what has being describe in the literature. The age of diagnosis remains on the fifth decade of life (55 % female vs 44% of men, the most common symptoms were 62.6% abdominal pain, 21.3% bleeding. 70% of tumours were of fusiform C-KIT was expressed in 98.5%. 57.5% were primarily gastric, 24.9% small intestine, 3.1% colorectal and 14.5% extragastrointestinal. CD34 was positive in 83.8%, DOG1 45.8% and PDGFR in 1.7%. 51.2% of tumours classified as high risk at the time of diagnosis. In terms of treatment, 35.5% received surgical treatment and among these 13.8% had received targeted therapy, Imatinib.
Conclusion: This study represents an approximation to the current situation of GIST tumours in a pathology reference centre in Colombia. Most of the patients are woman and at the time of diagnosis presented with a high-risk tumour, in contrast with what is referred in the literature. This differences in incidence reflect variation in population risk and warrants further investigation in our Country.

PS-21-050
HER2 expression pattern in gastric adenocarcinomas in a Nigerian tertiary hospital by immunohistochemistry
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Background & objectives: The demonstration of HER2 in gastric adenocarcinoma (GA) tissues by immunohistochemistry assists in deciding whether targeted therapy would be optimal for HER2 positive GAs patients. HER2 status of GA patients in this environment is unknown, hence the need for this study.
Methods: Data on age, gender, site of lesion and histological subtype of gastric adenocarcinomas were retrieved and reviewed. Tissue array blocks were made from archived formalin fixed paraffin embedded gastric tumour tissue. Slides cut from these blocks were stained with anti-human HER2 antibody by immunohistochemistry and scored using ToGA trial criteria. Ethical approval was obtained from the institutional ethical review committee
Results: There were 80 cases with a male to female ratio of 1.9:1. The mean age was 55.65 ±13.50 years whilst the modal age group was 60-69 years. Only 7 (8.75%) of the tumours involved the proximal part (cardia) of the stomach whilst 73 (91.25%) involved the distal parts (pylorus, body and fundus). The intestinal, diffuse and mixed morphological subtypes constituted 53.8%, 31.2% and 15.0% of the cases respectively. Overall, A great majority of the tumours (92.5%) showed negative HER2 expression with only 6 cases (7.5%) showing strong positivity for HER2. The HER2 positive tumours include 2 of the 7 (28.6%) proximal and 4 of the 73 (5.5%) distal tumours.
Conclusion: HER2 showed slightly lower overexpression rate than studies from many parts of the world. This overexpression was significantly higher in proximal than distal tumours suggesting differences in their molecular pathogenesis and more likelihood of response to trastuzumb by proximal tumours.

PS-21-051
Biological and molecular profile of colorectal cancer is dependent on the tumour microenvironment

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Background & objectives: Colorectal cancer (CRC) has been stratified into prognostic groups based on gene expression profile and tumour microenvironment (TME) composition.
The goals of this study are to identify prognostic biomarkers within TME using immunohistochemistry and to improve understanding of tumour biology.
Methods: This study utilized 281 CRC samples for immunohistochemical stainings with biomarkers for T-cells (CD3, CD8), B-cells (CD20), macrophages (CD68, CD163), cancer associated fibroblasts (CAF) (α-SMA, FAP). Biomarker expression has been quantified at the tumour core (TC) and invasive margin (in carcinomas) / neoplasia border (in adenomas) (IM/NB) as areal fraction with digital pathology software (Visiopharm).
Results: Expression of all biomarkers was strongly correlated in both regions but was significantly higher at the IM/NB compared to TC (except for anti-CD68 in adenomas). In more advanced pathological tumour stages T-cell expression and B-cell expression were decreasing, whereas CAF expression was increasing. CD68-positive macrophages were more prevalent compared to CD163-positive macrophages in carcinomas with no significant difference in adenomas. High expression of CD163-positive cells was associated with presence of BRAF mutation(s) and microsatellite instable tumours, whereas low macrophage expression was associated with microsatellite stable tumours. Moreover, high expression of T-cells was associated with microsatellite instable tumours and low expression group was associated with microsatellite stable tumours.
Conclusion: This study provides insight into relationship between TME and molecular/biological tumour profile. To improve our understanding of tumour biology and enhance personalized treatment it might be beneficial to combine TME with conventional patho-anatomical tumour classification/grading.
Funding: Health Research Fund of Central Denmark Region.

PS-21-052
The new scale for the semi-automatic assessment of the immune microenvironment in gastric cancer has great prognostic value compared to generally accepted scales
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Background & objectives: Generally accepted scales for assessing immune microenvironment in gastric cancer are based on manual calculation of average number of cells in hot spots (predominantly intratumoral and in invasive margin). This is time-consuming process, development of new assessment scales is required.
Methods: After immunohistochemical staining average area of CD8+ cells (square micrometres) in three fields of view (lens magn.x20) was assessed separately in central part of tumour and in morphologically normal mucous membrane of peritumoral region directly adjacent to tumour tissue. Automatic segmentation method based on colour separation (RGB system) implemented in the Leica LASX tool was used.
Results: We also counted average number of cells in three hot spots (lens magn.x20) in tumour and normal mucous membrane. Multivariate analysis of factors affecting overall survival was performed using Cox proportional hazard model (N=43). Risk ratio (RR) for intratumoral CD8+ cells using hot spot counts was 1,001 (CI: 0,995–1,008, p<0,01) and when using the new scale RR=1,009 (CI: 0,532–1,914, p<0,01). By using the hot spot count obtained RR for CD8+ cells in normal mucosa using hot spot calculation was 1,005 (CI: 0,999–1,011, p<0,01) and when using the new scale RR=1,599 (CI: 0,519–4,917, p<0,01).
Conclusion: Our proposed scale for assessing immune microenvironment in gastric cancer showed that average area of CD8+cells assessed in normal mucosa by automatic segmentation is strong negative prognostic factor. Values obtained using hot spot calculation were not significantly related to prognosis.

PS-21-053
Dysplasia in patients with Barrett's oesophagus
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Background & objectives: Barrett's oesophagus (BE) is a premalignant condition defined as any type of columnar metaplasia of the distal oesophagus higher than 1 cm above gastro-oesophageal junction. Intestinal metaplasia is well-known risk factor for developing oesophageal adenocarcinoma, while studies of cardiac-type metaplasia are controversial. The aim of our morphological study was to identify and characterize dysplasia in patients with BE.
Methods: We examined endoscopic biopsy specimens of 80 patients with BE, stained with haematoxylin-eosin. Combined PASD/Alcian Blue stain was used for detection of goblet cells. Immunohistochemical evaluation was performed in cases with dysplasia, including immunostaining with MUC1, MUC2, MUC5AC, MUC6, CDX2 and villin. Of 80 patients with morphological features of BE 50 had intestinal metaplasia and 30 – cardiac-type metaplasia.
Results: Dysplasia was found in 12 patients (15%). Dysplasia in most cases (83,3%) was multifocal. Among patients with dysplasia 11 showed evidence of intestinal metaplasia and one patient with high-grade dysplasia had cardiac-type metaplasia. Immunohistochemical evaluation in foci of dysplasia revealed pure cardiac phenotype (MUC1+, MUC5AC+, MUC6+, MUC2-, CDX2- and villin-) in 3 cases (15%) and mixed adenomatous phenotype (MUC1+, MUC5AC+, MUC6+, MUC2+, CDX2+ and villin+) in 9 cases (75%).
Conclusion: Dysplasia is much more frequent in patients with BE with intestinal metaplasia and in most cases is multifocal. Mixed adenomatous immunophenotype is the most common immunophenotype in BE with dysplasia.

PS-21-054
Alteration of circadian rhythm proteins expression in inflammatory bowel diseases
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Background & objectives: Inflammatory bowel disease (IBD) is considered to be a chronic, relapsing, multifactorial disease. Over the past years a possible connection of IBD with circadian system has been proposed, which we further explored in this work.
Methods: We performed a semiquantitative immunohistochemical analysis of the expression of 8 core circadian proteins (BMAL1, BMAL2, PER1, PER2, PER3, CLOCK, NPAS2 and TIMELESS) in the epithelial cells of intestinal mucosa of 24 patients with Crohn's disease (CD) and 26 patients with ulcerative colitis (UC), which we subsequently compared with 25 control samples.
Results: The expression of 5 core circadian proteins (BMAL1, PER1, PER3, TIMELESS and NAPS2) was statistically significantly decreased in patients with IBD in comparison to control samples, whereas expression of BMAL1 and PER1 was more noticeably decreased in UC patients and PER3, TIMELESS and NPAS2 in CD patients. The most pronounced changes were noted in BMAL1 protein expression, where larger segments of neighboring epithelial cells showed loss of staining in inflamed mucosa. Our work represents a complex immunohistochemical

study evaluating the changes in circadian proteins expression in intestinal mucosa of IBD patients.
Conclusion: We demonstrated apparent changes of circadian proteins expression in patients with IBD, confirming connection between IBD and disruption of circadian rhythms. Our results suggest a number of possible new diagnostic or prognostic markers, with BMAL1 protein being the most potent one.
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PS-21-055
HER2 status in gastric precancerous lesions
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Background & objectives: Amplification of HER2 gene can occur early stages of gastric cancer, but information about that is extremely scarce. The aim of the study was to reveal the frequency and patterns of HER2 protein and gene expression on the spectrum of carcinogenesis.
Methods: The study included 82 gastric biopsy samples: atrophic gastritis (18), 17 - uncertain dysplasia (17); intestinal type adenomas and non-polypoid lesions with low grade dysplasia (14) and high grade dysplasia (17); invasive adenocarcinoma (18). Serial sections of tissues were used for routine examination, HER2 immunohistochemistry and silver-enhanced in situ hybridization (SISH) with adapted manual tissue microarray technique.
Results: Overexpression of HER2 (2+ and 3+) with the presence of a membrane or basolateral immunohistochemical label was found in 3 cases among invasive carcinoma group only with SISH confirmation of all 2+/3+ positive cases. The presence of non-conventional staining variants of HER2 expression were revealed in 62 cases: apical label (partial membrane staining of the apical edge of the cell), cytoplasmic (diffuse staining of cell cytoplasm), "strip form" (focal cytoplasmic staining of the cell, forming a strip) and nuclear staining. There were no statistically significant differences in the expression of HER2 between different categories of dysplasia and invasive adenocarcinoma as well as between variants with different phenotypic differentiation (($p<0,05$).
Conclusion: We did not reveal the presence of HER2 overexpression during early precancerous changes. Non-conventional HER2-staining needs more data and additional analysis for practical interpretation and implementation. These results don't exclude the possibility of using this marker in differential diagnostics in the situations of small volume or low informative biopsy material as a method with high specificity.

PS-21-056
Orientation of the biopsy material as a way to increase the informativeness of the pathologists' conclusion in assessing of gastric mucosal atrophy
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Background & objectives: The diagnostic value of the study of gastric biopsy specimens can be reduced due to the artificial changes especially lose of appropriate orientation. The possible way to reduce the interpretation difficulties is orientation of the gastric mucosa fragments.
Methods: 60 diagnostic cases (248 biopsy fragments) were divided into 2 groups: oriented and not oriented. The orientation of tissue samples was performed by using specialized orientation strip. After that biopsy fragments were embedded and stained according to the standard methods. 3 pathologists assessed the gradation of atrophy in the obtained biopsy material with the calculation of the agreement level (Cohen's kappa).
Results: A comparative analysis of the diagnostic effectiveness of the gastric mucosa atrophy evaluation was performed on both groups. In group with oriented specimens 119 from 124 (95.97%) remained orientation regardless of the side of biopsy material in contact with the strip. Appropriate orientation was not reached with an extremely small volume of biopsy material. Cohen's kappa was 0,92. In second group only 59 fragments (47.58%) remained the appropriate orientation under microscopy examination with impossible to make a diagnostic judgement on atrophy and kappa level 0,58.
Conclusion: The orientation of gastric biopsy specimens improves the quality of morphological diagnosis. The best way to orient is to use specialized strips for biopsy material, which is due to the high effectiveness of reaching the orientation of tissue fragment and low level of artificial deformation. The use of adhesive strips significantly increases the level of diagnostic agreement due to the objective detection of atrophy.

PS-21-058
High micro-vessel density correlates with higher peri-tumoral immune response in colorectal cancer
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Background & objectives: Microvessels, a significant component of the tumour microenvironment in colorectal cancer (CRC), have traditionally been assessed in full-face sections. This study aimed to assess the microvessel density (MVD) in CRC tissue microarrays (TMAs) and determined correlations with clinicopathological variables.
Methods: TMAs from 1000 consecutive cases (2008-2014) of CRC from a tertiary centre were immunostained with clinical grade CD34 antibody (1:500 dilution). Stained microvessels and core areas were annotated on digital images (Nanozoomer) and assessed (3D Histech). The MVD was adjudged in luminal, central and peripheral tumour cores as well as adjacent normal, and results correlated to clinicopathological variables (SPSS).
Results: Of 985 assessable cases, 490 had a high overall tumour MVD. The mean tumour MVD was lower than the mean MVD in the adjacent normal area ($p<0.001$). A higher overall and peripheral tumoral MVD was associated with lower T stage ($p=0.04$) and lower overall stage ($p=0.02$). Average tumour MVD (as well as peripheral and luminal specific MVD) correlated with a conspicuous peri-tumoral lymphocyte density ($p<0.0001$). Higher tumour MVD also correlated with mismatch repair (MMR) proficient state ($p<0.001$). The MVD in the adjacent normal neither correlated with the immune response nor with the MMR status. Higher overall tumoral MVD was associated with alive survival status at 5 years ($p=0.045$).
Conclusion: MVD in the CRC microenvironment is correlated with lower stage, a conspicuous peri-tumoral lymphocyte response and is higher in MMR proficient tumours. Digital annotations of core stromal areas may further refine clinical correlations of MVD in CRC.
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PS-21-059
Searching for the aetiology of gastric mucosa pigmentation – sometimes a teamwork
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Background & objectives: Gastric mucosa pigmentation is a rare finding and it can be associated with exposure to exogenous agents including hydralazine, thiazide, furosemide, beta blockers and iron supplements, the pigment deposits consisting of iron, calcium, barium sulphate, charcoal, melanin, lipofuscin and others.
Methods: We report two cases of a 34-year-old and 40-year-old female patients with dyspeptic syndrome and oral treatment with bismuth tripotassium (De NOL, respectively Ulcamed) and PPI. Because of

persistent symptoms and black stools, gastroscopy was performed in both cases.
The first gastroscopy revealed a diffuse inflammatory mucosa, with a friable and "solid plaque"-like aspect, suspicious for a gastric lymphoma.
Results: The biopsies taken from the body of the stomach showed a diffuse chronic gastritis, erosive, non-atrophic, negative for Hp, with mild hyalinosis of the lamina propria and the presence of amorphous black-brown pigment deposits on the mucosal surface, within the exudate and under the superficial regenerative epithelium.
The second patient had a friable and erosive gastric mucosa. Biopsies showed oxyntic type mucosa with lesions erosive gastritis, with abundant neutrophils, discrete exudate and focal grey-black pigment covering the mucosa and beneath the regenerative cubic. Hp was absent. Both cases presented negative Pearls stain.
After a detailed discussion with the patients and the gastroenterologist the on-going treatment containing Bismuth was revealed.
Conclusion: These cases highlight the need for the differential diagnosis and show the importance of communication between the gastroenterologist and pathologist. Bismuth is known to induce oral pigmentation and even mucosal oesophageal necrosis when associated with salicylates.

PS-21-060
Markers of epithelial-mesenchymal-transition in oesophageal adenocarcinoma for decision strategy of surgical versus endoscopic therapy
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Background & objectives: The decision for endoscopic submucosal dissection (ESD) versus esophagectomy of oesophageal adenocarcinomas (EACs) is based on clinical evaluation of tumour depth and invasion, whereby marker profiling of the epithelial-to-mesenchymal-transition (EMT) could be helpful to ordain which procedure is more appropriate.
Methods: We investigate retrospectively the immunohistochemical expression levels of several EMT-related proteins (Claudin-1, E-Cadherin, Ki67, P53, SNAIL/SLUG, Vimentin, ZEB1, ZEB2) and microRNAs (141, 200a, 200b, 200c, 429, 205) in ESD- and surgically resected samples of EACs. By doing this we aim to evaluate whether pre-operative measurement of EMT marker expression might support the decision regarding ESD versus surgery of EACs.
Results: ESD resected samples display high expression of epithelial protein markers, whereas surgically resected samples display high expression of mesenchymal markers. Additionally, the anti-EMT microRNA-205 was significantly higher expressed in ESD-resected samples, whereas we found no significant differences in the expression levels of microRNA-200 family members. Additionally, statistical cluster and regression analysis reveal a significant cluster determination based on the EMT and miRNA expression pattern.
Conclusion: On molecular level, tumour invasion is strongly associated with epithelial-to-mesenchymal-transition (EMT) and microRNAs. Our retrospective approach demonstrates that measurement of selected EMT markers and microRNA-205 has significant discrimination power to distinguish ESD-resected and surgically resected samples. We suggest the assessment of EMT status of EAC samples on molecular level might support clinical evaluation regarding the applicability of ESD in future.
Funding: Cancer Cluster Salzburg

PS-21-061
Non-genetic HER2 intratumoral heterogeneity with newly discovered HER2 positive tumour cells in gastric cancer: HER2 mRNA expression in amplified HER2 gene tumour cells without HER2 protein over-expression
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Background & objectives: HER2-positive gastric cancer (GC) demonstrates more HER2 intratumoral heterogeneity (ITH) compared to breast cancer (BC) and GC patients don't respond to HER2-targeted therapy well. Our objective was to investigate HER2 ITH at HER2 gene, mRNA, and protein levels in GC.
Methods: GC tissue biopsy and post-HER2 therapy surgical resection samples of previously diagnosed HER2 positive GC patients were analysed for HER2 ITH statues with consecutive sections using: 1) HER2 gene-protein assay (GPA) for concurrent detection of HER2 gene, chromosome 17 centromere, and HER2 protein at the individual cell level and 2) HER2 RNA in situ hybridization (ISH).
Results: We discovered a new type of HER2 positive cell populations that are amplified-HER2 gene tumour cells without HER2 protein over-expression among HER2-positive GC cases with ITH using GPA (non-genetic ITH). This new HER2-positive tumour cell type could be found in mucosal and more deeply invasive cancer areas of submucosa and disrupted muscularis propria. HER2 genetic ITH was also observed in GC. HER2 gene and protein negative GC cells lacked HER2 RNA expression while homogeneous HER2 gene and protein positive tumour cells demonstrated high HER2 RNA expression levels. However, HER2 RNA ISH revealed that over-expression of HER2 RNA was detected in the newly discovered HER2-positive tumour cells without HER2 protein over-expression.
Conclusion: Non-genetic HER2 ITH in GC was confirmed by a discovery of the new type of HER2 positive tumour cells presenting amplified-HER2 gene and over-expressed-HER2 RNA, but without HER2 protein over-expression. This unique HER2 ITH might be a cause of inefficient efficacy of HER2-targeted therapy that requires HER2 protein as the target. Thus, we propose to redefine the definition of GC HER2 ITH by including non-genetic HER2 ITH.

PS-21-062
The correlation between metastatic lymph node ratio, location of the tumour, and tumour differentiation in 97 colorectal cancers with lymph node metastasis
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Background & objectives: The proportion of the number of involved lymph nodes (LNs) to the number of examined LNs—defined as metastatic LN ratio (mLNR)—has been considered as a prognostic parameter in colon cancer.
Methods: We conducted a retrospective study of 97 patients (55 males and 42 females) who were initially diagnosed with colon cancer at General Hospital Asklipieion Voulas from 2010 to 2019. In our study, a cut-off of 0.4 was used for the mLNR. The distributions of the patient characteristics were assessed by the Chi square test.
Results: A high mLNR (≥0.4) was significantly correlated with tumour differentiation. No significant correlation was observed between mLNR and the location of the tumour.
Conclusion: Many authors have introduced the metastatic lymph node ratio (mLNR) in examining various malignant tumours. Berger et al. first reported the prognostic role of mLNR in colon-rectal cancer, though no detailed information regarding the criteria for high mLNR is currently available. Recently, the mLNR has been explored as a prognostic factor on survival outcomes and time to progression for patients with colon cancer. Further detailed cumulative assessment is needed to confirm the optimal criteria of high mLNR.

PS-21-063

High expression of PLK4 as a predictor of poor prognosis for locally advanced rectal cancer patient: a prospective analysis

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Background & objectives: Recent studies highlight the importance of regulating PLK4 on the basis of PLK4 overexpression in various neoplasms. Meanwhile, radio resistance is an important issue in rectal cancer treatment. Therefore, it will be demonstrated PLK4 as a novel target to overcome radio resistance.
Methods: We constructed the tissue microarray, containing of 73 paired rectal cancer tissues, both pre- and postoperative specimens. PLK4 expression was evaluated by immunohistochemistry. Response to therapy was evaluated after surgery by pathologic tumour regression grade. And the association between PLK4 immunoreactivity levels and clinicopathologic parameters were evaluated. Functional studies for tumour proliferation and migration were performed in cell line models.
Results: Overexpression of PLK4 in pre-radiotherapy specimens is significantly associated with better overall survival. And our results were consistent with large cohort public data analysis. In addition, it was proved in vitro study. However, expression in post-radiotherapy specimens was not associated with survival.
Conclusion: Based on our human tissue study results, PLK4 expression can be suggested as a potential prognostic factor and predictor of preoperative radiotherapy resistance. Therefore, clinical development of PLK4 could be an effective therapeutic strategy for radioresistant locally advanced rectal cancer.

PS-21-064

Mismatch repair (MMR) protein expression and next-generation sequencing (NGS) result in microsatellite instability-high (MSI-H) colorectal cancer

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Background & objectives: MSI-H CRC accounts for 15% of all CRCs. MSI phenotype can be
detected by PCR-based molecular test or immunohistochemical (IHC) staining for MMR
proteins. Recently, NGS has been increasingly utilized. We compared and analysed the IHC staining and NGS results.
Methods: We reviewed the medical records of 625 colon cancers, collected from 2005 to 2017 in our institution. 60 cases of 625 cases (9.6%) were MSI-H tumour detected by PCR-based molecular tests. We evaluated MMR proteins (MLH1, MSH2, MLH6, and PMS2) expression by IHC staining method. And NGS was performed using dissected Formalin-Fixed Paraffin-Embedded (FFPE) tumour tissue.
Results: Among the 60 MSI-high patients, MMR protein expression pattern was categorized to 7 groups(group1, loss of MLH1 and PMS2(n=28); group2, loss of PMS2(n=4); group3, loss of MSH2 and MSH6(n=11); group4, loss of MSH2, MSH6 and PMS2(n=1); group5, loss of MSH2(n=1); group6, loss of MSH6(n=9); and group7, retained expression of 4 MMR proteins(n=6)).
NGS using 44 tumour tissue showed the following results : group1, pathogenic MLH1 mutation(n=6) and pathogenic PMS2 mutation(n=2); group2, pathogenic MSH6 frameshift variant mutation(n=1) and MSH2 Conflicting interpretations of pathogenicity(n=1); group3, MSH2 mutation(n=5), MSH6 mutation(n=2) and pathogenic MSH3 mutation(n=3); group4, pathogenic MSH6 and MSH3 mutation(n=1); group6, pathogenic MSH6 mutation(n=7), MSH2 mutation(n=7) and Pathogenic MSH3 mutation(n=1); group7, MSH2 mutation(n=1).
Conclusion: NGS is useful to understanding the molecular mechanism of MMR protein deficiency in CRCs.

PS-21-065

KRAS and NRAS mutations and histopathological characteristics of colorectal adenocarcinoma in vojvodina

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Background & objectives: RAS pathway alteration is important in colorectal carcinogenesis. Detections of KRAS and NRAS mutations are a standard in the management of metastatic colorectal cancer. We evaluated histopathological characteristics of colorectal adenocarcinoma between tumours with RAS mutation and wild type tumours.
Methods: 100 formalin-fixed paraffin-embedded samples of colorectal adenocarcinoma were analysed for KRAS mutations and NRAS mutations (exons 2, 3 and 4). Analysis was performed at Oncology Institute of Vojvodina. Results were compared with histopathological characteristics of diagnosed tumours. Patients were divided into two groups: I – patient with RAS mutations (n=44) and II – patient with wild type (n=56).
Results: KRAS mutations were detected in 86.36% of patients (exon 2 in 82%) and 15.9% of patients had NRAS mutations (exon 3 in 70%). The average age of patients in group I were 64.5 years and 65.3 years in group II. Most frequent tumour sites were rectum (group I 31.8%; group II 32.14%), sigmoid colon (in both groups 25%) and rectosigmoid junction (group I 18.2%; group II 12.5%). Most subjects had the tumour descriptor status T3 (group I 63.6%, group II 64.3%) and the node descriptor status N0 (group I 40.9%, group II 41%). 70.45 % of tumours from group I and 76.78% of tumours from group II were medium grade.
Conclusion: This study proved higher rates of KRAS mutations and low rates of NRAS mutations. Most frequent tumour localisation was rectum. In both groups, most of the tumours had the same: histological grade (medium), tumour descriptor status (T3) and node descriptor status (N0).

PS-21-068

Inflammatory spectrum of Crohn's terminal ileitis

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Background & objectives: Crohn's terminal ileitis (TI) may present with a histopathologic spectrum ranging between active ileitis to chronic active/inactive ileitis.
Aim of this study was to evaluate inflammatory patterns of Crohn's TI in initial & follow-up biopsies.
Methods: Initial biopsies(IB) and follow-up biopsies (FUB) of 152 patients diagnosed as Crohn's disease were reviewed in correlation with their clinical and endoscopic records. Inflammatory patterns were grouped as chronic active (CA), chronic inactive (CI) and active/acute ileitis (AI). Accompanying colonic biopsies were evaluated for involvement patterns classified as TI, TI with segmental colitis (SC), and TI with diffuse colitis (DC).
Results: There were 63 CA, 63 CI and 26 AI in TI biopsies with no difference found between IB and FUB. Ulcer, basal lymphoplasmocytosis, foveolar metaplasia were significantly more frequent in the CA group, followed by CI and AI groups($p=0.008$ and $p<0.001$, respectively). Predominant involvement pattern was TI(n=98) followed by SC(n=45), and DC(n=9). Majority of the cases (n=126, (82,9%)) had patchy lamina propria inflammation which was significantly higher in TI group(n=87, 88.8%) compared to SC group(n=32, 71.1%)($p=0.009$) in both IB and FUB. Granuloma was significantly more common in DC (n=2, 22.2%) than SC group (n=5, 5.1%) ($p=0.025$). No difference was observed between TI, SC, DC groups for inflammation patterns of TI.

Conclusion: Our results suggest that chronic ileitis characterized by patchy inflammation, either active or inactive, is the predominant inflammation pattern of Crohn's terminal ileitis, regardless of the time of the biopsy.

PS-21-069

Clinical implication of ABC transporters and cancer stem cell markers expression in colorectal cancer

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Background & objectives: The prognostic implication of cancer stem cell (CSC) and protective function of ATP-binding cassette (ABC) protein for CSC have been suggested. We aimed to assess the prognostic significance of CSC markers and ABC transporters in colorectal cancer.
Methods: Expression of ABC transporters, including ABC subfamily C member 2(ABCC2), ABCC3 and ABC subfamily G member 2(ABCG2) and CSC markers including aldehyde dehydrogenase 1(ALDH1), leucine-rich repeat-containing G protein-coupled receptor 5(LGR5) and sex determining region Y-box 2(SOX2) were determined by immunohistochemistry in 331 colorectal cancer tissues and were assessed according to the patients' prognoses.
Results: ABCC2 and SOX2 expression was associated with lower pathologic T stage (P=0.001, each). SOX2 was associated with favourable overall survival rate (OS; P=0.001), and ABCG2 and SOX2 were associated with increased disease-free survival rate (DFS; P=0.029 and 0.005, respectively). SOX2 was the prognostic factor for OS in multivariate Cox proportional hazard model for overall survival (HR=2.641, P=0.048).
Conclusion: The expressions of ABCG2 and SOX2 in colorectal cancer tissues were associated with patients' prognosis. Especially, SOX2 can be a potential predictive marker for patients with colorectal cancer.

PS-21-070

Predictive and prognostic value of Peritoneal Regression Grading Score (PRGS) in peritoneal metastasis

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Background & objectives: Peritoneal biopsies are increasingly used to evaluate therapy response of peritoneal metastases. Peritoneal Regression Grading Score (PRGS) is a new, reproducible tool to determine histological regression of PM. Study aim is examination of possible predictive and/or prognostic significance of PRGS.
Methods: Registry study. Explorative analysis. Prospective cohort 97 pre-treated patients with histologically proven PM: Gastric (n=33); CRC/appendiceal (n=25); HBP (n=20); ovarian/tubal (n=8); others (n=11) treated with various regimen. 4 biopsies taken from abdominal quadrants. Analysis by independent pathologist. Calculation of mean PRGS from all available biopsies. Increasing PRGS was considered as POD, decreasing PRGS as OTR. Survival statistics: Kaplan-Meyer, Cox regression.
Results: Out of 97 patients, 36 (37%) has a PRGS < 2 (favourable), 61 (63%) PRGS ≥ 2 (unfavourable) at first laparoscopy. Favourable PRGS predicted favourable overall survival (median (CI 5-95%): 12.1 (7.8-16.4) months vs. 8.0 (5.1-10.8) months, p < 0.001. Out of 62 patients (64%) eligible for histological response assessment (≥ 2 laparoscopies), 42 (70%) had a histological OTR. Median survival was 14.6 (CI 95% 6.0-23.2) months in OTR vs. 6.9 (CI 95% 0-14.9) months in POD patients.
Conclusion: This is the first evidence suggesting a predictive and prognostic value for PRGS in PM. This pilot data should now be confirmed in adequately powered studies. If this data is confirmed, PRGS might have a clinical potential for individualized therapy of PM of various origin.

PS-21-071

Duodenal neuroendocrine cells hyperplasia in coeliac disease

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Background & objectives: Several studies have reported increased number of neuroendocrine (NE) cells in the duodenal epithelium of patients with celiac disease (CD). We investigated if the hyperplasia of NE cells in CD correlates with the Marsh-Oberhuber classification of histological findings.
Methods: Immunohistochemistry with an antibody against Chromogranin A was performed on formalin-fixed paraffin-embedded sections of biopsies obtained from the 2nd segment of duodenum. Biopsy samples were obtained from control group (n=5), CD Marsh I patients (n=5), CD Marsh II patients (n=5) and CD Marsh III (n=6 including IIIa, IIIb and IIIc). NE cells number was quantified per 1mm2 of duodenal mucosa.
Results: Biopsies from CD patients had visually increased number of NE cells in crypts in comparison to the control group. Furthermore, in 2/6 samples from CD Marsh III group we noticed clusters of 3-5 NE cells in crypts. There was a statistically significant difference in number of NE cells between groups as determined by one-way ANOVA (p=0.04). Tukey's post-hoc test revealed that there was only a statistically significant difference between CD Marsh III group and control group (p=0.03) and not between the CD groups or between CD Marsh I-II groups and the control group.
Conclusion: Our pilot study confirmed the hyperplasia of NE cells in CD, especially in cases classified as Marsh-Oberhuber III. Further studies are needed to characterize which subtypes of NE cells are increased and how the inflammatory milleu drives NE cell hyperplasia.

PS-21-072

SOX2 expression in serrated neoplasia pathway

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Background & objectives: Many sessile serrated lesions (SSLs) and some colon cancers (CCs), especially BRAF-mutant cases, express SOX2. Additionally, most of BRAF-mutant CCs probably derive from SSLs (so-called serrated neoplasia pathway: SNP). Therefore, we aimed to investigate the role of SOX2 in SNP.
Methods: In order to clarify the association of SOX2 with SNP, we evaluated SOX2 expression profile in SNP and compared to that in traditional adenoma-carcinoma sequence. The expression of SOX2 was investigated by applying immunohistochemistry in SSL (n=50), SSL with cytological dysplasia (n=20), carcinoma in SSL (n=13), conventional adenoma (tubular and tubulovillous) (n=53) and carcinoma in adenoma (n=27).
Results: SOX2 was expressed with significantly higher frequency in SSL (54%, 27/50) than in adenoma (11.3%, 6/53) (p<0.0001). SOX2 expression of the dysplasia part and the carcinoma part in SSL, and the carcinoma part in adenoma were 20% (4/20), 30.8% (4/13), and 14.8% (4/27), respectively. SOX2 expression rate was considerably higher in advanced stage of histology in SSL than that in adenoma, though the difference was not statistically significant.

Conclusion: These results indicate that SOX2 may be associated with histogenesis, rather than carcinogenesis, of SSL. However, this may possibly be attributed to the present small-sized sample study. Thus, further validation of the present results with additional samples is ongoing.

PS-21-073

Analysis of clinical and histopathological findings in microscopic colitis

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Background & objectives: Microscopic colitis is a chronic inflammatory bowel disease encompassing a triad of chronic diarrhoea, normal endoscopy and characteristic histological findings. Based on the histological features, it is divided into collagenous colitis (CC), lymphocytic colitis (LC) and incomplete microscopic colitis (MCi).
Methods: The histopathological parameters were evaluated in 53 microscopic colitis (37 CC, 7 LC, 9 MCi) diagnosed between 2012 and 2019. The presence of a broad subepithelial collagen band ≥10 μm in thickness and ≥20 intraepithelial lymphocytes(IELs)/100 enterocytes were considered diagnostic for CC and LC respectively. The presence of 5-10 μm in thickness or 5-20 IELs/100 enterocytes were evaluated as MCi.
Results: CC had female predominance (%70) with a mean age of 59 (22-87) while LC and MCi showed male predominance (%100,%78). The most distinct localization for CC and LC was right colon (%60,%77) while for MCi left colon (%60).
All of CC,LC,MCi had lymphoplasmocytosis in lamina propria (slight %46,%86,%100, moderate/severe %54,%14,%0). The majority of CC (%97) showed 5-19 IELs/100 enterocytes. The striking point was the presence of ≥20 eosinophils/1HPF in lamina propria in %78,%43,%11 of CC,LC,MCi respectively. Desquamation, flattening, vacuolization, loss of mucin in the surface epithelium were %73,%51,%65,%62 of CC, %21,%86,%43,%71 of LC while %33,%11,%22,%33 of MCi respectively. None of CC,LC had crypt distortion, crypt abscess, giant cell, granuloma, ulceration.
Conclusion: Histopathologically the presence of distinct lymphoplasmositosis, increased eosinophili and epithelial damage should alert for the diagnosis of complete microscopic colitis. Collagenous colitis may demonstrate intraepithelial lymphocytosis. Awareness of microscopic colitis that is common treatable cause of chronic diarrhoea needs to increase and we should be careful on histopathological examination in order not to miss the diagnosis of hidden cases.

PS-21-074

Combined eosinophilic oesophagitis and lymphocytic oesophagitis: a new entity?

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Background & objectives: Combined eosinophilic oesophagitis(EoE)-lymphocytic oesophagitis(LyE) has recently been reported in literature. Whether or not EoE/LyE is a separate entity is yet to be determined. In this study, eosinophil and lymphocyte counts were determined and their diagnostic significance for EoE/LyE was evaluated.
Methods: Oesophageal biopsies of 75 patients including 29 EoE (10 had follow-up biopsies), 6 LyE, 20 gastroesophageal reflux disease(GERD) and 20 controls were evaluated for histopathologic features comprising papillary elongation, basal cell hyperplasia, vascular congestion while eosinophils and lymphocytes were counted in hot spots at x40 magnification, on H&E and CD3 stained sections, respectively. Clinical findings were retrieved from electronic records.
Results: There were 22 males and 7 females, with a mean age of 10.8 years. Mean number of eosinophils and lymphocytes were significantly (p=0,000) higher in EoE (47.2; 58) compared to LyE (0; 46.8), GERD (1; 21), and controls (0; 11). Lymphocytes ≥29,5 and eosinophils ≥12 yielded the highest sensitivity and specificity (100% & 87.5%, 100% &100%, respectively) for EoE. Lymphocytes were above the cut-off in 87.5% of EoE, 84% of LyE, and 25% of GERD. Eosinophil count (100%) followed by lymphocytes (94%) and basal cell hyperplasia (78%) were the most important discriminant parameters EoE/LyE. No significant difference was found between initial and follow-up biopsies for eosinophil and lymphocyte counts.
Conclusion: The diagnosis is compatible with EoE, when eosinophils, LyE, when lymphocytes, combined EoE/LyE, when both are above cut-offs, and GERD when both are below cut-offs. We suggest that eosinophil and lymphocyte counts should be routinely evaluated for a diagnostic algorithm.

PS-21-077

Clinical and pathological features of rectal neuroendocrine tumours: experience from a single centre in Singapore

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Background & objectives: Rectal neuroendocrine tumours (recNETs) constitute one-quarter of gastrointestinal NETs and are often managed by endoscopic mucosal (EMR), submucosal (ESD) or full-thickness (EFTR) resection. A retrospective review was performed to assess the clinicopathological features and management of recNETs in our institution.
Methods: A search of pathology database for recNETs between January 2016 and December 2019 was performed and slides of biopsy and resection specimens [polypectomy, EMR, ESD, EFTR transanal minimally invasive surgery (TAMIS)] were reviewed. Clinicopathological parameters of identified cases were analysed.
Results: 58 specimens (29 biopsy, 14 polypectomy, 5 EMR, 3 ESD, 3 EFTR, 4 TAMIS) from 39 patients were identified (male: female=26:13; mean age=57.9 range 35-83). Indications for colonoscopy were usually altered bowel habits and haematochezia.
64.1% recNETs were solitary sessile polyp. 82.1% (32/39) were <1 cm (0.2-2.5 cm). 95% were grade 1 tumours [G1 37 (94.9%); G2 2 (5.1%)]. Histologically, 13 recNETs showed intratumoral dense sclerotic stroma. Positive margin was reported in 4 of 11 endoscopic (ESD/EMR/EFTR) resection specimens and 3 of these (75%) were associated with dense sclerotic stroma. Most (38/39) were stage I. 27 patients had follow-ups until 48 months. No local recurrence was observed after definitive ESD/EMR/EFTR/TAMIS.
Conclusion: Most recNETs were G1 and <1cm with a favourable prognosis. Local recurrence and distant metastasis were rare. Endoscopists need to be aware that it is more difficult to achieve a pathological negative endoscopic resection margin for sclerotic recNETs.

PS-22 Digestive Diseases Pathology - Pancreas

PS-22-001

Sensitivity and specificity of pancreatic EUS-FNA cytology: a retrospective review from a National Surgical Centre for Pancreatic Cancer

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Background & objectives: Endoscopic ultrasound and fine needle aspiration (EUS-FNA) is the preferred method for assessing solid pancreatic lesions.
We aimed to retrospectively review patients with solid pancreatic lesions who had EUS-FNA cytology and compare the diagnosis with the subsequent histological diagnosis.
Methods: EUS-FNA cytology from January 2016-December 2019 was identified using our laboratory system. Cystic lesions were excluded. Standard cytological terminology was used: C1 non-diagnostic, C2 benign, C3 atypia, C4 suspicious for malignancy, C5 malignant. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated twice, firstly considering C4/C5 test positive and again with only C5 considered positive.
Results: 386 patients were identified with solid pancreatic lesions who underwent FNA. 76% had a C5 diagnosis; 4% C4, 6% C3, 10% C2, and 3% C1. Subsequent histological specimens were available in 28%.
When C4 and C5 diagnoses were considered positive cytology, sensitivity was 86%, specificity 64%, PPV 95% and NPV 35%.
When only C5 was considered positive cytology sensitivity was 76%, specificity 91%, PPV 99% and NPV 31%.
Conclusion: Multiple factors affect the sensitivity of EUS-FNA. Our sensitivity is in keeping with international standards (85-93%) and our non-diagnostic category was superior to international standards (4.7-9.2%). EUS-FNA provides valuable diagnostic information in appropriately selected patients.

PS-22-002
The combined benefit of cystic fluid biochemical markers and cytology in assessing cystic pancreatic lesions: a review from a National Surgical Centre for Pancreatic Cancer
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Background & objectives: Cytological and biochemical analysis of pancreatic cyst fluid facilitates the detection of neoplastic mucinous cysts.
Our aim was to retrospectively review patients with cystic pancreatic lesions who underwent endoscopic-ultrasound -fine needle aspiration (EUS-FNA) for cytology and fluid biochemical markers (amylase, CEA).
Methods: EUS-FNA cytology from January 2016-December 2019 was identified using our laboratory system. All cytology reports were interpreted using a standardised five tier diagnostic criteria. The cytological diagnosis was correlated with biochemical markers and surgical resection specimens. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated.
Results: 77 patients with cystic lesions who underwent FNA were identified. 27% had subsequent biopsy or surgical resection. 60% of the total number of patients had cystic biochemical markers performed and these were only performed on C1 C2 and C3 specimens. 20% had raised CEA (>192) and 91% had elevated CEA and or amylase. The cytological diagnoses were: C1 30%, C2 40%, C3 8%, C4 3%, C5 19%. Final histological diagnoses were: mucinous cysts 57%, pancreatic ductal adenocarcinoma 28%; neuroendocrine tumour 5%; pancreatitis 5%; serous cystadenoma 5%.
When we considered C3/C4/C5 or raised cystic CEA (>192) and or amylase as test positive sensitivity was 85%, specificity 100%, PPV 100% and NPV 40%.
Conclusion: Cytology alone usually has poor diagnostic accuracy in cystic lesions compared with solid. Cystic fluid biochemistry has a role in ruling out malignant neoplasms. Our cytology-biochemistry results are sensitive and highly specific for mucinous cystic neoplasms of the pancreas.

PS-22-003
Epithelial-to-mesenchymal transition in undifferentiated carcinoma of the pancreas with osteoclast-like giant cells
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Background & objectives: Undifferentiated carcinoma of the pancreas with osteoclast-like giant cells is a peculiar tumour, characterized by the presence of undifferentiated neoplastic cells intermingled with histiocytes and giant cells resembling osteoclasts. This study aims at clarifying if the process of epithelial-to-mesenchymal transition.
Methods: Twelve cases of UCOCG were stained for two well-known EMT markers, Twist1 and Slug. Immunohistochemistry was performed with anti-Twist1 (clone: Twist2C1a, 1:80 dilution, Santacruz/USA) and anti-Slug (clone: rabbit, 1:350 dilution, Xeptagen/Italy) antibodies, using 4 μm formalin-fixed paraffin-embedded sections. The evidence of a positive staining was defined as the presence of a nuclear pattern of staining in the neoplastic cells.
Results: Two cases of UCOCG showed a nuclear staining pattern for Twist1 and Slug. This result highlights that EMT is not a key process in UCOCG and cannot explain the peculiar morphology of this entity. Future research should focus on the inflammatory landscape of these rare cancers.
Conclusion: Two cases of UCOCG showed a nuclear staining pattern for Twist1 and Slug. This result highlights that EMT is not a key process in UCOCG and cannot explain the peculiar morphology of this entity. Future research should focus on the inflammatory landscape of these rare cancers.

PS-22-004
Standardised pathology reporting in donor pancreata within the quality and safety in organ donation (QUOD) tissue bank: a new resource for pancreatic research
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Background & objectives: The MRC-funded Quality and Safety in Organ Donation (QUOD) Expand programme enabled the creation of a tissue biobank of whole donor pancreata for multimodality phenotyping of defined anatomical regions underpinned by standardised clinical pathologist reporting.
Methods: Examination of 8 anatomical regions (anterior/posterior) resulted in 16 FFPE tissue blocks with corresponding fresh frozen and electron microscopy (EM) samples. A standardised semi-quantitative histological scoring system has been developed for reporting human pancreatic tissue, assessing lobular/perilobular/peripancreatic compartments for inflammation, fibrosis, PanIN and other changes. Duplex-immunohistochemistry was applied to characterise pancreatic islets for hormone expression and identify PP lobe.
Results: To date 63 donor pancreata have been collected with comprehensive clinical and laboratory data. Thus far, donor organ sub-cohorts have been fully characterised to assess the applicability of the histological scoring system (n=10) and underwent quantitative assessment of acute cellular stress using the Newcastle EM Ischaemia Score (NEMIS) (n=16). PanIN was found in 14/24 organs (58%) and in 33/188 tissue blocks (18%). Fibrosis varied between organs, although was mostly mild following a spectrum of severity and patterns. Islet amyloidosis (n=1) and peliosis (n=1) were noted. The PP lobe has been identified in all pancreata.
Conclusion: Extensive sampling of 8 pancreatic regions and a detailed fully searchable scoring system is valuable for deceased donor human pancreatic tissue / islet provision to the research community to maximise translational impact. PanIN is an unexpectedly common finding. The presence and underlying cause of pancreatic fibrosis requires further investigation.

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PS-22-005

Solid pseudopapillary neoplasm of the pancreas: analysis of clinicopathological characteristics and immunoreactivity of BAP1 in 9 cases

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Background & objectives: Solid pseudopapillary neoplasms of pancreas almost always present somatic activating mutations of CTNNB1. Inactivating mutations of epigenetic regulators like BAP1 may play role in their malignant behaviour. Our aim was to investigate the role of BAP1 in this sense.
Methods: We investigated a retrospective clinicopathological analysis of patients (n=9) who were diagnosed as solid pseudopapillary neoplasm between 2010 and 2019 in our department. BAP1 antibody (Santa Cruz Biotechnology, clone C-4, 1:100 dilution) was used in paraffin-embedded tissue sections. Nuclear immunostaining for BAP1 was defined as 'negative' or 'positive', without considering a cut-off value.
Results: The median follow-up time for the patients was 31 months (range 6-102 months). There was no local recurrence or metastasis. Aggressive tumour behaviour was defined as having at least two of the histopathological features including parenchymal invasion, vascular invasion, perineural invasion, cytological atypia, adipose tissue invasion and > 5% Ki67 index. 'Aggressive' group (n=4) and relatively low-risk group (n=5) were compared in terms of BAP1 expression but there was no statistically significant relationship (p=0.722). However, there was one case with loss of BAP1 expression showing five out of six aggressive histopathological features and also with a short survival time (12 months).
Conclusion: Loss of BAP1 expression may be associated with more aggressive clinicopathological features in solid pseudopapillary neoplasm of the pancreas. Larger case series are needed to reveal the possible effects of BAP1 expression on the prognosis of this unique neoplasm.

PS-22-006

Assessing the impact of neoadjuvant therapy on lymph node yield, lymph node status and excision margin status in pancreaticoduodenectomy specimens: a ten-year review

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Background & objectives: Pancreaticoduodenectomy is the primary surgical treatment for pancreatic malignancies. Pathological examination of the specimen including lymph node dissection, is essential for staging. We assessed the effect of neoadjuvant therapy on lymph node yield and lymph node and resection status.
Methods: All pancreaticoduodenectomy specimens at St Vincent's University hospital between January 2009 and December 2019 were retrieved via a SNOMED search of the laboratory information system (n=714). Margin status, lymph node yield and lymph node status was obtained from pathology reports. Details of neoadjuvant therapy were retrieved from the patient chart or the clinical history provided on the specimen request card.
Results: 272 pancreaticoduodenectomy (PD) specimens contained pancreatic ductal adenocarcinoma and neoadjuvant therapy (NAT) was administered to 61 patients. The mean lymph node yield for NAT patients was equivalent to that of non-NAT patients (14.7 versus 14.6). The mean nodal positivity for patients without NAT was 2.6 versus 1.7 for patients treated with NAT. R0 margin status was achieved in 135 (64%) cases with no NAT versus 49 (80.3%) of NAT cases.
Conclusion: Our study has shown that neoadjuvant therapy has a positive impact on both the nodal status (N) and the resection (R) status. We have also shown that neoadjuvant therapy does not reduce lymph node yield in pancreaticoduodenectomy specimens.

PS-22-007

Immunohistochemical profile of galectin-8 in pancreatic ductal neoplasia – a preliminary report

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Background & objectives: Galectin 8 (Gal8), a "tandem-repeat"-type galectin, is currently studied in numerous tumours as prognostic factor, but limited data for pancreatic malignancies are available. Our study aims to analyse the immunohistochemical profile of Gal8 in pancreatic ductal neoplasia.
Methods: We investigated 25 cases of pancreatic ductal carcinoma, 13 of them associating intraductal proliferation (PanIN). Gal8 was assessed qualitative and semiquantitative (based on the percentage of positive cells and intensity of reaction). The semiquantitative assessment allowed the stratification in three classes: low Gal8, moderate Gal8 and high Gal8. The Gal8 immunoprofile was correlated with pTNM stage and histological variants.
Results: Qualitatively, 21 cases of pancreatic ductal carcinoma presented cytoplasmic and nuclear Gal8 expression, with low/moderate intensity; 3 cases displayed exclusively cytoplasmic expression, 1 case – only nuclear. In PanIN, Gal8 was strong cytoplasmic or cytoplasmic and nuclear, similar with normal pancreatic tissue. Semi-quantitatively, 11 cases had low score, 9 cases – moderate score, and 5 cases – high score. Significant correlations were noted between high Gal8 and pN stage (p=0.019).
Conclusion: Overall, our results indicated a loss of Gal8 expression from normal exocrine pancreas to preneoplastic and neoplastic lesions. To the best of our knowledge, our study represents the second report regarding Gal8 profile in pancreatic malignancies, preneoplastic lesions and normal pancreatic tissue, opening interesting perspective for larger studies in order to define a better stratification of cases and to correlate Gal8 expression with clinico-pathological features.

PS-22-008

Transcriptomic correlation of fine-needle aspiration samples and paired surgical specimens from pancreatic ductal carcinomas

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Background & objectives: There is evidence of transcriptomic signatures obtained from surgical specimens associated with survival in pancreatic ductal adenocarcinoma (PDAC). Most cases were diagnosed by endosonography-guided fine needle aspiration (EUS-FNA). We aim to evaluate the molecular concordance between EUS-FNA and surgical specimens.
Methods: We used a 52-gene signature by NanoString technology that identifies three populations: Cluster-1 (inflamed, stromal-dependent) characterised by upregulation of CAF and EMT-related genes. Cluster-2 (inflamed, non-stromal-dependent) presents enrichment for immune checkpoint genes and features of EMT. Cluster-3 (non-inflamed) lacks such upregulated genes. The percentage of fibrosis/epithelium was evaluated in all samples.
Results: Paired samples from 18 PDAC patients who underwent EUS-FNA for cytological diagnosis and surgical resection were analysed. The study was closed prematurely due to low concordance (5%). All three clusters were identified in EUS-FNA samples in 1 (6%), 8 (44%), and 9 (50%) cases, respectively, whereas all resected specimens where classified as cluster-1. There was less fibrotic component representation in FNA specimens (mean 10%) than in surgical specimens (mean 60%), associated with cluster-1 features.

Conclusion: The epithelial compartment is well represented in EUS-FNA samples, but fibrotic transcriptomic information is under-represented, which poses the question whether FNA material is adequate or not for molecular classification of PDAC. Further analysis with microdissection is required in order to identify the cell population aspects that explain molecular discrepancies and their impact in the prognosis.

PS-22-009

Tumour regression grading of pancreatic ductal adenocarcinoma: value of immunohistochemical and molecular markers

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Background & objectives: Tumour regression grading (TRG) of pancreatic ductal adenocarcinoma (PDAC) based on histomorphology is non-standardized. Only limited data support its prognostic significance. The aim of this study was to evaluate the prognostic value of immunohistochemical (IH) and molecular parameters in PDAC-TRG.
Methods: Tissue samples from patients with neoadjuvant treated PDAC were reviewed (n=18). CAP (College of American Pathologists) TRG score was determined for primary tumour, lymph node metastases, and distant metastases, if present. Expression of p16, p53, SMAD4, and proliferation index (Ki67) were evaluated by IH. Additionally, next generation sequencing (NGS) using the Cancer HotSpot Panel v2 (ThermoFisher) was performed.
Results: Most cases were CAP score 2 (partial response; 78%). Based on IH, co-existent aberrant p16 and p53 expression showed association with reduced overall survival (OS) (p=0.06). SMAD4 loss was also associated with poor OS (p=0.07). NGS was successful in n=16. Pathogenic variants found in n=14 included variants of KRAS (87.5%), TP53 (68.7%), CDKN2A (25%) and SMAD4 (25%). Identical variants were found pre- and post-therapy (n=3). SMAD4 variants were correlated with poor OS (p=0.02). TP53 variants correlated with the presence of distant metastasis (p=0.03). CAP-TRG was not correlated with OS. However, high CAP score (poor regression) showed a trend for positive correlation with the total number of mutated genes (p= 0.07).
Conclusion: CAP was not correlated with patient survival, questioning its role as prognostic factor. However, an association of CAP with the number of mutated genes was noted, suggesting that the mutational burden of PDAC might be involved in therapeutic response. Adding IH and molecular analyses may be more reliable for PDAC-TRG compared to using histomorphology alone. Evaluation in larger independent cohorts of patients is needed to validate our preliminary results.

PS-22-011

Nerve fibres in the tumour microenvironment are co-localised with tertiary lymphoid structures and is associated with a better survival in pancreatic cancer patients

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Background & objectives: Pancreatic Cancer (PDAC) is a lethal cancer. Here we want to define the role of small nerve fibres in cancer stroma and determine the influence on survival. We hypothesize that small nerve fibres are important in progression.
Methods: 155 PDAC slides were stained with immunostaining PGP 9.5 Nerve Fibre Density (NFD) was evaluated by counting the nerves and scored into 3 categories:
1. none
2. 1-10 nerve fibres
3. >10 nerve fibres

The dominant type of immune cells was scored into three categories:
1. lymphocyte predominant
2. neutrophil predominant
3. no immune cells.

Results: We found a highly significant correlation in the group with a high NFD (group 3; having more than 10 positive nerve fibres) and an overall survival. Univariate analysis showed that lymphocytes are present in the tumours containing more stroma. By machine learning we determined the mean distance from the nearest tumour gland from each immune cell. The patients with a high Nerve Fibre Density have lymphocytes more distant from the nearest tumour gland. These lymphocytes stain positive for B-cells (CD20), T-cells (CD8) and dendritic cells (CD21), matching a Tertiary Lymphoid Structure (TLS).
Conclusion: In this study we found a high NFD correlates with a better survival in PDAC. The spatial distribution of the lymphocyte predominant phenotype showed lymphocytes more abundant from the tumour in high NFD cases. The nerve fibres are co-localized with TLS.
We have shown that small nerve fibres in PDAC are co-localized with TLS. This can be a new therapeutic strategy in increasing life expectancy of patients with PDAC.

PS-22-012

Predicted prognosis of pancreatic cancer patients by machine learning

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Background & objectives: Pancreatic cancer remains a disease of high mortality. Mucins play crucial roles in carcinogenesis and tumour invasion. This study investigates whether the methylation status of three mucin genes from specimens could serve as a predictive biomarker for outcome after surgery.
Methods: We evaluated the methylation status of MUC1, MUC2, and MUC4 promoter regions in pancreatic tissue samples from 191 patients with various pancreatic lesions using methylation-specific electrophoresis. Then, integrating these results and clinicopathological features, we used support vector machine-, neural network-, and multinomial-based methods to develop a prognostic classifier.
Results: Significant differences were identified between the positive- and negative-prediction classifiers of patients in 5-year overall survival (OS) in the cross-validation test. Multivariate analysis revealed that these prognostic classifiers were independent prognostic factors analysed by not only neoplastic tissues but also non-neoplastic tissues. These classifiers had higher predictive accuracy for OS than tumour size, lymph-node metastasis, distant metastasis, and age and can complement the prognostic value of the TNM staging system.
Conclusion: Analysis of epigenetic changes in mucin genes may be of diagnostic utility and one of the prognostic predictors for patients with pancreatic ductal adenocarcinoma.

PS-22-013

Rapid on-site evaluation of endoscopic ultrasound-guided fine-needle aspiration of pancreatic lesions reduces repeat procedures and inadequate samples: a retrospective study from a national centre in Ireland

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Background & objectives: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is the preferred diagnostic procedure for tumours involving the pancreas. The aim of this study was to evaluate the influence of rapid on-site evaluation (ROSE) by a pathologist on specimen adequacy for pancreatic EUS-FNA.

Methods: All patients who underwent EUS-FNA for a pancreatic lesion between 2016 and 2019 whose cytology was reviewed in our centre were retrieved from the laboratory information system, which included specimens reviewed from outside institutions. Information on cytological diagnosis, presence of ROSE, subsequent histological specimens and repeat procedures was collected.
Results: Four-hundred-and-sixty-three patients underwent pancreas EUS-FNA. Of the 242 patients with ROSE performed at least once, 4%(n=10) did not achieve an adequate sample, compared to 11%(n=25/221) of patients who never had ROSE. Repeat procedures were performed on 12%(n=57), including 8%(n=18) of patients who never had ROSE and 15%(n=37/241) of those who did not have ROSE on a first procedure, versus 5%(n=10) of those who had ROSE on the first procedure.
Conclusion: This study found that ROSE in our national centre was associated with reduced inadequate sample rates and a reduced need for repeat procedures. Our findings support the practice of ROSE during pancreatic EUS-FNA as an effective and efficient means of procuring high-quality specimens.

PS-22-014

A multicenter interobserver study identifies the International Tumour Budding Consensus Conference-scoring as a reliable and reproducible method for the assessment of tumour budding in pancreatic ductal adenocarcinoma

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Background & objectives: Tumour budding (TB) is a strong and independent prognostic factor in pancreatic ductal adenocarcinoma (PDAC). Its implication into daily diagnostics would improve prognostic stratification. We performed a multicenter interobserver study to identify the optimal method of TB assessment in PDAC.
Methods: TB was scored by independent observers at five participating centres in Switzerland, Germany and Canada. Two serial sections were stained for H&E and pan-cytokeratin. Pathologists assessed TB on a digital pathology platform comparing H&E with pan-cytokeratin staining in 10 high power fields (10HPF) and one HPF hotspot (1HPF), as well as in one H&E hotspot at 20x magnification.
Results: 50 resected PDACs TNM-stage I-III were evaluated. Correlation coefficients for TB-counts between centres ranged from r=0.58648 to r=0.78641 for H&E and from r=0.69288 to r=0.81764 for pan-cytokeratin stained slides. Interobserver agreement across all centres was excellent for pan-cytokeratin 10HPF: ICC=0.81764 followed by one H&E hotspot at 20x magnification: ICC=0.78641. Assessment of TB on 1HPF reached only moderate agreement both for H&E (ICC=0.59526) and pan-cytokeratin (ICC=0.69288).
Conclusion: Based on the rates of interobserver agreement and the practicability of the method, we recommend the one H&E hotspot at 20x magnification score - as suggested by the International Tumour Budding Consensus Conference (ITBCC) 2016- as a simple, reliable and reproducible method for assessing TB in PDAC.

PS-22-015

Pancreatic neuroendocrine tumours, experience in a reference hospital in Bogotá, Colombia - a series of cases

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Background & objectives: Pancreatic neuroendocrine tumours (pNET) are a rare and heterogeneous group of tumours with very variable morphologies, functional and behaviours characteristics. Usually grow slowly and behave indolently. However, they have the metastatic potential being difficult to predict their behaviour
Methods: Patients were selected from the pathology databases; reclassified according to the 2017- WHO-Classification. A retrospective analysis of pathological characteristics found in the surgical specimens of the adult population, the correlation with pathological data and overall survival (OS), disease-free survival (DFS) and progression-free survival (PFS) as the outcome measures. Univariate analysis, the Kaplan–Meier method and log-rank test were used.
Results: There were 29 female and 26 male patients with a mean age of 53 (31-77 range), median follow-up 42 months. Well differentiated Grade 1, Grade 2 and Grade 3 (n=47:85.4%) and Poor differentiated/ Neuroendocrine Carcinoma (n=8:14.5%). CK-19 expression was correlated with 9 months less PFS and 12 months less OS. A significant difference in PFS, NETG2 had more PFS than NETG3. Surgical treatment had 26 months longer OS than other treatments.
Conclusion: Pancreatic neuroendocrine tumours are rare tumours comprising 2% of all pancreas neoplasms. In the last decade, our understanding of this disease has increased allowing for advancements in the treatment of pNETs. Positive CK-19 expression can be used as a predictor of poor prognosis. The surgical treatment is the only potentially curative therapeutic modality if resection can be complete which is associated with increased OS.

PS-22-016

Endoscopic ultrasound-guided sampling of solid pancreatic masses: the role of aspiration in fine needle biopsy

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Background & objectives: Endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) play an essential role in the diagnosis of pancreatic cancer, providing a minimally invasive method of obtaining tissue for pathological examination.
Compare the accuracy of diagnosis of specimens collected with EUS-FNB with or without aspiration.
Methods: We performed a prospective study in a general hospital, with 34 patients undergoing EUS-FNB for a solid pancreatic mass (May 2019 to January 2020). All the samples were collected in 2 passes (with and without aspiration). Pathologists were blinded to the sample collection method. The evaluated criteria were: Papanicolaou category; hematic contamination; suitability for diagnosis and best sample (size according).
Results: The results from EUS-FNB analysis were accurate for 82%(n=28) of all cases (19 adenocarcinomas, 6 neuroendocrine tumours, 2 metastasis and 1 chronic pancreatitis), without significant differences between the samples obtained with and without aspiration. However, the quality of the samples with aspiration, according to the size, was better in 55% of the cases, regardless of the hematic contamination.
Pancreatic lesions features, like size and location, didn´t interfere with the accuracy of the diagnosis.
Conclusion: In our study no differences were found in the diagnostic accuracy of EUS-FNB with or without aspiration. Our results, in spite of the small cohort, are in line with the literature.
More studies are needed in order to optimize the tissue obtained, not only aiming an accurate diagnosis but also to acquiring enough sample for ancillary studies and target therapy evaluation.

PS-22-017

Pancreatic neuroendocrine tumours treated with CAPTEM or everolimus. A multicentric study of MGMT, NDRG-1 and PHLDA-3 immunohistochemistry expression as predictor of outcome

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Background & objectives: Previously our group showed the use a score (SPI) of MGMT, NDRG-1 and PHLDA-3 immunohistochemistry expression as predictor of outcome in operated Pancreatic Neuroendocrine Tumours.
Objective: To analyse the predictive role of SPI in advanced PanNET treated CAPTEM or everolimus.
Methods: 60 of 105 patients have been fully analysed. 30 treated with CAPTEM and 30 with everolimus. Paraffin-embedded tissues from resected tumours were stained. Immunohistochemistry (IHC) nuclear staining for MGMT and PHLDA-3 is being scored: 0, 1-5%, 6-50% and ≥ 51%. For NDRG-1, we are using a cytoplasmic score from 0 to 2 based on distribution pattern (null, patched or diffuse).
Results: Median lines were 1 (21.7% chemotherapy previously), and 91.7% of patients had ki67 <20%.
65.5%, 10.2% and 29.1% were null for MGMT, NDRG-1 and PHLDA-3 IHC analysis. Analysis showed significant differences for PFS or OS based on best response observed and number previous lines received. Patients treated with CAPTEM, showed significant differences for PFS (p=0,047) and OS (p=0,040). Similar, although not significant, results were observed in everolimus-treated cohort for PFS
Conclusion: As it was described previously in operated PanNET, our SPI also seems to own predictive role in patients with advanced PanNET treated with CAPTEM or everolimus.
The present project is funded by grant from 2016 GETNE.

PS-23 Electron Microscopy

PS-23-001
Ultrastructural features of angiogenesis in invasive carcinoma of no special type

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Background & objectives: Activation of angiogenesis is a key step in the invasion and metastatic spread of malignant tumours.
Methods: We studied 86 cases of invasive carcinoma of no special type (IC NST). Tumour sizes ranged from 1 cm to 8 cm, the average size of the tumour node was 2.8 + 2.6 cm. Ultrathin sections were examined by using a «Zeiss Libra 120» electron microscope.
Results: Proliferation of the endothelium, dissociation of interendothelial contacts with the intercellular clefts and canals, and local lysis of the basement membrane with endothelial cords resembling growth buds were noted in the vascular bed in the zone of the epithelial-mesenchymal transition
The vessels didn't reach full maturity and were represented by microvessels of the capillary, venular and sinusoid type, which had an abnormal wall structure, which made it difficult to limit the type.
Tonofilaments and a small accumulation of cytoplasmic organelles were in the cytoplasm of the endothelium of tumour capillaries. We noted an accumulation of luminal and cytoplasmic micropinocytotic vesicles, which were an indicator of the activity of cell metabolism.
Conclusion: Ultrastructural changes (absence of pericytes and a formed basement membrane) clearly indicate the presence of microvascular mimicry in the tumour, imperfect angiogenesis, accompanied by the appearance of tumour nests without endothelial lining, shows the presence of retraction gaps with a thinned wall.

PS-23-002
Ultrastructural and immunohistochemical evaluation of breast cancer fibroblasts

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Background & objectives: It is known that tumour cells interact closely with their microenvironment, which includes tumour-associated fibroblasts (CAFs), immune cells, endothelial cells, pericytes, and extracellular matrix components. All these components induce the development of an epithelial-mesenchymal transition (EMT).
Methods: 82 cases of invasive carcinoma of no special type (IC NST) were studied. Transmission electron microscopy, histochemical analysis (PAS reaction) and immunohistochemical analysis using EMT markers were used. Ultrathin sections were studied in a Zeiss Libra 120 electron microscope.
Results: We identified 3 varieties of CAF in invasive carcinoma of no special type: those associated with α-SMA, subplanin, and CD44. Expression of all 3 markers was maximally expressed in zones of invasive growth. At the ultrastructural level, tumour stromal fibroblasts have a different degree of maturity, in their structure they do not differ from non-tumour tissue fibroblasts. in the narrow tanks of which an accumulation of fine-fibrous flocculent material and its entry into the extracellular space is noted. The Golgi apparatus is well expressed, large single mitochondria are noted. There are fibroblasts in which vesicles of the type of cross-secretory granules are formed, with microfilaments inside the expanded GER (myofibroblasts).
Conclusion: When studying the stroma of invasive carcinoma of no special type (IC NST), 3 types of CAF were identified with ultrastructural features of proliferating, able to migrate and possessing secretory fibroblast activity. CAFs are maximally represented in invasive growth zones (EMTs).

PS-23-003
Ultrastructural diagnosis of neonatal herpes simplex virus infection presenting as fulminant hepatitis

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Background & objectives: Among neonatal fatal diseases noteworthy is the Herpes Simplex Virus (HSV) infection as cause of fulminant hepatitis as viral diagnosis may be difficult to establish. A healthy new-born male hospitalized for status epilepticus worsened rapidly to death.
Methods: A metabolic disease with multi-organ involvement was firstly suspected and skin and muscle biopsies were obtained. Muscle biopsy was routinely processed for histoenzymatic and ultrastructural analysis. Autoptic samples, kidney, liver and myocardium were routinely processed for histology and immunohistochemical (IHC) analysis and some also for ultrastructural analysis.
Results: Muscle biopsy showed unspecific myopathic damage with mitochondrial alterations. Ultrastructurally, liver samples showed many rounded-polygonal viral particles (70 nm) with an electrondense core (herpes-like virus), mainly detectable both in the nucleus and cytoplasm of hepatocytes. IHC analysis defined viral particles as type I HSV. Moreover, type I HSV positivity has been confirmed also in cortical adrenal glands.
Conclusion: Ultrastructural analysis, even in autoptic cases, allows to make a precise diagnosis when clinical features are not suggestive: fulminant hepatic and multi-organ failure can be induced by HSV infection. It has high mortality for untreated neonates and early diagnosis is difficult as the characteristic vesicular rash may be absent, early symptoms often nonspecific and HSV infection maternal history not evident. Neonatal HSV infection, although rare, can cause neonatal hepatic failure.

PS-24 IT in Pathology

PS-24-001
Digital pathology; awareness, practice, and challenges in a developing country like Pakistan

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Background & objectives: In the past decade, a revolution in pathology, digital pathology, is defined as the electronic capture, analysis, and distribution of gross or microscopic specimens. The aim of this study is to determine the perception of various pathologists regarding digital pathology, its applications, and challenges.
Methods: A cross sectional descriptive survey was conducted involving 76 surgical pathologists including postgraduate residents of different levels and consultants belonging to different governmental and private institutions of Pakistan. The respondents were evaluated by means of a self-designed questionnaire prepared after extensive literature search. Data was entered and analysed using SPSS version 21.
Results: The overall response rate was 98%. The awareness regarding digital pathology and its uses varied among respondents depending upon their level of residency. Many practical perspectives of this field were either missing or not being followed in spite of provision in some institutions. However, majority of the institutions were lacking in this facility. Many challenges in implementation included lack of awareness, financial constraints, improper technical support and backup, and disinterest in the new technology.
Conclusion: Awareness among residents and practicing surgical pathologists can be increased by encouraging their participation in dedicated workshops thus familiarizing them to its various advantages. Teaching undergraduates using different digital pathology techniques is perhaps the best way to demonstrate its effectiveness.

PS-24-002
Low cost diagnosis support system using the remote desktop

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Background & objectives: Although WSI scanners have become more sophisticated in recent years, they are still expensive. For consultation, WSI is useful, but small hospitals need cheaper systems. Therefore, the usefulness of the system using the remote desktop (RDP) was verified.
Methods: We collected 50 intraoperative diagnostic specimens. On the RDP distribution side, a pathologist or clinical technician operated the microscope and displayed the image obtained from the CCD camera. On the receiving side, a RDP connection was made from a smartphone via a 4G line, and pathologists diagnosed while instructing the viewing site via telephone. Then, we compared the coincidence rate.
Results: Regarding diagnostic accuracy, no statistical difference was found between the diagnosis using RDP and using microscope. However, the diagnosis time tended to be slightly longer when RDP was used. This tendency was remarkable when the laboratory technician operated the sender. In addition, in the diagnosis by RDP via the 4G line, there was almost no problem of the diagnosis due to the delay of the image and the unclear image.
Conclusion: It was shown that even a low-cost system using a conventional CCD camera and RDP can provide sufficient performance for consultation for rapid intraoperative diagnosis. If it is a small specimen, it can be applied to a consultation system for routine diagnosis. This system can be configured at about one tenth the price of a WSI scanner and can be installed in many small hospitals. It is considered that this system may contribute to the equalization of diagnostic accuracy.

PS-24-003
Views on digital pathology: a departmental survey

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Background & objectives: Prior to the changeover to digital pathology at the Queen Elizabeth University Hospital Glasgow (QEUH) we aimed to investigate the views that pathologists held towards it, to allow a comparison with a repeat questionnaire once the changeover is complete.
Methods: A printed questionnaire was handed to all trainee and consultant pathologists (total=59) in October 2019. Participants were asked to rate their views towards the plans to change to digital pathology and whether they thought reporting biopsy and resection specimens would be faster or slower. Free text fields for perceived advantages and disadvantages of digital pathology were also given.
Results: 44 completed questionnaires were returned (14 trainees, 26 consultants). Feelings towards the introduction of digital pathology were generally positive (average = 4.1, 1 being very negative and 5 being very positive), particularly amongst trainees (average = 4.4). The main perceived advantages were measuring, sharing slides with colleagues and experts, access to archive and ergonomics. The main perceived disadvantages were IT issues, costs, image quality and a delay caused by scanning.
Conclusion: At the QEUH there is a positive attitude towards digital pathology, but concerns remain. The changeover to digital pathology is now underway and digital workstations are being installed for both consultant and trainee pathologists. This study serves as a baseline measurement and will allow for a meaningful comparison with a repeat questionnaire in 2 years' time, to see if real-life use of digital pathology changes pathologists' views towards it.

PS-24-004
Detection of lymph node metastasis in colorectal cancer with the help of deep neural network

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Background & objectives: Lymph node status predicts prognosis and guides management in colorectal cancer. At least 12 lymph nodes are to be assessed for proper staging. The examination of lymph node metastasis is an important but tedious task for the pathologist.
Methods: The primary aim was to develop a deep learning algorithm that can detect and outline metastatic cancer in digitalised histologic sections of colorectal lymph nodes with at least the same sensitivity and specificity as pathologists. Lymph nodes with and without metastases from patients with colorectal cancer operated at Västmanlands Hospital were included and the glasses scanned on a Hamamatsu scanner.
Results: To maximize the performance of the deep learning algorithm two pathologist annotated, on pixel level, areas of metastases in each positive node. A deep learning algorithm pre-trained with Camelyon data was trained on 270 (138 with cancer and 132 benign) whole slide images (WSI). The performance was evaluated on 26 WSI with cancer and 9 benign. The median sensitivity for cancer images was 0.88 and the median specificity for benign images was 1.00.
Conclusion: These encouraging preliminary results indicate that a deep neural network could be developed to identify and outline lymph node metastasis in colorectal resections. This deep neural network will be further developed and in the future may serve as a decision support tool for pathologists in their routine diagnostic process.

PS-24-005

Deep learning as a tool for the diagnosis of mycosis fungoides

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Background & objectives: Mycosis Fungoides (MF) is a form of cutaneous T-cell lymphoma where lymphoid cells with atypical nuclei infiltrate epidermis. Nuclei detection is an application of deep learning and in this study, we utilized deep learning for the diagnosis of MF.
Methods: 25 MF and 25 non-MF cases were enrolled in this study. Photographs of cases were then classified via a deep learning algorithm. Nuclei are detected, features are extracted, values are visualized and integrated on to the same image with colour codings above each lymphocyte as to whether that lymphocyte nucleus is atypical or not.
Results: Nucleus area, hue, saturation, heterogeneity, roundness, convexity extracted from each nucleus showed that all features showed statistically significant difference between MF and non-MF cases. The deep learning algorithm developed during this study achieved 85% accuracy in classifying lymphocytes as atypical or normal.
Conclusion: MF is a type of cutaneous lymphoma that is potentially fatal, so correctness of the diagnosis is of utmost importance. In order to diagnose MF, pathologist should determine if the lymphocytes seen in the biopsy specimen are atypical or not. We developed a deep learning algorithm that can achieve high accuracy in this task. This algorithm may be used as a secondary tool in the diagnosis process in the future.

PS-24-006

The efficacy of virtual microscopy in teaching practical pathology to medical students at an international college of medicine in Thailand: a comparison of pre-test and post-test scores with student satisfaction

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Background & objectives: Historically, conventional light microscopy (CLM) was the preferred learning modality in pathology courses for almost two centuries. Virtual microscopy (VM) has been recently challenging traditional practices and providing a new realm for pathology diagnostics. However, most medical schools in Thailand still use CLM to teach pathology for medical students. This study aims to evaluate the effectiveness of digital pathology in terms of undergraduate teaching, which is the first experience at Thammasat University.
Methods: Participants were 29 second-year medical students who sat in the practical session of the alimentary system pathology using VM as a teaching modality. Students took pre- and post-test with 12 items covering common alimentary diseases, followed by ten survey questions with a five-point Likert-style scale. Test and satisfaction scores were analysed.
Results: There was a significant difference ($p<0.01$) between students' pre-test scores (mean±SD, 1.7±2.1) and post-test scores (7.1±3.4). VM was viewed as efficient in terms of undergraduate education, mainly because of its portability (mean: 4.9 on the five-point Likert-scale), satisfactory quality of images (4.4), allowing learning in less time (4.3), and stimulating cooperation between students with improving interaction with teachers (4).
Conclusion: The students' perceptions regarding VM as a new teaching-learning tool and their excellent performance on the knowledge exam suggest that VM has a potential role in undergraduate teaching. Further studies with a comparison with CLM, recruiting more participants, and other practical sessions are needed to prove whether VM is useful in terms of undergraduate teaching in Thailand.

PS-24-007

Evaluation of Ki67 stained neuroendocrine tumours of the gastrointestinal tract

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Background & objectives: Despite the established role of the Ki67 labelling index for neuroendocrine tumours (NET), its evaluation suffers from subjectivity and technical shortcomings. We perform a study to assess different Ki67 quantification techniques including manual evaluation, traditional image analysis, and machine learning.
Methods: Eighty regions of interest from ten Ki67 stained NETs were chosen randomly. To assess the ground truth, an experienced pathologist counted positive and negative tumour cell nuclei on digital slides. For traditional image analysis, the Aperio Nuclear Algorithm was applied. Finally, a machine learning system (Aiforia™) was trained with a training data set (29 digital slides).
Results: The observed correlation between traditional image analysis and ground truth was not significant ($R2=0.4$). This may be justified by the difficulty of the Nuclear Algorithm to only include tumour cells and ignore interstitial cells and lymphocytes nuclei. We also found that the algorithm could not properly separate overlapping tumour cell nuclei. On the other hand, an intra-observer study noted that traditional image analysis offers increased reproducibility compared to manual evaluation ($R2=0.9$). Finally, the machine learning approach successfully identified and segmented tumour cell nuclei and offered a performance, in one test sample, of overall 90% precision and 94% sensitivity.
Conclusion: Nuclear detection and segmentation in NET for assessing the Ki67 labelling index is a challenging task for traditional image analysis. A machine learning solution on the other hand, once trained and verified, delivers reliable and reproducible results and is hence preferable.

PS-24-009

Blinded external validation of a multi-feature AI-based algorithm in prostate core needle biopsies

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Background & objectives: There is high demand to develop clinically useful computer-assisted diagnostic tools to evaluate prostate core needle biopsies (CNBs). Clinical validation of AI systems able to analyse histopathology images of prostate cancer, especially in large independent blinded studies, is still lacking.
Methods: Ibex Medical Analytics has developed an AI-based algorithm that identifies various cell types, tissue structures and morphological features within whole-slide-images (WSI) of prostate CNBs trained on 1,357,480 image patches.
Results: We validated the performance of the algorithm on detection of adenocarcinoma, Gleason scoring, identification of perineural invasion, and calculation of cancer proportion in an external dataset of 100 consecutive cases (1,627 slides) from UPMC digitized on an Aperio AT2 scanner. Ground truth ascertainment was conducted for a subset of the slides with two independent pathologists, resulting in adjustment of diagnoses in accordance with the algorithmic output in some cases.
The algorithm demonstrated high AUCs for all parameters, and specifically an AUC of 0.991 for adenocarcinoma detection, the highest reported in the field in a blinded data set.
Conclusion: These results suggest that this AI-based algorithm can be used as a computer-assisted diagnostic tool to automate screening of

prostate CNBs for primary diagnosis, assess signed-out cases for QA purposes, and standardize reporting to improve patient management. We will further discuss the performance of the algorithm and its clinical utility in routine use in a pathology lab.
Ibex Medical Analytics funded the study.

PS-24-010
Going virtual: a medical students' performance assessment
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Background & objectives: The change to virtual microscopy in our Pathology Department approaching, we aimed to compare long term information retention following a classical power point (PPT) presentation versus virtual slides (VS) as tutorial teaching material, in order to assess students' performance.
Methods: We recruited 3rd year medical school students, French Division, from the University of Medicine and Pharmacy Victor Babes Timisoara. A cross-over design was employed, and students were randomly allocated into 2 study groups: G1(n=14) – 1st lab PPT and 2nd lab VS and G2(n=18) – vice versa. Student performance was assessed on memory retention MCQ tests, administered two weeks later.
Results: Significant higher scores were found in favour of VS, in between comparisons when comparing G1 with G2, with a mean difference of 3.32 points with 95%CI (1.86;4.79) in lab 1 and a mean difference of 2.23 points with 95%CI (0.67;3.79) in lab 2 and within each group: a mean difference of 3.1 points with 95%CI (1.23;4.9) for G1 and a mean difference of 2.5 points with 95%CI (1.35;3.64) for G2.
Conclusion: Our results show that for our French Division students, the change of the teaching materials used in the tutorial part of the microscopy labs from PPT to VS is beneficial from the point of view of long-term information retention.

PS-25 Other Topics

PS-25-001
Predictive value of serial daily platelet count in assessing progression to Dengue shock syndrome amongst Dengue patients
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Background & objectives: Early identification of adults presenting with dengue who are likely to develop DSS can decrease mortality and resource allocation in endemic areas. The objective of this study was to assess the values of haematocrit and platelet count in predicting DSS.
Methods: In a prospective observational study, we analysed data of 325 adult patients admitted between May-Nov 2019. The population comprised of all adults with laboratory-confirmed dengue enrolled between days 1–4 of illness. Logistic regression was the main statistical model for all univariate and multivariable analyses. Prognostic value of daily haematocrit levels and platelet counts were assessed on each day of illness.
Results: Amongst the 325 patients included in our study, 29 (9%) progressed to DSS. Significant baseline risk factors for DSS included a history of vomiting, higher temperature, cough, and hepatosplenomegaly. Prediction models that included serial daily platelet counts demonstrated better ability to discriminate patients who developed DSS from others, than models based on enrolment information only. However, inclusion of daily haematocrit values did not improve prediction of DSS.
Conclusion: It was concluded that serial daily platelet counts provide useful additional information to identify adults at an early stage who are likely to develop DSS, in addition to other risk factors e.g., hepatosplenomegaly, cough, vomiting, and high temperature.

PS-25-002
Challenges of participation in proficiency testing by different surgical pathology laboratories; a perspective from Pakistan
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Background & objectives: Proficiency testing is mandatory for any surgical pathology laboratory in order to achieve accreditation and for improvement. Aim of this study is to determine the perception of laboratories regarding PT, their routine practice and challenges in a developing country like Pakistan.
Methods: A cross sectional descriptive survey was conducted involving 35 surgical pathology laboratories including both private and government, from different regions of Pakistan. Their participation in various proficiency testing modules was evaluated. The respondents were evaluated by means of a self-designed questionnaire prepared after extensive literature search. Data was entered and analysed using SPSS version 21.
Results: The different PT providers included; CAP, UKAS and RCPATH Australia. Only one laboratory was CAP accredited while some of them were just participating in either technical or diagnostic modules of PT. Many laboratories were accredited for ISO15189 by Pakistan National Accreditation Council. Laboratories which were not participating in PT were either unaware of it or had financial constraints. Few of the laboratories were participating in inter-laboratory comparison as part of external quality assurance program.
Conclusion: PT results in improved laboratory standards and performance. Laboratories especially in developing countries should be encouraged to participate in PT by easy accessibility to various PT providers, maintaining their performance graphs, awareness workshops/seminars and offering them discounted rates for different modules.

PS-25-003
Pan-TRK immunohistochemistry in 9 secretory carcinomas
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Background & objectives: Neurotrophic tyrosine receptor kinase (NTRK) gene family encodes tropomyosin receptor kinases (TRKA, TRKB, TRKC) in which gene fusions are oncogenic drivers of various tumours, one of them, secretory carcinoma. Immunohistochemistry (IHC) can be used as a screening for those alterations.
Methods: We reviewed information from the medical records of 9 patients aged from 4 to 68 years with pathologic diagnosis of secretory carcinoma between 1990 and 2019 at our institution. Tumours were located in the parotid gland or breast parenchyma. NTRK overexpression was studied by immunohistochemistry.
Results: We reviewed information from the medical records of 9 patients aged from 4 to 68 years with pathologic diagnosis of secretory carcinoma between 1990 and 2019 at our institution. Tumours were located in the parotid gland or breast parenchyma. NTRK overexpression was studied by immunohistochemistry.
Conclusion: Secretory carcinomas are invasive tumours composed of epithelial cells with intracytoplasmic vacuoles often associated with E7V6- NTRK fusion.
IHC can be used to detect TRK overexpression and be useful as an effective screening tool for NTRK gene fusions. Positive results should be followed with a confirmatory molecular test if TRK inhibitors treatment is considered.

PS-25-004

Gliclazide suppresses inflammation via modulation of cyclooxygenase and immune pathways in an experimental diabetic model

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Background & objectives: N-(2-cyclohexyl-4-nitrophenyl) methane sulfonamide (NS-398), a reported inhibitor of cyclooxgenase-2 (COX-2) belongs to sulfonylurea group. In this study we aim to assess and explore anti-COX-2 and β-cell protective activity of Gliclazide (sulfonylurea) an antidiabetic drug using both in-silico and in-vivo tools.
Methods: COX-2 (PDB: 3QMO) was docked with Gliclazide using AutoDock Vina (Lamarckian Genetic Algorithm) and ArgusLab software. Prostaglandin E2, EP4, COX-2, COX-1, IL-1β and TNF-α were measured in STZ-induced diabetic models (β-cells), carrageenan-induced paw oedema and peritonitis in albino rats treated with Gliclazide (i.e. Sulfonylurea) using ELISA and RT-PCR. β-cell functional genes PDX1, NKX6.1 and MAFA expression were quantified using RT-qPCR.
Results: Binding interaction of Gliclazide with the side chains of R120 and Y355 in COX-2 channel were same as NS-398. H-bonding and van-der-Waal interaction were appreciated with R120, W387, A527, S530 and L531. Expression levels of COX-1, COX-2, TNF-α and IL-1β were inhibited 96±2.1%, 73±0.8%, 93±0.7% and 63±0.3%, respectively. Paw oedema, PEG2 levels and expression of PDX1, NKX6.1 and MAFA showed promising results with the therapeutic doses of Gliclazide. Inhibition of carrageenan induced paw-oedema and peritonitis, reduced levels and expression of PGE2, EP4, COX-1/2, IL-1β and TNF-α along with improved expression of β-cell functional genes (PDX1, NKX6.1, MAFA) revealed gliclazide anti-inflammatory potential and supported its interaction with catalytic residues of COX-2.
Conclusion: Taken together, breaking IL-1β/COX-2/PGE2 pathway loop using single therapeutic dose of Gliclazide revealed its therapeutic potential to improve β cell function and insulin secretion by its anti-COX-2 and β-cell protective activity besides its antidiabetic activity.

PS-25-005

Companion diagnostics in immunotherapy: evolving role and impact of PD-L1 testing within a referral laboratory

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Background & objectives: Cancer management guidelines continue to evolve by merging PD-1/PDL-1 testing with introduction of companion diagnostic approaches. Aim of this study was to provide a comprehensive overview of the requirements and potential challenges for laboratories resulting from introduction of PDL-1 assessment.
Methods: Histopathology reports (5-year period - Jan 2014 to Jan 2020) incorporating PDL-1 test results were identified and analysed for tumour type, clone and result (as per recommendations).
Results: PDL-1 testing requested in 238 cases was undertaken in 199 of them - with a clear majority in the last two years. Commonest tumour types included pulmonary (76%) and urological (15%) with remaining 9% including eight other tumour sites/ types. Majority (59%) of cases were reported to be PD-L1 positive.
Conclusion: This study highlights an interesting recent trend for test requests in cancer settings, with resulting reporting challenges in the absence of similar defined guidelines and, potential requirement for validation of more than one antibody clone to meet test recommendations.

PS-25-006

Assessment of immune cell heterogeneity in the tumour microenvironment

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Background & objectives: Levels of tumour infiltrating lymphocytes are critical biomarkers for quantifying the therapeutic value of cancer immunotherapies. We sought to understand marker variability across and/or within patients, with diversity including indications, treatment history, tumour heterogeneity, lesion site and type.
Methods: Utilizing data from >1000 baseline tumour samples from clinical trials and commercially available sources, we compared how markers of immune activation (Ki67+ CD8A+ T cells/mm2) or tolerance (FOXP3+cells/mm2) varied by demographics, indication, lesion site, lesion type, fresh or archival status, and treatment history. Where multiple tumours were available from the same patient, we evaluated how densities fluctuated within individuals.
Results: We found meaningful and statistically significant differences in both proliferating CD8+ T cells and FOXP3+ cells by indication, lesion type and site, and prior treatment with immune checkpoint inhibitors, chemotherapy or hormone-related therapies. There was no significant linear relationship between time since treatment and density of either cell population. Within-patient differences by lesion site and type were smaller than between-patient differences but still statistically significant. Fresh core needle biopsies had almost twice the density of Ki67+ CD8 T cells than archival tissue and the difference was meaningful even within patients. We found no statistically significant difference in either immune cell marker level by age or gender.
Conclusion: We identified factors that vary in baseline and on-treatment samples and are associated with immune infiltrate levels, creating bias—even within patients. Applying our results towards an algorithm for biomarker analysis will improve the accuracy of measuring treatment-related effects on the tumour microenvironment. Understanding lymphocyte heterogeneity can provide opportunities for patient selection and define new markers of tumour and immune cell engagement to predict susceptibility to immunotherapy or identify biological modulation.

PS-25-007

The evaluation of fixation practices on VENTANA immunohistochemical assays

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Background & objectives: During the development of VENTANA immunohistochemical (IHC) assays, fixation studies are conducted to ensure assay performance is acceptable within established standards and to provide information on any limitations observed with fixatives or fixation times that may yield inaccurate results.
Methods: Fresh tissues well characterized for biomarker expression were harvested to limit ischemic time. Samples were immediately subjected to various fixatives for a range of 1-72 hours. The samples were then compared to a reference fixed within established guidelines. This data set compiles the results of these studies across eleven VENTANA assays tested with various formalin, alcohol, and glyoxal based fixatives.
Results: Across all VENTANA IHC assays tested, crosslinking formalin-based fixatives yielded more consistent results within 6-72 hours by demonstrating overall percent agreement (OPA) rates of 95.4% and 98.5%, respectively, to the reference sample. Comparatively, 1-72 hours in formalin fixatives yielded 88% and 87.6% OPA, respectively. Alcohol and glyoxal-based fixatives exhibited more variability within 6-72 hours of fixation resulting in OPAs of 12.8% and 38%, respectively.

Conclusion: The potential of fixative types and fixation times to yield inaccurate results necessitated the need for standardization such that The College of American Pathologists (CAP) and American Society of Clinical Oncology (ASCO) developed guidance for HER2 Testing in Breast Cancer (2018). These data corroborate the established CAP/ASCO guidelines and demonstrate the importance of standardization in fixation practices to yield accurate IHC results, particularly for predictive assays that aid in determining patient treatment regimens.

PS-25-008

Twitter is a useful and effective tool for pathologists worldwide in the diagnosis of breast pathology

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Background & objectives: In Pathology the use of Twitter with educational purposes has increased recently. Under the hashtag #breastpath is tagged reliable information about breast pathology. The aim of this study is to highlight Twitter as a tool to share educational information.
Methods: Using the advanced Twitter search tool we tracked the #breastpath tag during the period between April 2018 and June 2019. We studied this variables: author, number of comments, retweets and "likes". We added together tweets according to its objective (teaching, consultation, sharing information of congresses or papers) and according to the type of Breast pathology (special subtypes, benign pathology,...).
Results: 300 tweets from 136 pathologists from 27 countries were reviewed. The pathologists who most frequently publish came from the US, Spain and Brazil, the most active being Jenny Pincus (@jennpincus, USA), Gerônimo Junior (@GeronimoJrLapac, Brazil) and Idaira Expósito (@ijexpafo, Spain). The user with the highest average of likes/tweet was Mario Prieto (@dr_MPrieto, Spain) and retweets was Kalyany Bambal (@kriyer68, USA). The goal of the tweet was 59% for teaching purposes, 7% to share doubts, 22% related to congress and 13% to highlight a paper. Regarding pathologies tweets were about: benign lesions (35%), special subtypes (16%), NOS carcinoma (5%), metastatic lesions (4%) and molecular pathology and immunohistochemistry (5%).
Conclusion: Twitter is a useful and effective tool for sharing and teaching information about breast pathology. It also generates a valuable interaction between professionals around the world involved in the diagnosis of breast cancer and benign breast lesions.

PS-25-009

Quality improvement project: a survey on the use of photography during cut-up at Wycombe Hospital, United Kingdom

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Background & objectives: We sought the views and experiences of Histopathologists in our department regarding the use of photography during specimen cut-up, with the aim to determine whether the creation of a Standard Operating Procedure (SOP) would be useful.
Methods: We asked all the Histopathology consultants, staff grades and trainees in our department (n: 16) to complete a qualitative and quantitative survey comprising a combination of 13 open and close-ended questions. The survey was open for 1 month, after which the data was analysed.
Results: The response rate was 87.5%. 100% of the respondents answered they thought it was useful to take photographs of specimens during cut-up, mostly on a case-by-case basis. 64% answered they were aware of consent and data protection issues. 64% answered they had used photography during cut-up before, but 93% said they did not know where to find the camera and 79% did not know how to use it. 93% did not know where to upload the images and 79% did not know how to make users aware of them. Finally, 86% answered that it would be useful to have an SOP to guide through the process of specimen photography.
Conclusion: The survey showed an awareness of the need for photography during cut-up in our department, but highlighted a lack of knowledge of the processes involved and how to access the images, deeming the creation of an SOP appropriate. We therefore propose a potential SOP for our department, to include the designation of a 'Camera Supervisor' to oversee any issues related to the camera and/or images.

PS-25-010

Importance of the size of the field of view for standardized biomarker evaluations

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Background & objectives: Interest in digital microscopy has increased exponentially. Guidelines for standardized evaluation of biomarkers are mainly defined for light microscopy (LM). This study aimed to define parameters for alternative standardized use of digital and light microscopy for biomarker evaluations.
Methods: Microscopes with field numbers (FNs) 23 and 18, respectively, a HD computer monitor with diagonal of 56 cm, 100% size scaling and 1920x1200 resolution and a 3K computer with monitor diagonal of 31 cm, 200% size scaling and 2736x1824 resolution were used. PD-L1 stained cancer sections were scanned with Leica Aperio AT2 slide scanner and evaluated with Aperio ImageScope.
Results: Field of view (FOV) adjustment was required to enable standardized PD-L1 scoring. Light microscopic FOV was calculated using the FN of the ocular, and digital FOV using Aperio ImageScope. At 20x setting identical size areas could be examined in 10 and 16 LM FOVs using the microscopes with FNs 23 and 18, and 23 and 45 digital FOVs for computers with monitor diagonals of 56 and 31 cm, respectively.
Conclusion: This preliminary investigation has helped to identify field of view (FOV) and field number (FN) as the two key parameters for standardized evaluation of biomarkers by physicians and scientists in multicenter studies equipped with different light microscopic and digital imaging apparatus. The adjustment for these two parameters could also facilitate a comparison of retrospective research data obtained with different microscope or digital image settings, and standardized training of pathologists in scoring of PD-L1 on glass slides and digital images.

PS-25-011

Computer-assisted analysis of sources of variability in PD-L1 combined positive score (PD-L1cps) estimation

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Background & objectives: PD-L1cps is used for immune-oncological typing of solid tumours. Study investigated sources of variability in estimation of its constituent parameters: number of viable tumour cells (vTC), PD-L1-positive tumour cells (PD-L1PTC) and PD-L1-positive immune cells (PDL1PIC), in head-and-neck cancer (HNC).
Methods: A digital image of HNC stained for PD-L1 with 22C3 pharmDx kit, was analysed for vTC, PD-L1PTC, and PD-L1PIC using Visiopharm tissue selection application, to determine PDL1cps in 3 non-overlapping 0.64 mm2 digital fields, 3 independent times by an expert trained medical student. Mean % coefficient of variation (MCV% of the 3 repeats) was calculated as an index of variability.

Results: The mean (range) counts of vTC, PD-L1PTC, and PD-L1PIC included within 0.64mm2 digital image frames (n = 9) as manually determined on three repeat analyses, were found to be 819 (478-1559); 165 (75-255); 125 (89-166), respectively. For each of these three parameters, the relative variability (MCV% = 1 standard deviation/mean x 100) was calculated to be 33, 50 and 19, respectively, and that for PD-L1cps to be 21. According to statistical criteria applied to small samples MCV% of <20 is considered to be a reflection of good reproducibility; <30 as indicative of acceptable reproducibility; and that of >30 as representative of overall poor reproducibility.
Conclusion: Visiopharm tissue selection application provides a means of determining the sources of variability in PD-L1cps estimation by allowing simple manual annotation of individual cells of interest in predefined areas of digital images. The poor reproducibility of vTC and PD-L1PTC estimation indicates need for more objective methods for identification of viable tumour cells and PD-L1-labelled tumour cells, whilst the higher precision noted in estimation of PD-L1IC acknowledges its greater clinical utility.

PS-25-012
Immunohistochemical detection of FAS in formalin-fixed paraffin embedded tissues

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Background & objectives: FAS is a receptor protein of the the tumour necrosis factor receptor superfamily. Engagement with its ligand FASLG induces the formation of death inducing signalling complexes triggering apoptosis. FAS is a pivotal immune-regulator involved in peripheral tolerance and other processes.
Methods: Various mAbs were batch-tested for suitability in IHC of FFPE tissues. Various tissues and antigen retrieval methods (AGR) were tested. All assays were performed on a Leica automated stainer platform.

Clone	Company	Order #
EPR5700	Abcam	ab133619
B-10	Santa Cruz	sc-8009
C18C12	Cell Signalling	4233S
Y599	abbexa	abx233017
LT95	Novus	NB500-503
DX2	BioLegend	305614
APO-1-1	eBioscience	BMS151
UB2	MBL	MD-10-3

Results: All antibodies were tested on a panel of ten normal tissues and modifications of the staining protocol employing different buffer solutions as well as enzyme pre-treatment. However, most antibodies did not render any staining at all or demonstrated diffuse overall labelling not compatible with FAS expression. Clone EPR5700 showed moderate good staining congruent with FAS expression employing heat-based AGR and a hipH buffer. Best and most consistent immunostaining was achieved with clone mAb LT95 when employing enzyme pre-treatment (Leica, Enzyme 1). Staining was intense and membranous with variable cytoplasmic component. Specificity was confirmed by comparative analysis of LT95 staining with immunostaining of FAS-defining mAb APO-1 on frozen tissues.
Conclusion: Proper evaluation of molecules involved in immune-regulatory processes is mandatory for the understanding of tumour biology especially in the context of novel immunotherapeutic approaches such as checkpoint therapy. Interestingly, few data about death receptor FAS are available. Moreover, most data were gathered on frozen specimens and/or with discontinued polyclonal reagents. Our present study allows for accurate assessment of FAS in archival pathology material using commercially available reagents and equipment.

PS-25-013
South-south collaboration as a mechanism to strengthen pathology residency training in Africa: Tanzania and Rwanda experience

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Background & objectives: African medical schools have traditionally focused to western collaborators for technical assistance to strengthen their education and research programmes. The disproportionate cost and the advanced pathology diagnostics don't match with treatment protocols which affect the realization of the intended goals.
Methods: African pathology residency elective's placement model under GEMx in partnership with COPECSA was initiated in 2019. Among the participants, three MUHAS senior residents were placed to Rwanda University in exchange of three residents from Botswana and Rwanda for 4-8 weeks. Total cost was provided by GEMx through COPECSA. Every participating resident submitted a semi-structured report to programme organizers.
Results: The semi-structured reports of the six elective residents, showed the following: i) significant improvement in their diagnostic skills, knowledge, attitude and professionalism ii) development of cultural and interpersonal competences iii) professional and career development, iv) a cost-effective model in comparison to a similar placement in Western countries was observed. This model initiated a practical and sustainable program, if well adopted can progressively improve the diagnostic skills, knowledge and attitude which is relevant to Africa context.
Conclusion: Regional exchange programme for pathology residency have a potential to produce highly competent pathologists who are able provide quality laboratory services. Identification of strengths in each institution and a well-planned programmes for pathology residents is mandatory to improve the model.

PS-25-014
Expert assessment of damages on the clothes and skin of a person

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Background & objectives: Injuries caused by blunt objects are a common type of mechanical injury in forensic medicine. However, the issues of identifying traces caused by different models of shoes with rubber soles remain poorly studied to date.
Methods: The purpose of the work is to identify the features of damage by various models of shoes and identification of the rubber trace-forming surface using spectral methods. Samples of rubber soles of various models of shoes and traces on various tissues and skin flaps of corpses removed from the hip areas within no more than a day after death were examined.
Results: The analysis of the results showed that contact-diffusion and x-ray methods were not effective for detecting metals in traces. Visualization of traces on black tissues using research in infra-red rays in most cases was inconclusive. Direct stereomicromorphoscopy revealed overlays of grey foreign matter of different intensity in the areas of traces on non-biological and biological objects, and separate black foreign microparticles of various shapes similar to rubber particles. The conducted spectral studies have shown the identity of the qualitative chemical composition of the rubber sole of various models of "civilian" Shoe samples, the marking elements of which are zinc and iron, as well as admixtures of calcium, silicon, aluminium, magnesium and manganese.

Conclusion: The data obtained prove the need to study the damage and traces on the skin of the victims ' clothing in order to establish the possibility of their cause by a foot shod in tight shoes with a rubber sole.

PS-25-015

Pathological study of stillbirths' placentas at Muhimbili National Hospital, Tanzania

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Background & objectives: Stillbirth is foetal death that occurs at gestational age of ≥28 weeks. Majority of causes of stillbirths can be identified by placenta examination hence the study aimed to describe fatal pathological changes in the placentas of stillbirths
Methods: A descriptive cross-sectional study done for the period of 6 months, it involved examination of 80 placentas of stillbirths born at gestational age of ≥ 28 weeks, placentas were fixed in 10% neutral buffered formalin for 8-12 hours. Grossing and interpretation of placenta pathology was according to Amsterdam Placental Workshop Group Consensus Statement.
Results: Out of 80 stillbirths, 32(40%) had unknown clinical diagnosis. Majority of stillbirth placentas 71(91%) found with either one or combined pathologies with the risk to cause stillbirth. Maternal vascular malperfusion was the commonest pathology and was significantly associated with preterm stillbirths. Maternal floor infarction, a placenta pathology with risk to cause foetal death and high risk of recurrence was among the pathologies found, was seen in 4(5%) of stillbirth placentas.
Conclusion: Findings in this study clearly indicated the importance of pathological examination of placenta in determining cause of stillbirth. Placenta examination in stillbirths can identify more pathology related to stillbirths than clinical assessment alone. Placenta examination is not routinely done in our setting and it highlighted its importance as more pathologies are identified some of them with risk of recurrence which necessitate counselling and close follow up of the future pregnancies. Placenta examination is recommended in each case of stillbirth.

PS-25-016

Hyperbilirubinemia improves clinical course of autoimmune arthritis

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Background & objectives: Rheumatoid arthritis is relatively common multisystem chronic disease that causes mainly inflammatory arthritis of the peripheral joints. In the present work, we examined the effect of bilirubin administration in experimental adjuvant-induced arthritis in rats
Methods: Male Lewis rats were randomised into four groups: control, adjuvant-induced arthritis, adjuvant-induced arthritis with bilirubin administration and control group with bilirubin administration. Bilirubin was administered intraperitoneally from day 14 till the end of the experiment at day 28. The volume of the hind paw was the marker of clinical progression. Blood cell count, DNA and tissue damage were evaluated.
Results: Clinical signs of disease progression evaluated as the volume of hind paws, significantly decreased after 7 days of bilirubin administration. Bilirubin administration leads to a significant decrease of leukocyte, lymphocyte and erythrocyte counts, increase of platelets, to significantly decreased C-reactive protein and ceruloplazmin plasma levels. DNA isolated from lymphocytes showed significantly lower damage after bilirubin administration. Joint damage assess by granulocyte invasion and fibrin deposition was a significantly reduced in rats with bilirubin administration.
Conclusion: Bilirubin significantly reduces markers of inflammation, white blood count, inflammatory cells and fibrin accumulation in joints in the animals with adjuvant-induced arthritis. One of the possible protective mechanisms might be the reduction of oxidative stress by bilirubin.

PS-25-017

Hypoglycaemic properties of 2-morpholino-5-phenyl-6h-1,3,4-thiadiazine hydrobromide are correlated with increased extra-islet insulin and PDX1 expression

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Background & objectives: Previous studies show anti-hyperglycaemic properties of 2-morpholino-5-phenyl-6H-1,3,4-thiadiazine hydrobromide (L-17) in diabetic rats. However, mechanisms of L-17 anti-diabetic action are not completely clear. Our study aimed to characterize regenerative process in the pancreas in streptozotocin-induced diabetic rats treated with L-17.
Methods: Forty male Wistar rats were divided into 4 groups: control, control plus L-17, streptozotocin diabetes (T2DM) and T2DM treated with L-17. T2DM was induced by intraperitoneal injection of nicotinamide (110 mg/kg) and streptozotocin (65 mg/kg). L-17 was injected intramuscularly (40 mg/kg/day, 12 injections for 4 weeks). Biochemical, haematological, histological and immunohistochemical investigations were performed.
Results: L-17 decreased fasting blood glucose, glycated haemoglobin, urea and alkaline phosphatase in diabetic rats. Haematological analysis did not reveal any negative effects of this substance. L-17 treatment had no impact on the pancreatic islets' quantity, their diameters, β-cells number and CD117 expression (both in islets and acinar part). However, L-17 caused increasing of total islet cells, extra-islet insulin-producing cells (especially in acinar part), PDX1+cell in acini and ducts in T2DM-rats.
Conclusion: Our studies suggest that observed plasma glucose and glycated haemoglobin improvement appears to be occurred by the way independent from islet β-cells recovery. However, it may be related to extra-islet acinar and ductal insulin-positive cells development, as indicated by increased insulin and PDX1 expression in these areas.
This work was supported by the Russian Science Foundation grant (16-15-000390-П).

PS-25-018

A quality review of amended reports in the histopathology department of a tertiary referral hospital and cancer centre

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Background & objectives: Amended reports are issued when the final report diagnosis changes due to either a change in interpretation or new pathological information. We reviewed 24-months of amended reports to assess reporting standards, identifying areas of good practice and areas requiring improvement.
Methods: Our histopathology department participates in the Irish National Quality Improvement Programme (NQIP) and thereby a quality code is applied to all amended reports (Q021). Using the Q021 code, all amended reports issued from January 2018 to December 2019 were identified and reporting standards were assessed. The cases collected spanned multiple reporting pathologists and included all speciality practices within the department.
Results: In 53 of 73,610 cases, an amended report was issued (0.07%). Of these, the change in final diagnosis occurred as a result of

interpretive discrepancy (n=40), external review (n=4), levels (n=4), new clinical information (n=3) and immunohistochemistry (n=2). Of the 6 cases where levels or immunohistochemistry changed the final diagnosis, 5 final reports did not document the request for additional information nor label the original report provisional. 35 amended reports (66%) did not document notifying the clinician of the change. The importance of clinical correlation was seen. In 3 cases, evaluation of the clinical picture at MDT led to a review of histology and a change in final diagnosis.
Conclusion: The percentage of amended reports (0.07%) met the Irish Quality Improvement target of <1%. It is local policy that all amended reports should be communicated to the clinician. This is an area that should be improved upon by the department.

PS-25-019
Reducing turnaround times Tallaght University Hospital Department of Cellular Pathology: from red to green
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Background & objectives: TUH Department of Cellular Pathology has struggled to reach the National Quality Assurance Scheme turnaround time (TAT) standards for a number of years.
Objectives: Achieve national NQAIS TATs by reviewing end to end processes in the laboratory and introduce change improvement.
Methods: A working group was established to review work practices, workflow and to assess potential areas of change. A lean improvement approach was used to identify and eliminate waste with the use of process maps and risk assessments. All staff – clerical staff, medical laboratory aides, medical scientists & consultants -were consulted and were encouraged to propose areas for improvement
Results: The changes were introduced into the department from February 2019. Multiple changes were identified starting at receipt and booking in of samples by MLAs, typing priorities by the secretaries, re-categorisation of samples in line with TAT targets and, Scientific/Consultant rota changes and introduction of voice recognition reporting. There has been a dramatic improvement in achievement of TATs since introduction of the changes. All day 5 TATs were improved from 38.5% in 2018 to 88% in 2019, and all day 7 TATs improved from 67.5% in 2018 to 90.5% in 2019.
Conclusion: Through the collaboration and cooperation from all staff, the multiple changes in work practice had a compounding positive effect on the TATs in the laboratory. The quality improvement intervention achieved an effective and streamlined histopathology service with reduced TATs within a challenging work environment, resulting in an improved patient care pathway.

PS-25-020
Cancer incidence and survival among young adults in Hospital Prof. Dr. Fernando Fonseca in young adults (2008-2018)
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Background & objectives: The incidence of cancer in younger adults is lower but carries a higher burden.
Our goal is to evaluate the incidence and mortality of malignant neoplasms diagnosed in our hospital among patients, aged 15-39 years, during a 10-year period.
Methods: Cases of cancers diagnosed in patients aged 15-39 years, were collected from our hospital oncologic registry between 2008 and 2018. Two different age subgroups were analysed: 15-24 and 25-39 age-groups. Descriptive statistics and incidence rates were calculated. Vital status was determined until December 2014; survival was estimated using the Kaplan-Meier survival function.
Results: A total of 524 cancer cases were diagnosed from 2008 to 2018: 40 males and 30 females in the 15-24 age-group; 159 males and 295 females in the 25-39 age-group. Overall incidence rate was 10.7 and 33.6 per 100.000 young adults, respectively.
A tendency for lower incidences over time was observed in the 25-39 age-group.
The 5-year overall survival was 93.3% in the 15-24 age-group and 74.5% in the 25-39 age-group, with 69.7% for males and 77.5% for females (P = 0.04) in the 25-39age-group.
The most frequent tumours were: Hodgkin's lymphoma, thyroid and testis in the 15-24 age-group; Breast, cervix-uteri and thyroid in the 25-39 age-group.
Conclusion: Comparing with European population the most frequent tumours were similar, incidence rates were lower, with higher survival in the 15–24age-group, but lower in the 25-39age-group.
This study is important to strengthen prevention and therapeutic approaches, and ramp-up future studies.

PS-25-021
Effect of zinc and selenium deficiency on haemoglobin level, linear growth, and sexual maturation in Sudanese children with sickle cell anaemia
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Background & objectives: Sickle cell disease is an inherited haemolytic anaemia. Trace elements have been claimed to affect growth and Hb level. The objective is to measure the levels of Zinc, selenium, Hb in those patients & correlate them with linear growth and sexual maturation.
Methods: This is a case control study. 31 patients with sickle cell anaemia, attending the referred clinic in Jaafer Ibn Auf Hospital in the period between October to December 2010, and 19 healthy children were studied. Plasma zinc and selenium were measured chemically by Atomic Absorption Spectrophotometry. patients were studied by means of questionnaire, clinical examination, growth measurements and laboratory investigations.
Results: 51.6% of the patients had zinc deficiency, and 71% had selenium deficiency as compared to control (p=0.00). The Hb levels were lower in those with zinc deficiency with a mean of 6.2g/dl as compared to a control group in whom the mean zinc level was 7.2g/dl (p=0.837). In the studied patients, heights were below normal 51.6% were at (-2SD) and 16.1% were at (-3SD) as compared to the control group of whom 78.9% were normal (p=0.00). Seventy one percent of the patients were children, the rest 29% were found to have delayed sexual maturation. The difference in results were statistically significant.
Conclusion: Most of patients with sickle cell anaemia have low plasma zinc and selenium levels. Lower Hb level, growth retardation and delayed sexual maturation have been found in zinc and selenium deficient patients. These differences are statistically significant, it is anticipated that supplementation of these trace elements may improve growth and well-being of these children.

PS-25-022
Mechanisms of macrophages effect on extra-islet insulin-positive cells in experimental diabetes
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Background & objectives: In diabetes insulin-positive cells can be detected outside of the islets of Langerhans in the pancreatic acini and ducts. Macrophages can affect the formation of such cells. We aimed to detect the mechanisms of macrophages' action on extra-islet insulin-positive cells.

Methods: Immunohistochemical staining for insulin, f4/80, PDX1 and c-kit at formalin-fixed pancreases from male Wistar rats with streptozotocin-nicotinamide-induced type 2 diabetes and after injections of 3-aminophthalhydrazide derivatives (APH), which is a macrophage activity modulator, were made. Content of stem cell factor (SCF), TNFα, Ifnγ and TGFβ were determined in blood and pancreas by ELISA.
Results: After administration of APH the number of extra-islet insulin-positive cells and optical density of insulin in them increase. Blood glucose significantly decreases vs. diabetic rats from 11.64±0.93 mmol/L to 7.18±0.19 mmol/L. APH administration is accompanied by increase in the number of macrophages and expression of PDX1 transcription factor in non-endocrine part of the pancreas and a shift in the macrophage production towards anti-inflammatory cytokines. The effect of APH on the number of c-kit+ cells in non-endocrine part of the pancreas, reduced in diabetes, was not detected. However, concentration of c-kit ligand SCF after injections of APH decreases in blood and increases in pancreas vs. diabetic meanings.
Conclusion: Mechanisms of macrophages effect on extra-islet insulin-positive cells in non-endocrine part of the pancreas may be associated with the activation of PDX1 gene, decrease in the content of pro-inflammatory cytokines and increases of SCF amount.
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PS-25-023
Systematic review for tumour classification
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Background & objectives: New methods of evidence synthesis are necessary to classify/reclassify histologically similar tumours. Our objective was to assess the distinction between adenosquamous (ADSQ) and mucoepidermoid carcinomas (MEC) using systematic review methodology to summarise published molecular information on these two tumours.
Methods: We performed a systematic literature search of Medline, Embase and Web of Science from 1990-2019 for articles studying molecular alterations in MEC and ADSQ from any site. Retrieved citations were screened and reviewed for eligibility by two independent reviewers. A third reviewer arbitrated. Two reviewers independently extracted data and conducted a Risk of Bias assessment of included studies
Results: Of 6688 references, 113 met the criteria for further review. Only 3 articles directly compared these two tumour types. They showed that MAML2 rearrangement was present in 29/44 (66%) MEC and in none of 67 (0%) ADSQ. 53/113 articles studied MAML2 rearrangement in MEC only. 57 of 113 articles studied commonly mutated genes, and in these EGFR mutations were reported in 33% (526/1594) of ADSQ versus 4% (8/202) MEC. Mutations in KRAS were found in 19% (85/451) ADSQ versus 2.5% (4/161) MEC. 100% (51) pancreatic ADSQ had mutations in KRAS.
Conclusion: We found no published molecular evidence to support similarities between ADSQ and MEC, supporting the separation of these neoplasms. Systematic review methodology provides a tool for assessing molecular data accruing on tumours and may assist in their classification/reclassification.

PS-25-024
When immunohistochemistry may be useful in the evaluation of necrotic tumour tissue?
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Background & objectives: Immunohistochemistry (IHC) enables the visualisation of the distribution and number of specific molecules present in tissues using antigen-specific antibodies. IHC technique enables the differentiation of benign and malignant tumours, as well as determine the site and origin of primary tumour.
Methods: We investigate the sensitivity and specificity of IHC studies on necrotic samples derived from adenocarcinoma, squamous cell carcinoma and melanoma with different markers.
Results: The morphological analysis of necrosis within tumours revealed 88% sensitivity and 56% specificity for Melanoma TC, 95% and 92% for CK5/6, 95% and 83% for CK20, 37% and 95% for p63, 69% and 97% for Melan A, 88% and 92% for SOX-10, 98% and 56% for CKAE/AE3 and 75% specificity for CK7. Our results demonstrated good preservation of cytoplasmic markers. Antibodies such as CK5/6, CK20 and CKAE1/AE3 should be considered reliable markers in demonstrating the epithelial nature of suspected tumour mass, especially SCC. A combined panel of Melan-A and SOX-10 also showed excellent preservation of markers in necrotic melanoma tissue; however, when used individually, these markers may give false-negative results.
Conclusion: Immunohistochemistry of necrotic tissues cannot exclusively be used to establish a definitive diagnosis; however, it is a useful tool in directing further clinical evaluation and may provide clinically useful information when conventional histology fails to give a diagnosis.

PS-26 Soft Tissue and Bone Pathology

PS-26-001
Solitary fibrous tumour of head and neck - a distinct entity
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Background & objectives: Solitary fibrous tumour (SFT) of head and neck region is a distinct entity with characteristic morphological features. The objective of this study is to bring this entity to light and to study the clinicopathological features.
Methods: 24 cases of head and neck SFT were identified from the archives of histopathology at AgaKhan University Hospital between 2010-2019. The cases were reviewed by two consultant histopathologists. Clinical data was obtained from histopathological reports and follow up was obtained via telephonic conversation.
Results: The median age was 45 years. The tumour site showed a predilection for nasal cavity. A total of 17 cases could be retrieved from the archives for review, out of which, 88.23% showed necrosis,41.17% showed fascicular and storiform arrangement, amanthoid fibres were seen in 35.29% cases and hemangiopericytoma like vasculature was seen in 94.11% cases. Six cases showed features of malignancy such as mitosis, necrosis and pleomorphism. 87.5% cases were CD34+ and 62.5% were STAT6+. Follow up of 9 patients could be attained and one was found to have expired due to some undiagnosed pulmonary disease, rest were all healthy. Most of the patients were treated with surgical excision.
Conclusion: SFT of head and neck is a distinct entity with majority of them behaving in a benign fashion, commonly treated by local excision. IHC stain CD34 was consistently positive in all of the cases. Chances of recurrence and need for neoadjuvant therapy is restricted for those with positive margins. A NAB2-STAT6 gene mutation has been reported. Hence, recently STAT6 has been considered as a reliable marker for diagnosis.

PS-26-004
Histological and molecular characteristics of primary solitary fibrous tumours of the bone – diagnostic pitfalls and criteria of aggressiveness

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Background & objectives: Primary solitary fibrous tumour of the bone (SFTB) is a rare entity, and it is crucial to use proper ancillary tests for correct diagnosis. Herein we report four SFTB cases and discuss histological-radiological correlation in regard to their malignant behaviour.
Methods: Clinical data pertaining to age and sex of patients were gathered. Known malignant histological features of SFTB, i.e. hypercellularity, marked atypia, tumour necrosis and mitotic activity (MA) more than 4/10 HPF were assessed. The microscopic findings were correlated with imaging studies. IHC for STAT6 and other markers were carried out. FISH and NGS analyses were performed in each case.
Results: SFTB showed spindle-shaped to round cell morphology with pattern-less pattern and HPC-like vessels. In all cases MA was more than 4/10 HPF and radiologically destructive growth pattern was evident. Other malignant histological features of SFTB were not present. STAT6 IHC was positive in all cases (100%). FISH confirmed STAT6 rearrangement only in two cases (50%). NGS detected NAB2-STAT6 fusion in all cases (100%).
Conclusion: - All SFTB were radiologically aggressive and 50% metastasised to other bones.
- MA more than 4/10 HPF seems to be sufficient to render a diagnosis of malignant SFTB.
- STAT6 is a specific and sensitive IHC marker for SFTB. CD34 can be negative. SATB2 is negative.
- NGS/rtPCR is the best genetic test to confirm SFTB.

PS-26-006
Extrapulmonary inflammatory myofibroblastic tumours occurring at unusual locations: a report of 30 cases
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Background & objectives: The study aims to describe the clinicopathological features and occurrence of IMT in unusual locations. Although the lung is the best known and most common site, IMT occurs in diverse extrapulmonary locations and in any age group.
Methods: 94 cases of IMT were retrieved from the archives of Histopathology at The Aga Khan University Hospital between years 2006-2019.Out of these,30 cases involved quite unusual sites. H&E slides were evaluated for characteristic findings. Relevant IHC stains performed were CKAE1/AE3, ASMA, ALK protein, Desmin, CD34, S100 and CD117.FISH analysis for ALK gene rearrangement had been done on two cases. Treatment/follow up details were obtained by calling the patients.
Results: The described unusual tumour sites were abdominal wall(n=2) kidney(n=3), eye(n=1),orbit (n=2),intracranial but extra-axial (n=2) and rest included cheek, parotid gland, oropharynx, epiglottis, supraclavicular area, hypochondrium, vocal cord, liver, adrenal gland, urinary bladder, gluteal region, popliteal fossa and big toe.14 patients were female and 16 were male. Ages ranged from 01-64 years with a mean age of 21 years. Specimen were received as trucut biopsies, excised nodular masses or in multiple pieces. The IHC results were CKAE1/AE3(n=19),ASMA(n=30),ALK protein(n=30) Desmin (n=21),CD34(n=13), S100(n=23),CD117(n=12).Follow up of 13 patients was attainable.6 found to have expired of their disease. Of the remaining 7 alive patients, 3 were alive with recurrence. Of the 4 alive patients without recurrence, 3 received chemo and radiotherapy while 01 was treated by resection alone.
Conclusion: Inflammatory Myofibroblastic Tumour (IMT) is an uncommon neoplasm with intermediate behaviour. Because of its variable presentation but possible highly aggressive course and tendency to recur, occurrence of IMT should always be suspected whenever a spindle cell lesion with marked inflammation arises at unusual sites in body specially in children and young adults. Long-term follow up with serial imaging techniques may be recommended to clinch possible local aggressive behaviour and recurrence.

PS-26-007
Infiltrative growth of retroperitoneal liposarcoma may cause recurrence
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Background & objectives: Atypical lipomatous tumour (ALT) and dedifferentiated liposarcoma (DDLPS) arising in the retroperitoneum recur frequently and are associated with a dismal outcome. To address this issue, the growth pattern of retroperitoneal ALT/DDLPS was pathologically studied.
Methods: The materials consisted of surgical specimens of two cases of ALT and seven of DDLPS, all of which arose in the retroperitoneum. The surgical margins were retrospectively re-evaluated in all tumours. Immunostainings for p16 and HMGA2 were applied to investigate the growth pattern of tumour cells.
Results: In all tumours, we confirmed tumour cell infiltration at surgical margins. Tumour cells including lipogenic cells and atypical stromal cells were diffusely positive for p16, whereas they were sparsely positive for HMGA2. The boundaries between tumours and surrounding tissues were well-demarcated or infiltrative. At the latter, p16-positive atypical stromal cells infiltrate along fibrous septa of normal-appearing adipose tissue. Besides, daughter nodules were occasionally found apart from main tumours.
Conclusion: As the retroperitoneal ALT/DDLPS are usually large in size, they tend to be marginally resected. Infiltrative growth of atypical stromal cells and daughter nodules may also cause recurrence. The p16, rather than HMGA2, immunostaining is useful to detect infiltrating tumour cells and to evaluate the surgical margins. As the complete excision may be impossible, novel, molecular target therapies are desirable for the treatment of the retroperitoneal ALT/DDLPS.
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PS-26-009
TFE3-rearranged pecoma: expanding gene fusion knowledge
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Background & objectives: TFE3-rearranged PEComas are rare mesenchymal tumours morphologically similar to other TFE3-associated neoplasms. Data on the molecular alterations in these tumours are limited. We analyse 2 cases of TFE3-rearranged PEComas using RNA-sequencing to identify gene fusion partners.
Methods: Clinical and morphologic features were reviewed. We performed immunohistochemistry for mismatch repair deficiency (case1), TFE3, SMA, and HMB45; FISH (TFE3), and RNA-sequencing.
Case1 was a 49-year old male with a Lynch syndrome and a previous rectal carcinoma, presenting with a suspicious 2.5 cm pelvic tumour.

Case2 was 20-year old man with a 1.7 orbital mass clinically diagnosed as a haemangioma.
Results: Histologically, both tumours were composed by nests of epithelioid cells with clear cytoplasms, separated by delicate fibrovascular septa. Both positive for HMB-45, TFE3, and focally for SMA. RNA sequencing revealed gene fusion PSF/SFPQ-TFE3 in case1 and NONO-TFE3 in case2. Both patients had no evidence of disease at 20 and 10 months, respectively.
44 TFE3-rearranged PEComas have been reported, 28% showing an aggressive behaviour, and 75% show PSF-TFE3 gene fusion.
Conclusion: TFE3-rearranged PEComa is a recently described tumour clinically mimicking different neoplasms. We report a second case of a TFE3-rearranged PEComa in the orbit with an unusual NONO-TFE3 gene fusion. In summary, our data may expand further the clinicopathologic features and the gene fusion knowledge of TFE3-rearranged PEComas.

PS-26-010
Prognosis and survival of patients diagnosed with well differentiated and dedifferentiated retroperitoneal liposarcoma - tertiary hospital experience
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Background & objectives: Retroperitoneal liposarcomas (LPSR) have a steep growth and poor prognosis compared to other tumours. We analyse the clinical presentation in patients with differentiated and dedifferentiated LPSR in the last 15 years, identifying histopathological variables affect patients' morbidity and mortality.
Methods: Cases between January 2002 and May 2019 will be reviewed. 85 patients with primary LPR were treated between this period and 33 of them with well-differentiated or dedifferentiated LPR subtypes. Variables (survival, affected surgical margins and recurrence) will be compared between patients diagnosed with LPS (well or dedifferentiated). A value of $P < 0.05$ will be considered statistically significant.
Results: The overall survival at 5 years was 60%, with a disease-free survival at 38% per year. The recurrence of the disease occurred in 42% of cases, especially in those where the margins were affected, being associated in this group with a lower survival, especially when the histological type is dedifferentiated or affected kidney and large vessels. Surgical complications from wide resections reached 23%. The presence of the dedifferentiated component and its degree of malignancy were independent prognostic factors for disease-specific survival and survival free from local recurrence.
Conclusion: The histologic subtype, margin of resection and wide surgical resections are prognostic for survival in LPSR. Dedifferentiated histological subtype and the need for contiguous organ resection (excluding nephrectomy) was associated with an increased risk of local and distant recurrence. Nephrectomy may be necessary to achieve complete resection, but its absence does not increase survival. Pathological studies on new multimodality approaches are warranted.

PS-26-012
Deep learning algorithm support classification of small round cell sarcomas: a proof of concept study
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Background & objectives: Ewing sarcoma (ES) and Ewing-like sarcoma (ELS) are aggressive mesenchymal tumours with overlapping morphology that makes diagnosis challenging. Aim of this study is to implements a computational pipeline in order to distinguish ES versus ELS using hematoxylin/eosin stained virtual slides.
Methods: ES and ELS (comprising BCOR/CIC-rearranged) slides were retrieved and digitized. Tumour area was outlined in each virtual-slide and divided into a set of tiles creating three categories (BCOR, CIC, and EWING). An automatic classification system based on Convolutional Neural Networks (CNNs) was trained and then tested in order to automatically assign each tile to the correct category.
Results: A total of three CNNs were implemented in order to classify each category versus the others. Each network was trained on a dataset composed of 20.000 images (size 384x384 pixels) for each category. Based on a test dataset of 16.000 tiles, preliminary results show that the three categories can be well discriminated using trained CNNs, with an average recognition accuracy of 94.3%.
Conclusion: CNNs-based algorithms are promising tools to support pathologist. Future work will focus on retrieve more cases for each category; add new categories as monomorphic synovial sarcoma and desmoplastic round-cell sarcoma; implementing CNNs complexity in order to increase recognition accuracy.

PS-26-013
Femoral head trabecular architecture in patients with osteoporotic hip fractures and correlation with vitamin D levels
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Background & objectives: Hip fracture is a devastating event with a high risk of death. Approximately 5% of all-cause mortality is attributable to hip fracture. Hip fractures have been found to be related to vitamin D (Vit-D) deficiency.
Methods: In a group of 11 patients, who had undergone surgery after a hip fracture the femoral head was histologically studied. Blood levels of 25(OH)D3 were also measured. All patients had also a DEXA scan for the diagnosis of osteoporosis.
Results: Histological analysis revealed thinning/loss of bone trabeculae. In 2 patients extreme thinning of bone trabeculae was observed. In 3 patients extreme loss of bone trabeculae was observed. Patients with low Vit-D levels had extreme thinning and loss of bone trabeculae. It appears that in patients with osteoporosis who had undergone a hip fracture thinning and loss of bone trabeculae is noted and this seems to be related to Vit-D deficiency.
Conclusion: In the current era of effective drug treatment for osteoporosis and effective surgical management for a hip fracture the acquirement of deeper knowledge regarding the histology of the bone in patients with a hip fracture is extremely interesting and important, as it may aid into the deeper understanding of the biology of osteoporosis and fracture.

PS-26-015
Clinicopathological, immunohistochemical and molecular cytogenetic profile of 32 cases Ewing sarcoma with epithelial differentiation, including cases with "adamantinoma-like" features: a single institutional experience, India
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Background & objectives: Ewing sarcomas(ESs) with epithelial differentiation, including "adamantinoma-like" features are rare tumours.32 cases of ES with epithelial differentiation, diagnosed during 2011-2018, in 17 males and 15 females (M:F ratio=1.1:1), were included after critical review.
Methods: Immunohistochemistry was performed on formalin-fixed/paraffin-embedded tissue sections by immunoperoxidase method using a MACH2 Universal HRP-Polymer detection kit. Twenty-five tumours(78.5%) were confirmed by EWSR1 rearrangement, using fluorescence in-situ hybridization(FISH).Twenty-seven tumours

were either diagnosed as ES(n=23) or favoured as ES over synovial sarcoma(SS)(n=4). Three were diagnosed as 'preferably' SSs and single case, each, as a poorly differentiated carcinoma(PDCA) and undifferentiated sarcoma.
Results: Age range was 8-61 years(average=23, median=23.5). Common locations were upper extremities(9), pelvis(7), paravertebral tissues(5), lower extremities(7), followed by neck region(3) and lung(1). Most common histopathologic pattern was nesting-type, containing round to oval basaloid cells. Immunohistochemically, tumour cells showed membranous positivity for MIC2(32/32), Fli1(19/19); synaptophysin(6/16); variable positivity for pancytokeratin(AE1/AE3)(29/30) and EMA(4/5). Therapeutically (n=19, 59%), most patients(12/19)(63.1%) were treated with resection and specific neoadjuvant chemotherapy(CT), neoadjuvant, including 6 with adjuvant radiotherapy. Four(21%) patients were offered CT and radiotherapy, 2, CT and single RT(palliative). Three cases developed recurrences and 4 developed metastasis. Finally(n=8, median follow up=18 months), 6 patients were alive-with-disease; 2 free-of-disease.
Conclusion: This study constitutes one of the largest documentation of these rare tumours. Diagnosis of ESs with epithelial differentiation requires molecular confirmation. Exact diagnosis has treatment implications, as these tumours are treated differently from their mimics, especially SSs and PDCAs.

PS-26-017
Soft tissue tumours of the skin with aneurysmal features: a comparative morphological, immunohistochemical and molecular study
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Background & objectives: Fibrohistiocytic tumours of the skin with aneurysmal features are rare and challenging lesions. We aimed to characterize a series using morphological, immunohistochemical and molecular methods, to identify new possible markers that can help in the differential diagnosis.
Methods: Twenty-four aneurysmal dermatofibromas (AD), 5 angiomatoid fibrous histiocytomas (AFH) and 4 pleomorphic dermal sarcomas with aneurysmal features (PDS) were studied using immunohistochemistry for CD10, EMA, desmin, ALK, P53, Rb1 and p16. FISH analysis was conducted on AFH, while 4 AD, 3 AFH and 1 PDS were also studied with a 15 gene mutation panel and 507 gene RNA fusion panel.
Results: AD: all positive for CD10, 68% for p16; EMA, desmin and ALK negative. AFH: negative for CD10 and p16; all positive for EMA and desmin, ALK in 60%. UPSs: positive for CD10 (75%) and for EMA (33%), negative for ALK and desmin. Rb1 protein: always retained. P53: wild-type in 96% of cases. EWSR1 rearrangement. found in AFHs. RB1 mutated in one PDS. Mutations or fusions in AD or PDS: negative.
Conclusion: While AFH has a peculiar immunohistochemical and molecular profile, AD and PDS require careful evaluation of cytological and morphological features including atypia and pleomorphism, number of typical and atypical mitosEs and infiltration of deep soft tissues. Significant molecular alterations were only found in AFH, despite the wide panel used in this study.

PS-26-018
Hepatic epitheloid hemangioendothelioma: clinicopathologic, immunhistochemical, and molecular genetic analysis of 15 cases
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Background & objectives: Epithelioid haemangioendotheliomas (EHE) of the liver are rare, malignant and often indolent vascular tumours that are known to demonstrate WWTR1-CAMTA1 fusion and YAP1-TFE3 fusion in a smaller subset, in which TFE3 immunohistochemistry is suggested to be positive.
Methods: 15 malignant vascular tumours of the liver, 12 of which are EHE, diagnosed in between 1996-2019 were re-evaluated and included in the study. A 4-mm diameter tissue microarray block was constructed. 4 micrometre thick sections were stained immunohistochemically with TFE3. WWTR1-CAMTA1 fluorescent in situ hybridization (FISH) was studied. Patients' files are used for the clinical information.
Results: Among all, 10 patients were female, 5 male. Mean age at diagnosis was 43.8 years. 9 patients presented with multiple intrahepatic nodules with a maximum size of 11 cm. at diagnosis. Follow-up information was available for 10 patients. 1 patient with transplantation was alive without disease, 6 patients were alive with disease and 3 patients died of disease. 5 patients were known to have lung metastases. 11 patient had immunoreactivity with CD31 and CD34, 6 with ERG. Immunohistochemically, TFE3 was studied in 9 patients and all found negative. WWTR1-CAMTA1 FISH results are pending.
Conclusion: Diagnosis of EHE is challenging and the course of the disease can be unpredictable. Identification of the fusion genes in EHEs provides significant diagnostic data, especially in cases with unusual morphology or when biopsy material is limited.

PS-27 Thymic and Mediastinal Pathology

PS-27-001
Giant mediastinal thymolipoma: a case report
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Background & objectives: Diagnosis of thymolipoma should be considered in case of mediastinal mass with fat density, especially if it is interspersed with strands of soft tissue attenuation on (CT) scans. Sometimes it is difficult to differentiate radiologically from other mediastinal fatty tumours.
Methods: A 44-year-old woman presented with chest discomfort on exertion for the past 4 years. A chest computed tomography (CT) showed a large heterogeneous fatty anterior mediastinal mass causing compression against right lung with no infiltration of the adjacent structures. The mass was excised surgically. The histopathological examination confirmed the diagnosis of thymolipoma.
Results: A 44-year-old woman presented with chest discomfort on exertion for the past 4 years. A chest computed tomography (CT) showed a large heterogeneous fatty anterior mediastinal mass causing compression against right lung with no infiltration of the adjacent structures. The mass was excised surgically. The post-operative period was incident-free, and the patient was discharged 5 days after surgery. Pathology examination results showed a tumour measuring 30x20x10 cm, consisting of large lobules of mature adipose tissue interspersed with small areas of thymic tissue and the diagnosis of thymolipoma was made.
Conclusion: Thymolipoma is a very rare benign mediastinal tumour, consisting of thymic and fatty tissue. Preoperative diagnosis is frequently based on CT and MRI findings. FNAB remains controversial. Surgical intervention is the only cure and also provides the definitive diagnosis.

PS-27-002
Clinico-pathologic study of 255 resected thymomas: a single institution experience
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Background & objectives: WHO scheme defines type B thymomas (B1-B2-B3), which is correlated with prognosis. Type A/AB tumours share similar features, including GTF2I mutation. A subset of them show

atypical features (so-called atypical type A), but this atypical category is not well-characterised.
Methods: 255 thymomas resected from 250 patients were retrieved and reviewed. A variety of clinical and histopathologic parameters were analysed, with particular emphasis on identifying prognostic factors in type A and AB group.
Results: There were 46 tumours (type A), 105 (AB), 22 (B1), 47 (B2), 32 (B3), 1 (metaplastic) and 2 (completely necrotic tumour). Type B group was more often of advanced stage compared to A/AB.
In A/AB group, multivariate Cox proportional hazard models demonstrated that mitotic count was the only independent prognostic factor as continuous variable (HR 1.15, 95%CI 1.07-1.24, p<0.001). A/AB patients were classified as typical if mitotic count was 0-19 / 2mm2 and atypical if ≥20 mitotic figures per 2mm2. Multivariate Cox proportional hazard models demonstrated that the strongest prognostic factors were the new subtype classification, the presence of necrosis, the status of surgical margins and neoadjuvant treatment.
Conclusion: Our results suggests that atypical type A and AB could be defined as tumours with ≥20 mitotic figures per 2 mm2.

PS-27-003
Follicular dendritic cell sarcoma of the mediastinum: a case report of a rare dendritic tumour of the right thoracic outlet
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Background & objectives: Follicular dendritic cell sarcomas are rare mesenchymal neoplasm arising from follicular dendritic cells of lymphoid follicles at nodal and extranodal sites. The patients are mainly adults, with a median age of 50 years and they present primarily with localized disease.
Methods: We describe a case of 74-year male with a tumour 5,5 cmin greater diameter at the region of the right thoracic outlet. The tumour, nine lymph nodes, a part of the right clavicle and a segment of mediastinal adipose tissue were submitted for histological examination. Diagnosis was set with Hematoxylin – Eosin stains and supported by the necessary immunohistochemical assays.
Results: Microscopy revealed a tumour showing nodular, diffuse or fascicular to storiform growth pattern, composed of oval to spindled, occasionally multinucleate, cells, with eosinophilic and fibrillar cytoplasm, small nucleoli and frequently pseudoinclusions. 15 mitoses per 2mm2 were counted. Perivascular lymphocyte cuffs and admixed population of lymphocytes, eosinophils, plasma cells and neutrophils were also observed. Tumour showed positivity for CD21, CD23, CD35, D2-40 and negativity for CD1a, CD4, CD14, CD15, CD30, CD68, Langerin, S-100 and HMB-45. One lymph node was infiltrated by the tumour, whereas the rest of the specimens did not show evidence of infiltration. Based on these findings, Follicular dendritic cell sarcoma was diagnosed.
Conclusion: Although follicular dendritic cell sarcomas are of intermediate-grade malignancy with low recurrence and distant metstasis rate (28% and 27% respectively), large tumour size (≥ 6 cm), high mitotic count (≥ 5 mitoses per 2mm2), coagulative necrosis and significant cytological atypia are associated with poorer prognosis. Lethal paraneoplastic syndromes (such as refractory pemphigus or myasthenia gravis) may also occur in some patients.

PS-27-004
Malignant solitary fibrous tumour and type B3 thymoma: a rare case of coexisting tumours
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Background & objectives: Malignant solitary fibrous tumours are rare fibroblastic neoplasms accounting for 10% of pleural solitary fibrous tumours. Type B3 thymomas are epithelium-predominant thymic epithelial tumours, representing 21% of thymomas. Our objective is to present a case of patient with coexisting tumours.
Methods: We report a 58-year old female patient who underwent surgery for a tumour at the right hemithorax, 16 cm in greater diameter and a tumour at the anterior superior mediastinum, 3 cm in maximum diameter. Both tumours were resected and sent together to our Department of Pathology with a segment of the right middle lobe of the lung.
Results: Microscopy revealed the following:
First Tumour: Hypercellular hyalinized tumour with fibroblastic spindle cell morphology, without specific architecture, with 47 mitoses/2 mm2. Tumour cells expressed STAT-6, CD34, CD99 and Bcl2.
Second Tumour: Thymic epithelial tumour composed of midly atypical polygonal tumour cells with solid growth pattern, with intermingled immature T-cells. Neoplastic cells expressed CK7 and CK19 and Immature T-cells Tdt.
Infiltration of the pulmonary parenchyma by tumour cells was not demonstrated.
Based on the microscopical findings, the diagnosis of Malignant Solitary Fibrous Tumour of the pleura was set for the first tumour and Type B3 Thymoma - Masaoka Stage IIb for the second tumour.
Conclusion: The coexistence of these tumours makes the prognosis for the patient rather unclear. The high mitotic rate of Malignant Solitary Fibrous Tumours is indicative for their aggressive behaviour, whereas the 10-year survival rates for Type B3 Thymomas are 81%.

PS-27-005
Myelolipoma of posterior mediastinum – a rare localisation for an extra-adrenal tumour
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Background & objectives: Myelolipoma (MYLP) is a benign neoplasm composed of mature adipocytes and haematopoietic tissue. It is commonly found in the adrenal gland with an incidence of 3-5%. However, extra-adrenal myelolipoma can also occur including the presacral region, retroperitoneum, liver, spleen, stomach, greater omentum, leptomeninges, and mediastinum.
Methods: The largest summary of mediastinal localization includes only 28 cases of MYLP. The patients remain asymptomatic or may present with endocrine disorders, anemia, hypertension, splenomegaly.
A 56-year-old male with a tumour localized in the posterior mediastinum was admitted to Maria Sklodowska-Curie National Research Institute of Oncology for diagnostics and treatment.
Results: The radiological imaging revealed a hypodense tumour on the Th10 level, in the largest diameter 190mm, with suspicion of malignant peripheral nerve sheath tumour. The tumour was surgically resected in thoracotomy and in microscopical examination presented as classical histological myelolipoma; among mature lipomatous tissue abundant haematopoietic tissue with erythroid and granulocytic, and megakaryocytic differentiation were identified. The immunohistochemical stainings (CD71, MPO, and CD61 respectively) were helpful in the differential diagnosis and the blastic change (CD34(-), CD117(-), TdT(-)) was eliminated as well. The clinical investigation was negative for any etiological factors i.e. splenomegaly, primary myelofibrosis, endocrine disorders. After 3 months patient remains with no evidence of disease (NED).
Conclusion: In conclusion, the described case represents a category: "common tumour in uncommon localization". At present, there is no

standard treatment for mediastinal myelolipoma. Surgical resection is an optimal treatment option that allows histopathological exclusion of other severe malignancies.
Funding: "This work has been implemented using the Project infrastructure POIG.02.03.00-14-111/13".

PS-27-006
Ectopic mediastinal parathyroid adenoma in association with metachronous intrathymic choriocarcinoma in an elderly woman. A coexistence never described before
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Background & objectives: Primary choriocarcinoma of the mediastinum is a rare form of extragenital germ cell tumour, occurring almost exclusively in young men. We present a unique-never described before-case of a postmenopausal woman with a coexistent ectopic parathyroid adenoma and intrathymic choriocarcinoma.
Methods: A 76-year old woman was admitted in our hospital for the investigation of blood loss from the rectum. At the same time, she was diagnosed with hypercalcemia, due to ectopic mediastinal parathyroid adenoma. Two years later she re-appeared with shortness of breath, due to a bulky anterior mediastinal mass. An attempt was made for surgical debulking of the tumour.
Results: Histologic examination of the mass was diagnostic of an intrathymic mediastinal choriocarcinoma in close proximity with an intrathymic parathyroid adenoma.
Conclusion: Our case indicates that the occurrence of a mediastinal mass in an elderly woman, cannot exclude an extragenital choriocarcinoma-although a curiosity- and also the coexistence with an ectopic parathyroid adenoma poses a base for consideration on the histogenesis of these tumours. Although, it has been hypothesized that extragonadal germ cell tumours are a consequence of aberrant midline migration of primordial germ cells, a somatic thymic stem cell derivation has not been excluded to date.

Poster Sessions

One-Day Computational Pathology Symposium
One-Day Molecular Pathology Diagnostics and Translational Research Symposium

PS-CP-01 Posters One-Day Computational Pathology Symposium

PS-CP-01-001
A novel deep learning-based diagnostic algorithm for detection and segmentation of amyloid in digital whole slide images
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Background & objectives: Amyloid identification on whole slide images can be diagnostically challenging due to its subtle appearance and lack of polarized filters. We aim to develop a deep learning-based computer-assisted diagnostic (CAD) tool for automated amyloid recognition to improve diagnostic accuracy and efficiency.
Methods: H&E and Congo Red slides of different tissue types from known cases of amyloidosis as well as normal control samples were retrieved, digitized and WSI extensively annotated to highlight amyloid as well as background in a training set. A deep learning-based segmentation model recently developed by our group named MILD-Net1was trained on both positive and negative examples.
Results: Our preliminary results have shown that the deep learning algorithm can predict the presence of amyloid in digitized histological samples confidently with desirable accuracy. When tested out on the held-out set, the algorithm was able to detect and segment amyloid with patch-level F1 score of 0.83 and recall of 0.9 within the equal proportion of positive and negative amyloid patches.
Conclusion: We report the first deep learning-based tool for amyloid detection which may overcome the requirement of Congo Red staining and polarized microscopy. Further testing and validation on a larger dataset could provide a reliable and fast method for amyloid detection in digital slides. The automated mapping and accurate quantification of amyloid produced by our tool has the potential to improve diagnostic accuracy, workflow, patient management and augment the pathologists' expertise.
Funding: BDIAP Fellowship

PS-MD-01 Posters One-Day Molecular Pathology Diagnostics and Translational Research Symposium

PS-MD-01-001
Role of histone H3 in high grade gliomas
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Background & objectives: The classification of gliomas is nowadays largely based on molecular findings. Along with other genes, such as *IDH* or *ATRX*, histone 3 (H3) plays an important diagnostic and prognostic role. We report an illustrative case where molecular pathology is crucial.
Methods: A 24-year-old man, without remarkable history, sought medical consultation for a two-month history of dysarthria. After an altered neurologic examination, a brain CT and MRI were performed, showing a mass in the left frontal lobe. A diagnostic biopsy was carried out.
Results: The histologic examination showed a dense cellular proliferation with small-sized and hyperchromatic nuclei, some with prominent nucleoli, pseudoinclusions and scarce eosinophilic cytoplasm. Mitotic activity reached 7 mitosis/10HPF. Neither necrosis nor vascular proliferation was identified.
Immunohistochemistry showed intense, patchy GFAP expression. No *IDH* R132H mutation was found, *ATRX* expression was lost, and p53 overexpressed. Ki67 reached 50% of the cells.
Molecular analyses of several genes were performed by PCR. *B-RAF*, *IDH1* and *IDH2* were wildtype, while the gene *H3F3A* showed a [c103G>A; p. G34R] mutation. With all these findings, a diagnosis of high-grade glioma, consistent with anaplastic astrocytoma, IDH-wildtype, 2016 WHO classification grade III, with H3 G34R mutation was achieved.
Conclusion: Although H3 K27M mutation is the best known H3 mutation, other alterations in this gene are important and have prognostic implications, like G34R in this instance.

PS-MD-01-003
Diagnosis of a paediatric renal tumour with the aid of molecular studies: a case presentation
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Background & objectives: An accurate pathological diagnosis of paediatric renal tumours is essential to determine therapy and prognosis. However, histological diagnosis may be difficult, even with

immunohistochemistry. Molecular studies may help in their classification, by either confirming or excluding entities with similar morphologies.
Methods: Case presentation of a 3-year-old girl with a kidney tumour in the setting of presumed nephroblastomatosis, who underwent a renal tumorectomy after pre-operative chemotherapy, in which the final diagnosis required the aid of molecular studies.
Results: The tumour was capsulated, had serpiginous architecture, with monomorphic oval and spindle cells, with scant cytoplasm, vesicular nuclei and high mitotic activity. Neither anaplasia nor areas of nephroblastomatosis were seen. Immunohistochemical studies showed positivity for PAX8, CCND1 and NSE, and negativity for WT1, cytokeratins and CD99. No rearrangements in YWHAE or ETV 6 genes were found by FISH, but there was deletion of the WT1 gene in 70% of the nuclei. CGH revealed a complex pattern of chromosomic alterations, with 1p-, 1q+, and deletion of the entire chromosome 11. A diagnosis of blastemal nephroblastoma was rendered.
Conclusion: In the present case, a final diagnosis was not possible without the aid of molecular biology studies. They are fundamental in the differential diagnosis of this tumours with clear cell sarcoma, neuroblastoma, primitive neuroectodermal tumours and other tumours with the same morphology. This case emphasizes the importance of an integrated approach between morphology, immunohistochemistry, and molecular studies to reach an accurate diagnosis.

PS-MD-01-004
Haemorrhagic vasculitis associated with the factor V Leiden mutation: difficulties of diagnosis and management
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Background & objectives: Atypical clinical pictures of many diseases could be resulted from the congenital or acquired thrombophilia, which is dangerous due to the development of acute thromboses and a chronic disorders of blood flows. One of the factors causing congenital thrombophilia is Leiden mutation.
Methods: Female patient 32 years old for 6.5 years suffered from various undifferentiated lesions of her hearing and vision organs, the gastrointestinal tract, the skin in the form of symmetrical, disseminated urticaria spots, ecchymosis and petechiae, periorbital oedema and scarring as a result of ulcerative defects in the history. To make a diagnosis, a biopsy was performed, and a study was conducted to identify genetic mutations.
Results: Skin biopsy specimen showing mild hyperkeratosis, focal lympho-macrophage (neutrophils, eosinophils) infiltration in the papillary layer of the dermis, leukoclastic vasculitis. According to the generic with G1691A polymorphism of the V factor gene (Leiden mutation)
Conclusion: This observation indicates that without genetic tests and careful analysis of the medical history, it is impossible to make an accurate diagnosis corresponding to the severity of organ damage that is the cause of an inadequate therapy.

PS-MD-01-005
Rare case of fibrolamellar variant of hepatocellular carcinoma (HCC) with DNAJB1-PRKACA fusion gene
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Background & objectives: Tumours of the liver are heterogeneous, with classic HCC as most common subtype, frequently associated with cirrhosis in over 80% (West). Rare subtypes of liver tumours can be difficult to diagnose in biopsy specimens due to tumour heterogeneity.
Methods: mRNA was extracted from the liver resection specimen and reverse transcribed in cDNA which was used for the detection of the fusion gene DNAJB1-PRKACA in RT-PCR. Aa product will appear on the gel if the fusion is present.
FISH (pending): BAC-clones will be established, and results will be presented.
Results: A biopsy specimen from a 28-year-old male patient with liver mass and no history of liver disease was diagnosed as classic hepatocellular carcinoma. In the subsequent resection specimen, the tumour showed a distinct heterogeneity with areas of classic fibrolamellar HCC morphology with hepatocytes with pale bodies, separated by broad fibrous septae. In addition, focal areas with classic HCC morphology were evident, explaining the discordant diagnosis in the biopsy. Surrounding liver parenchyma showed no signs of steatosis, fibrosis or inflammation, atypical for classical HCC. The detection of fusion transcript DNAJB1-PRKACA in RT-PCR confirmed the diagnosis in this case.
Conclusion: Morphology remains the mainstay for diagnosis of HCC, but molecular methods are useful in difficult biopsy specimens. The detection of the DNAJB1-PRKACA transcript can confirm the diagnosis of fibrolamellar variant of HCC.

E-Posters

E-PS-01 Autopsy Pathology

E-PS-01-001
Primary meningeal spinal cord melanoma: a clinical and morphological analysis of a 72-year-old patient's case
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Background & objectives: Meningeal melanoma is a rare tumour that occurs most often in the posterior cranial fossa and along the spinal cord, with severe neurological symptoms due to the appearance and growth of volumetric formation.
Methods: Analysis of clinical and anatomical data: CT and MRI of the brain and spinal cord, analysis of the autopsy protocol, followed by histological, immunohistochemical and genetic studies. IHC panel: HMB antibodies - 45, Melan A, EMA, Ki - 67, pancytokeratin AE1 / AE3, S100.
Results: The patient died of brain oedema. At autopsy: on the meninges of the spinal cord and subdurally at the Th8-L1 level, numerous merging foci of dark brown colour, friable consistency, with fuzzy borders, compression of the substance of the spinal cord with occlusion of the spinal canal were found. A sharp expansion of the spinal canal at all levels, above Th-8, with severe hydrocephalus dislocation of brain structures with the cerebellar hemispheres wedged into the large occipital foramen. Histological examination: dense infiltration of the meninges by tumour melanocytes. LV(+),Pn(+).The tumour grows by 0.5 s tissue of the spinal cord. An immunohistochemical study: a positive reaction with HMB-45, Melan A,S100;negative reaction to EMA,AE1/AE3;Ki 67-80%,BRAF mutations were not detected.
Conclusion: This clinical and anatomical observation demonstrates a rare tumour - primary meningeal melanoma, which is difficult to diagnose and leads to death early.

E-PS-01-002
Splenic littoral cell angiosarcoma with hepatic and pulmonary metastases
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Background & objectives: Splenic angiosarcoma (SAG) is a rare, aggressive and poor prognosis malignant entity, which apparently derives from the sinusoidal vascular endothelium in red pulp. SAG usually debuts with metastasis, with the liver being the most common site.
Methods: A 65-year-old woman presented with a general syndrome displaying joint pain and oedema, which had evolved during the three previous months. A PET-CT scan showed an uptake area of liver segment VIII, with no evidence of splenic alterations. Later, the patient presented hemodynamic instability with multiorgan failure, which evolved into refractory shock causing death. A clinical autopsy was performed.
Results: Post-mortem examination evidenced a subcapsular, poorly-defined lesion (2.5 x 1.5 cm) located in segments VII-VIII of the liver. Microscopically a marked hepatic infiltration caused by a malignant vascular tumour was detected; this neoplasm formed channels containing red blood cells delineated by histiocytoid-like tumour cells. Occasional mitoses and tumour projections could be seen. Spleen had massive AG infiltration and a similar morphological appearance was also found in metastatic lung microscopic foci.
Conclusion: Splenic littoral cell angiosarcoma is a neoplasm with aggressive behaviour and unfavourable prognosis due to high rates of metastasis caused by hematogenous spread. Early diagnosis and prompt splenectomy are very important for survival.

E-PS-01-003
Dandy-Walker syndrome - case report
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Background & objectives: Dandy-Walker syndrome is a congenital brain malformation. It's characterized by incomplete configuration of the cerebellum, dilatation of the fourth ventricle, an enlarged posterior fossa and the formation of cysts. Its incidence is 1-30.000 births and account for approximately 1-4% of hydrocephalus cases.
Methods: Histological examination of brain, heart, lungs, liver and kidneys of patient with history of Dandy-Walker syndrome. The measuring and weighing of these were within normal values. However, the brain was in places with indications of encephalopathy, hydrocephalus. The myocardium was in places with ischemic lesions and the lung tissue blocks were with oedema and in places with fibrosis and thickening.
Results: The results included brain in places with indications (macroscopic – microscopic) of encephalopathy, hydrocephalus, myocardium in places with ischemic lesions and lung tissue blocks with oedema and in places with fibrosis and thickening
Conclusion: Dandy-Walker syndrome is associated with chromosomal abnormalities, Mendelian disorders, syndromic malformations, congenital infections, CNS disorders, including various malformations. Hydrocephalus is a common complication of the disease in almost 80% of the cases. With regard to the diagnosis, it depends on ultrasound as the first imaging modality in assessing foetal brain and on MRI after the 20th week of gestation. Treatment is generally focused on alleviating hydrocephalus and posterior fossa symptoms and it consists of treating the manifestations and associated comorbidities.

E-PS-01-004
Sudden cognitive decline: a presentation of intravascular large B-cell lymphoma
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Background & objectives: Intravascular large B-cell lymphoma (IVLBCL) is a rare and aggressive subtype of non-Hodgkin lymphoma, characterized by growth of large cells within the lumen of blood vessels. We report a case, given an early diagnosis is crucial to altering the disease course.
Methods: We present a 72 year-old male patient who initially presented a sudden cognitive decline, with gait alterations, anaemia, thrombopenia, splenomegaly, asthenia and weight loss. MRI revealed leptomeningeal enhancement. Given the main clinical suspicion was autoimmune meningoencephalitis, steroids were administered, with no improvement, and Glasgow scale score fluctuations. Once in the ICU, a multidisciplinary committee decides to perform a diagnostic/therapeutical splenectomy.
Results: Large atypical lymphocytes with prominent nucleoli and scant cytoplasm were identified within capillaries, small arteries and veins. Tumour cells positive for CD20, CD79a, BCL-2, BCL-6 and Mum-1, while negative for CD3 and CD10. These findings suggested the diagnosis of IVLBCL. Despite therapeutical efforts, the patient died, and an autopsy was performed. The microscopical exam of sampled tissues, especially kidney and CNS, showed the same findings seen on the splenectomy specimen.
Conclusion: Uncommonly, our patient was diagnosed premortem, although not at an early stage. Since we are dealing with a rare and unusual disease, a diagnostic suspicion, communication among different specialties, along with early and adequate biopsy are critical to establishing an accurate diagnosis and initiating therapy.

E-PS-01-005
Aortic occlusion by tumour embolus complicating surgical resection of a pulmonary carcinosarcoma: a post-mortem case report
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Background & objectives: Occlusion of the aorta by embolic tumour material is rare, and, to our knowledge, has never been reported in association with pulmonary carcinosarcoma. Our objective is to review the literature and increase awareness of this uncommon complication of thoracic surgery.
Methods: Case Presentation (Methods/ Results)
A 69-year-old man underwent right pneumonectomy for a screen-detected, asymptomatic, 10 cm carcinosarcoma of the right upper lung. On recovery after anaesthetic, the patient developed immediate postoperative paraesthesia and mottling of both lower limbs. A computerised tomography (CT) scan revealed an aortic thrombus with focal ischaemia of the spleen and left kidney...
Results: Case Presentation (Methods/ Results) (continued)
…following failed angioplasty attempts and bilateral axillo-femoral bypass grafts, above-knee amputations were performed. However, despite these measures, the patient's clinical condition deteriorated and he sadly died.
The case was referred to the Coroner and post-mortem examination revealed occlusion of the aorta and other large arteries by firm pale material. This was histologically confirmed to represent tumour embolus and ischaemia and infarction were identified in multiple organ systems including the spleen, kidneys and intestine.
Conclusion: This patient died of arterial obstruction by embolic tumour, causing ischaemia of vital organs. Although rare, autopsy pathologists should be vigilant to the fact that advanced lung cancers can invade large pulmonary veins, facilitating embolization of tumour around the body.

E-PS-01-006
Primary liver chorioncarcinoma in a 36-year-old man: clinical anatomical analysis
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Background & objectives: Primary chorioncarcinomas of the liver are rare.A case of primary chorioncarcinoma of the liver in a 36-year-old man

flowing under the guise of a low-grade carcinoma of the stomach with metastases to the liver, lungs, and mesenteric root is presented.
Methods: A clinical and anatomical analysis of the case of primary chorioncarcinoma of the liver in a 36-year-old man. IHC was performed with antibodies: β-hCG, Pan-cytokeratin AE1 / AE3, CK 7 CD10, CD146, CD56, CD99, S-100, NSE, CD57, SMA, Melan-A, CD31, CD34.
Results: At autopsy, in the liver, a rounded knot of 18.0 cm, with haemorrhagic patches, friable consistency, in the centre of foci of necrosis. In the mesentery of the small intestine, a mottled-looking node is 9.0 cm. In the lower lobes of both lungs, subpleural foci are 0.5-0.8 cm with clear boundaries, of dense consistency. The tumour node of the liver consisted of cytotrophoblastic cells with homogeneous rounded nuclei, transparent cytoplasm, with large multinucleated syncytiotrophoblastic cells with bizarre nuclei, and abundant eosinophilic cytoplasm. In cells of a cytotrophoblast there are figures of mitosis. In a liver tumour: diffuse expression of β-hCG, Pan-cytokeratin AE1/AE3;CK7,CD10, CD146 - diffuse expression of intermediate trophoblast by cells.
Conclusion: Electron microscopy revealed syncytrophoblasts, but there were no open lacunae lined with microvilli. Most mononuclear cells with ultrastructural features of mature cells, as evidenced by a more complex cytoplasm than is observed in typical cytotrophoblastic cells.
Tumour wasn't detected in the testicals.
A case of primary chorionic carcinoma of the liver with an aggressive course is presented, with multiple distant metastases in a young patient without testicular damage.

E-PS-01-007
A case of sudden death associated with two incidental primary tumours
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Background & objectives: The prevalence of incidental cancers is low due to current advanced diagnostic methods. This study reports the case of a 64-year-old man who presented at the emergency room with dyspnoea at rest, orthopnoea, palpitations, and precordial pain.
Methods: Paraclinical tests revealed elevated serum pancreatic enzymes (lipase), lactate dehydrogenase and creatine kinase-MB. Electrocardiography showed ST-T wave changes in the inferior territory and atrial fibrillation with high ventricular rate. Thoracic front X-ray points out an irregular opacity in the left upper lobe, adjacent to the pulmonary hilum. The patient died within 2 hours and necropsy was performed.
Results: Necropsy findings show acute necrotizing pancreatitis, multiple small gallstones, macroscopic early changes of myocardial infarction, an advanced stage lung cancer extending to the oesophagus, and two tumours in the right kidney. These two renal tumours are both circumscribed, but they look differently: one is orange-yellowish, with cystic and haemorrhagic areas and the other one is tan and solid. We found multiple metastases in the mediastinal lymph nodes, brain, and liver.
Histological examination showed a poorly differentiated pulmonary adenocarcinoma, widely metastatic in mediastinal lymph nodes, brain, and liver. In the kidney, there was a conventional clear cell renal cell carcinoma (RCC) and a papillary RCC type 1, respectively.
Conclusion: Although incidental cancer is less common, there are some indolent cancers that remain undiscovered during life and do not contribute to death.

E-PS-01-008
Dressler's syndrome: an autopsy of a rare complication of myocardial infarction
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Background & objectives: To report an unusual complication of myocardial infarction in the age of reperfusion therapy. Dressler's Syndrome is a type of pericarditis that rarely occurs after damage to the heart, from occasions such as myocardial infarction or surgeries.
Methods: Review of autopsy report. The case was analysed both macroscopically and microscopically.
Results: A 71-year-old woman was referred for autopsy 4 days after hospital discharge, when she was treated for myocardial infarction. During the examination, pericardial cavity was filled with approximately 300mL of a reddish-brown fluid with cloudy appearance. The internal surface of the pericardial sac showed a fibrous exudate, as well as the epicardial surface. In cross section, there was marked concentric myocardial hypertrophy, especially in the left ventricle. The myocardial tissue on the anterior left ventricular wall showed a soft-elastic consistency and was dark red. Microscopically, the pericardium exhibited fibrinous exudate and inflammatory cells. Histology of the heart showed wavy cardiac muscle cells and presence of numerous immune cells, especially neutrophils.
Conclusion: Dressler's Syndrome occurred in approximately 1% - 5% of myocardial infarction cases. With the advancement of therapies for such condition, its incidence has dropped dramatically and nowadays it is estimated to be less than 1%, with some studies even suggesting that the syndrome may have disappeared.

E-PS-01-009
Hyperammonomemic encephalopathy in a patient with fibrolamellar hepatocellular carcinoma: autopsy at 25 years old
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Background & objectives: To report a case of a rare liver tumour, with an unusual complication.
Methods: Review of medical record and autopsy report.
Results: A 25-year-old woman was referred to Hepatology service due to an ultrasound finding that revealed a massive liver tumour. Imaging exams showed inferior vena cava thrombosis, that required an implant of a temporary filter. On the day following the procedure, patient decreased level of consciousness. Laboratory tests showed markedly elevated serum ammonia levels. Hyperammonemia was treated with ammonia scavengers, but the patient did not respond to treatment and died. At autopsy, a tumour measuring 21,3 x 16,4 x 11,6 cm was identified. Microscopic analysis leaded to the diagnosis of fibrolamellar hepatocellular carcinoma (FHCC). Neoplastic cells were large, polygonal, with oncocytic cytoplasm, accompanied by parallel lamellae of dense collagen bundles.
Conclusion: FHCC is a very rare tumour. In the United States, it corresponds to less than 1% of all liver tumours. Hyperammonemic encephalopathy in patients with FHCC is also a very rare complication; some aetiologies have been proposed for it's emergency, and one of them is intrahepatic shunting. As the clinical worsening occurred after placing the filter in intimate contact to the liver, it is believed that this was the cause.

E-PS-01-010
Ruptured ectopic pregnancy: autopsy at 42 years old
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Background & objectives: To report a ruptured ectopic pregnancy diagnosed at autopsy.
Methods: Review of medical record and autopsy report.

Results: A 42-year-old woman died few minutes after arriving at the hospital, complaining of abdominal pain in the last 24 hours. At autopsy, she exhibited marked cutaneous-mucous paleness. At laparotomy, there was a marked amount of haemorrhagic fluid in the abdominal cavity, and the focus was identified in the right uterine tube. At salpingotomy, a foetus was exteriorized measuring 3.5 cm in length, with genitalia still ambiguous - morphological characteristics compatible with 8-9 weeks of gestational age. Microscopic analysis showed large chorionic villi of the placenta inside the right uterine tube. The cause of death, therefore, was given as a hypovolemic shock due to ruptured ectopic tubal pregnancy.
Conclusion: In the present case, the early search for medical care would have a modifying impact on the prognosis. In cases of abdominal pain, especially in women of childbearing age, gynaecological causes should always be considered.

E-PS-01-011
Analysis of cases referrals for the Death Verification Service
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Background & objectives: The Death Verification Service (DVS) and the Institute of Legal Medicine, are responsible for performing the autopsies and sometimes cases are incorrect referral to each service and between them. Analysed the cases that were forwarded to Death Verification Service.
Methods: It was performed a retrospective cohort study, evaluating data from Death Verification Service of the state of Ceara, Brazil from 2019's January-February .
Results: During this period, there were more than 1300 deaths referred to the DVS and of these 28 cases were incorrectly referred to the DVS when they should have been sent to the Institute of Legal Medicine with 9 (33%) deaths from exogenous intoxication, 6 (21%) deaths without medical assistance, 5 (18%) due to falling from their own height, 2 (7%) due to aspiration of foreign bodies, 1 (3.5%) suicide, 1 (3.5%) drug addiction, 1 (3.5%) electric shock and the other 3 (10.5%) were due to other causes.
Conclusion: In conclusion, although there are very specific indications for referring a corpse to one of these institutions, erroneous referral of cases to any of these are still recurring and those mistakes may compromise future mortality indicators based assessments.

E-PS-01-012
Sudden death in young adults in Ceará, Brazil
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Background & objectives: Sudden death (SD) refers to a non-violent death occurring less than 24-hours from the onset of symptoms and in young adult is uncommon, but reaffirms its societal burden, especially for screening programs. Evaluate the causes of SD in young adults.
Methods: Cross-sectional study, evaluating autopsy data from Death Verification Service of the State of Ceara, Brazil from January to February of 2019.
Results: There were 195 cases of sudden death and of these, 26 were patients under 40 years of age, predominantly mixed race, average age of 28 years (median 36 years) and 80% were male. 61.5% deaths due to cardiac causes, 19.23% of which due to hypertrophic cardiomyopathy and 38.5% deaths due to non-cardiac causes.
Conclusion: Sudden death is rare in young people, but it has a disproportionate impact on the community and the most often, death is due to a heart abnormality. Even when analysed in a short period, many cases of SD are found and potentially preventable with correct diagnosis and risk stratification.

E-PS-01-013
A case of widespread metastatic pancreatic ductal adenocarcinoma, signet-ring cell variant
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Background & objectives: We report the case of a 58-years old man with multiple metastasis from unknown primary, who died from respiratory failure. Autopsy revealed a metastatic signet-ring cell adenocarcinoma of the pancreas, which is a very rare variant of pancreatic ductal adenocarcinoma.
Methods: A comprehensive autopsy study has been performed, which highlighted the presence of a large pancreatic mass, with extension to regional and distant lymph nodes. The lungs showed a solid aspect. The presence of gastric-intestinal primitive tumours was excluded. During autopsy, several specimens were collected for histological diagnosis.
Results: Histology revealed a signet-ring cell adenocarcinoma of the pancreas, with multiple metastasis. The pancreatic origin of the neoplasm was confirmed by immunohistochemical positivity for cytokeratin 7, 8/18 and for MUC1. Both lungs showed diffuse foci of tumour thrombotic microangiopathy (TTM), a rare condition caused by accumulation of neoplastic cells and fibrin clots within pulmonary vessels. This is the first report of TTM due to pancreatic signet-ring cell carcinoma.
Conclusion: Histology revealed a signet-ring cell adenocarcinoma of the pancreas, with multiple metastasis. The pancreatic origin of the neoplasm was confirmed by immunohistochemical positivity for cytokeratin 7, 8/18 and for MUC1. Both lungs showed diffuse foci of tumour thrombotic microangiopathy (TTM), a rare condition caused by accumulation of neoplastic cells and fibrin clots within pulmonary vessels. This is the first report of TTM due to pancreatic signet-ring cell carcinoma.

E-PS-01-014
Causes of lethal outcomes in children, born from mothers with type I diabetes
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Background & objectives: The pregnancy, complicated by diabetes of 1 type, is related to group of high risk of early reproductive losses, obstetric complications and congenital malformations of foetus. The aim of research is to study children, born from mothers with diabetes.
Methods: The 15 autopsies of new-borns, died in early and late neonatal period were researched. Their mothers had diabetes of 1 type.
Results: It was revealed that 88,8% of childbirths were premature, intrauterine infection was detected in 83,3% of childbirths, syndrome of respiratory dysfunction of new-born was detected in 12%, congenital anomalies were in 11% of cases. The direct causes of death of children, born from mothers with diabetes of 1 type were neonatal respiratory distress syndrome (50%), necrotizing enterocolitis (16.6%), cerebral oedema (16.7%), acute heart failure (11.1%), intraventricular haemorrhage (5.6%)
Conclusion: The pregnancy on background of diabetes of 1 type is accompanied by serious complications in foetus, what can lead to premature childbirths and further death of premature new-born.

E-PS-01-015

Fulminant myocarditis: a case report

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Background & objectives: Myocarditis is an inflammatory disease of the myocardium often associated with dilated cardiomyopathy and sudden cardiac death. The most frequent aetiology is viral infections; other causes are non-viral infections, drugs or autoimmune diseases, which could be diagnosed by endomyocardial biopsy.
Methods: We performed a complete autopsy. Samples of the heart´s myocardium were taken for its microscopic study. CD3, CD4, CD8, CD20, CD68, perforin and granzyme immunostains were made in order to identify inflammatory cells.
Results: We report a case of a 44-year-old female with a medical history of bilateral acute pyelonephritis, left renal abscess and obstructive ureteral lithiasis treated with JJ stenting. The patient presented with abdominal pain and fever. As acute pyelonephritis was suspected, she underwent several analytic and imaging tests, without any relevant results. The patient died three days later.
The macroscopic examination of the heart revealed no abnormalities besides a friable consistency of the myocardium. Microscopy exposed an intense inflammatory infiltrate in association with myocyte necrosis affecting both ventricles. Mature T lymphocytes, macrophages and isolated polymorphonuclear neutrophils constituted the main components of the infiltrate.
Conclusion: Myocarditis is an inflammatory disease that can lead to unexpected death, as in our case. Histologically, myocarditis is defined by the Dallas criteria, based in the presence of inflammatory infiltrates in the myocardium as well as non-ischemic myocyte necrosis.

E-PS-01-016

Bile pulmonary embolism in 81-year old male - case report and review of the literature

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Background & objectives: Bile pulmonary embolism (BPE) is a very uncommon process usually diagnosed post-mortem. Fistulation between biliary system and venous blood makes bile to reach lung vessels. We present the autopsy findings of 81-year-old man with BPE secondary to acute abscesified cholecystitis.
Methods: We perfomed clinical autopsy and after definitive diagnose, we made a systematic review of the Literature.
Results: The autopsy determined as primary cause of death sepsis secondary to an acute abscessified cholecistitis. Massive BPE in small sized pulmonary arteries were found, causing dyspnoea and cough with greenish expectoration.
Bilepulmonary embolism is a rare complication associated to fistulous communication between the bile ducts and the hepatic veins. The most commonly reported causes are iatrogenic medical procedures (ERCP), pancreatic or hepatic tumours and, less frequently, acute cholecystitis. Almost 20 cases reported since 1980's showed that this is an uncommon and severe event often presenting initially unspecific abdominal pain and progressive dyspnoea, leading to haemobilia, pulmonary hypertension, acute respiratory failure or acute right heart failure with fatal consequences.
Conclusion: Both clinicians and pathologists should be aware of this entity, whose incidence might rise during the next years since non-surgical treatment for acute cholecystitis is recommended in patients with comorbidities.

E-PS-02 Breast Pathology

E-PS-02-001

Traumatic neuroma after mastectomy for breast cancer: case report

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Background & objectives: Traumatic neuroma is a failed attempt to regenerate an injured or ruptured nerve from trauma or surgery. They are benign and non-neoplastic lesions that can appear in different parts of the body but are rarely seen at the mastectomy site. They are formed by a tangle of neural fibres, schwann cells and fibroblasts. The objective is describe and discuss a case of traumatic neuroma after mastectomy for invasive breast cancer.
Methods: This is a report of a case of traumatic neuroma close to the mastectomy scar in a 71-year-old woman who underwent mastectomy and chemotherapy for invasive breast carcinoma four and a half years ago and was being followed up at the mastology outpatient clinic. Clinical, diagnostic and literature data are presented for comparison.
Results: Asymptomatic patient with normal physical examination presented an ultrasound scan of a nodule in the right mastectomy store in the anterior axillary line measuring 0.4 x 0.3 cm. The microscopic analysis of the thick needle biopsy in hematoxylin and eosin staining showed proliferation formed by numerous nerve wires in the middle of the fibromyxoid connective tissue and concluded the diagnosis of post-mastectomy traumatic neuroma. Absence of breast cancer recurrence.
Conclusion: Traumatic neuromas occur in the age of 31 to 78 years, 2 to 22 years after mastectomy and measure from 0.2 to 1.6 cm. Rare after mastectomy with incidence of 0.09%. It´s necessary to distinguish from recurrence of breast carcinoma.

E-PS-02-002

Histopathological analysis of male breast cancer in Southwestern Nigeria: a single-centre retrospective study

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Background & objectives: Breast cancer in men is an uncommon disease accounting for 1% of all breast cancer cases. The study aimed to review all the male breast cancer cases over a ten-year period and to compare the findings with other similar studies.
Methods: This was a retrospective review of all histologically diagnosed cases of male breast cancers in the Department of Pathology, University College Hospital Ibadan over a ten-year period. Clinicopathological parameters and specific histological sub-types were extracted from surgical day book and Cancer Registry of the Department. The data was analysed using the Statistical Package for Social Sciences, version 22 (SPSS-22).
Results: Forty-two cases of male breast cancer were seen accounting for 1.7% of all breast cancer cases. The age range was between 22-91 years with a mean age of 60.3 years and a peak occurrence was in the 8th decade. The right breast was more commonly affected accounting for 52% of cases. Most of the patients presented with a retro-areolar mass. The commonest histological sub-type found in this study is the invasive ductal carcinoma accounting for 88% of the cases. The peak incidence of male breast cancer cases was in 2013 with 8 cases while the least incidence of 2 cases was seen in the year 2012 .
Conclusion: Breast cancer in men is relatively uncommon compared to female breast cancers. Breast cancer in males and females however share similar clinico-pathological features. Male breast cancer is more common in the older age group and invasive ductal carcinoma is still the

commonest histological subtype seen in our environment. Many gaps still remain in our knowledge about breast cancers in men.

E-PS-02-004

Florid Liesegang rings, closely mimicking filarial parasites within a screen detected breast lesion: a challenging diagnostic entity

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Background & objectives: 'Liesegang rings' are laminated globular structures that occasionally associated with mammary cystic, lactational or inflammatory conditions. Liesegang rings are rare but known diagnostic pitfalls, commonly misinterpreted as filarial parasites, resulting in inappropriate management.
Methods: A 72 years female presented with a screen-detected lesion in the right breast (R3/U3). Histology revealed microcalcification associating multi-cystic spaces, lined by bland cuboidal epithelium and appear partially filled with multiple globular pink structures, closely mimicking filarial parasites with focal areas showing granulomatous reaction (CD68 stain positive). There is also marked periductal chronic inflammation with no atypia or malignancy identified.
Results: Liesegang rings typically lack the internal structures of true parasites. The diagnosis, however, would be challenging in degenerative forms of filarial parasites. The experts' opinion (from The London Hospital of Tropical Diseases) described these structures as a special type of secretion, so-called 'Liesegang rings'. The variable size of rings, the absence of distinct internal organs of parasites in addition to the lack of relevant travel history (to an endemic place) in our case, all favoured Liesegang rings over filarial parasites. The special stains requested initially (Iron stain, Von Kossa, PAS, GIEMSA, MAST) were all negative.
Conclusion: We describe a rare histopathological finding 'Liesegang rings' that mimics parasites histologically. The recognition of such a rare entity is crucial to avoid labelling the case with a different disease process and targeting such patients with an inappropriate form of therapy and management.

E-PS-02-005

Unusual synchronous presentation of lobular breast carcinoma and anorectal melanoma

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Background & objectives: In women, 5 to 10% of breast cancers are attributed to mutations in predisposing genes.
Epidemiological studies have provided suggestive evidence of a link between skin melanoma and breast cancer. The association breast carcinoma and anorectal melanoma is somewhat exceptional.
Methods: We report the case of a 55-year-old patient with synchronous lobular carcinoma of the left breast treated by hormone therapy followed by mastectomy and lymph node dissection, and anorectal melanoma initially diagnosed as a poorly differentiated carcinoma, followed by primary radiotherapy with deferred surgery and where the diagnosis of melanoma was made on the rectal resection after an immunohistochemical study.
Results: The microscopic study of the anorectal tumour showed diffuse tumour proliferation with weakly cohesive cells with granular cytoplasm and nuclei with a prominent nucleolus.
The immunohistochemical showed a negativity of epithelial markers, GATA3 and the hormone receptors and positivity for anti-Melan-A, HMB45 and PS100.
The microscopic study of the tumour breast showed the presence of an invasive lobular carcinoma. The IHC showed a positivity for GATA3 and hormone receptors.
Conclusion: This observation raises the possibility that the pathways involved in the development of breast cancer and melanoma of the skin or mucous membranes overlap.

E-PS-02-006

Synchronous bilateral breast cancer of distinct histomorphologic and intrinsic subtypes: a case report

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Background & objectives: The incidence of bilateral synchronous breast cancer is accounting %1-%2.6 of all patients with breast cancer. These patients have relatively shorter overall survival rates. All patients with breast cancer should be carefully examined by radiological screening methods.
Methods: 81-year-old female patient presented with palpable mass in her right breast. Mammography demonstrated a spiculated contoured 25 mm sized upper quadrant mass on the right breast and 30 mm sized lesion under areola region of the left breast. Lesion on the right breast was classified as BI-RADS category 5, left breast lesion was classified as BI-RADS category 4.
Results: Tru-cut biopsy was performed for both breast lesions. On the biopsy of the right breast lesion, there was solid sheets of infiltrative ductal structures with desmoplastic stromal reaction. Left breast lesion, revealed an infiltration of neoplastic cells arranged in a single-file linear pattern in a fibrous stroma containing intracytoplasmic lumen. Bilateral mastectomy with bilateral axillary dissection was performed. Right breast lesion was diagnosed as invasive breast carcinoma of no special type and left breast lesion was diagnosed as invasive lobular carcinoma. Right breast tumour was ER, PR negative while HER2 was +++/+++. Left breast tumour showed %100 positive immunereactivity for ER and PR, HER2 was negative.
Conclusion: This case demonstrated that two distinct characterized tumours may develop in the same patient in bilateral setting.

E-PS-02-007

Adenosarcoma of the breast – a case report

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Background & objectives: Sarcomas account for less than 1% of breast malignancies. A 58-year-old woman without significant medical history noticed a lump in the right upper quadrant of her right breast. The clinicians asked for a second opinion on the tumorectomy slides.
Methods: The USG and FNAB results suggested a benign lesion (BI-RADS 3; epithelial cells without atypia). The tumorectomy specimen was 4x3x2 cm with greyish, lobulated cut surface. The original diagnosis of adenosarcoma was established basing on HE stain for the presence of both sarcomatoid and adenoma-like components. To exclude metaplastic carcinoma and determine the direction of differentiation, immunohistochemistry was applied.
Results: The tumour was biphasic: there was a poorly differentiated sarcomatoid stroma (suspected of having lipogenic lineage) with variable cellularity and admixed benign epithelial structures resembling adenosis and tubular adenoma, at the periphery and within the more cellular areas. There was no phyllodes tumour component and no necrosis. The mitotic index was about 8/10 HPF. Ki67 index was about 15%. The spindle-cell component was negative for CK AE1/AE3, CK 5/6 and MDM2. The glandular component was positive for ER, PR, with myoepithelia positive for p63 and CK 5/6.The consultation diagnosis was adenosarcoma, intermediate grade, originating from the breast stroma (ER, PR-positive), with myogenic differentiation (SMA-positive, actin, desmin and MyoD1 focally positive).

Conclusion: To our knowledge, similar lesions located in the breast have not been reported yet. As this abstract is being submitted, the patient is 5 months from primary tumorectomy and 6 weeks from radicalization due to narrow (0,1 mm) surgical margin (quadrantectomy - negative for neoplastic disease), with no signs of dissemination or recurrence. The Soft Tissue Multidisciplinary Team will continue the management, presumably requesting molecular tests on the tumour.

E-PS-02-008

Differences in GATA3 expression among histological/molecular subtypes and grades in infiltrating breast carcinoma (IBC)

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Background & objectives: GATA-binding protein 3 (GATA3) is a sensitive and relatively specific marker in IBC. Its relationship with different IBC histologic/molecular subtypes/grades has not been specifically defined. The aim was to determine GATA3 expression among different histological and surrogate molecular BT subtypes.
Methods: Immunohistochemical staining of ER, PR, ki67, HER2 and GATA3 was performed in a cohort of 84 consecutive cases of primary IBCs. The association of GATA3 expression with different histological subtypes, grades and surrogate intrinsic molecular subtypes was assessed.
Results: The overall positivity of GATA3 across various histological subtypes was 71.43% with no correlation with histological type (p=0.849). GATA3 expression was positively correlated with low histological grade (G1/G2 vs G3: p=0.001; OR=0.174 95%CI=0.057-0.535) with most of G3 (57.89%) cases being negative and with luminal A (72.22%) and B (84.62%) subtypes (p=0.00001; OR=17.544, 95%CI=4.202-71.429) while most of the triple negative (87.5%) and HER2-overexpressed (66.67%) being negative for GATA3 (p=0.0001).
Conclusion: GATA3 exhibits a relatively high sensitivity for IBC. GATA3 expression is associated with IBC most frequently encountered histological subtypes, with luminal A/B molecular subtype and low G1/G2 histological grade. Caution must be payed when dealing with an IBC metastasis of HER2-overexpressed or triple negative molecular subtypes or G3, since in these categories GATA3 is frequently negative and cannot be used for diagnosis of tumour origin.

E-PS-02-009

Human dirofilariasis: report of a case presenting as a breast lump

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Background & objectives: Human dirofilariasis (HD) is a rare zoonotic infection caused by filarial nematodes belonging to the genus Dirofilaria. The main clinical manifestations in humans are subcutaneous nodules and pulmonary lesions. We report a case of HD, presenting as a breast lump.
Methods: Our patient, a 75-year-old woman, presented with a mass in the left breast, measuring 1.5 cm in maximum diameter. Lumpectomy was performed.
Results: Macroscopically, the mass was well-circumscribed, white, solid and hard on palpation.
Histological examination revealed a lymph node with necrotic, granulomatous inflammatory reaction. In addition, within the necrotic tissue, a worm with histological features consistent with Dirofilaria repens was identified.
Conclusion: HD has been reported in countries with temperate, semi-tropical, or tropical climates.
The infection of humans occurs through a mosquito bite that has obtained larvae-containing blood from an infected animal.
The commonest Dirofilaria species are D. repens and D. immitis, responsible for subcutaneous and pulmonary dirofilariasis, respectively.
HD can mimic a tumoral process, so it is important to develop practical techniques for histological and serological diagnosis, to avoid radical surgery.

E-PS-02-010

Neuroendocrine neoplasm versus solid papillary carcinoma of the breast with neuroendocrine differentiation? Tricky lesion to recognise

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Background & objectives: Solid papillary carcinoma (SPC) is considered a rare malignant breast tumour.
Given its monomorphous aspect, other differential diagnoses are most often mentioned.
Herein a rare and tricky case of SPC with a neuroendocrine (NE) differentiation.
Methods: A 52-year-old female patient consulted for nodule in her right breast. Palpation revealed a firm, ill-defined nodule of upper external quadrant with palpable axillary lymph node. Mammography revealed an ill-defined opacity of 20mm classified BIRADS IV.
The patient underwent breast conserving surgery with axillary lymph node dissection.
Results: On macroscopy, there was a nodule of 19 mm.
On histology, it had a solid architecture with very unconspicious fibrovascular cores and nests of monomorphous oval and rounded epithelial cells, moderate to high in size. There was little nuclear pleomorphism, and numerous mitotic figures (up to 14,8/mm²). 1 lymph node was metastatic with capsule rupture.
Tumour cells were positive for Oestrogen and progesterone receptors, synaptophysin and chromogranin A, and negative for HER-2.
Given solid growth, monorphous cell tumours, reactivity to NE markers, we conducted firstly a neuroendocrine carcinoma.
we concerted breast pathologists who proposed as diagnosis: solid papillary carcinoma with a neuroendocrine differentiation.
Conclusion: SPC is characterized by solid growth pattern with delicate fibrovascular cores.
NE differentiation is frequent. Its important to differentiate it from other subtypes of breast neoplasms: papilloma with florid usual ductal hyperplasia, medullary carcinoma, pure neuroendocrine neoplasm .
Due to its rarity and lack of sufficient clinical data, treatment and prognosis are calculated as invasive breast carcinoma.

E-PS-02-011

Retrospective evaluation of breast carcinoma brain metastases

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Background & objectives: The second most common cause of metastatic brain tumours is breast cancer and lifetime risk of brain metastasis(BM)in breast cancer patients is 10-16%.In this study, we aimed to discuss immunohistochemical and prognostic features of patients diagnosed as BM of breast cancer.
Methods: Between January 2012 and April 2018, 28 patients diagnosed as BM of breast carcinoma in our department and patients with known follow-up were re-evaluated with age, gender, primary tumour diagnosis, survival time, immunohistochemical properties and histological degrees.

Results: When the cases were divided into groups according to hormone receptor and HER2 status; ER/PR positive in 17.85% (n = 5) of the cases (Hormone positive group); only ER positive (ER positive group) in 28.57% (n = 8); HER2 amplification in 32.14% (n = 9) (HER2 positive group); ER/PR/HER2 negative in 21,42% (n=6) (Triple negative group). Median overall survival was 8 ± 2.6 months (2.8-13.2) after diagnosis of brain metastasis, while 30 ± 10.9 months (8.5-51.5) in the hormone positive group; 7 ± 8.5 months(0-23.6) in the ER positive group; 10 ± 3 months(4.2-15.8) in HER2 positive group and 4 ± 1.6 months (1.7-6.3) in triple negative group (p: 0.03).
Conclusion: BM seriously affects the quality of life and survival in breast cancer patients, that's why development of effective treatment methods is more important and urgent. In our study the longest survival was detected in the hormone positive group and very low in the triple negative group. This result might be a guide in determining new treatment methods.

E-PS-02-012
Basaloid carcinoma of the breast: case report of a rare entity
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Background & objectives: Basaloid carcinoma of the breast (BCB) is a rare triple-negative breast tumour, with a difficult differential diagnosis with neuroendocrine neoplasms, adenoid-cystic carcinoma and secondary disease.
Methods: A 40-year old female patient with no prior history of malignancies was submitted to a magnetic resonance imaging of the breast, which showed a spiculated, irregular nodule measuring 1,4x1,1x1,5 cm located in the posterior third of the upper-outer quadrant of the right breast.
Results: The morphological study demonstrated a high-grade, solid malignant neoplasm, with groups of cells with scant cytoplasm and hyperchromatic nuclei organized in clusters with peripheral palisading and comedonecrosis. The immunohistochemical panel showed that the tumour cells were positive for Cytokeratin 7 and Cytokeratin 34BetaE12, but negative for Cytokeratin 20 and EPCAM. There was also focal positivity for GATA-3, BRST-2 and c-KIT, and the proliferative index assessed with Ki67 was 70%. There was no expression of Oestrogen Receptor, Progesterone Receptor, or HER2. The neuroendocrine markers Chromogranin and Synaptophysin were negative, as well as the myoepithelial markers p63, CD10, SMA and Cytokeratin 5. Finally, there was no staining with TTF1, CDX2 or PAX8.
Conclusion: Herein we reported a case of BCB, a rare tumour of the breast. Exclusion of the main differential diagnosis is necessary and was performed with a thorough immunohistochemical study assessing the presence of myoepithelial cells, neuroendocrine characteristics and the possibility of metastasis. Awareness of the characteristic morphology of this tumour is warranted for its correct diagnosis.

E-PS-02-013
Polymorphous adenocarcinoma of the breast: a rare salivary gland-like tumour
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Background & objectives: Salivary gland-like tumours of the breast are rare entities with a wide clinic-morphological spectrum. Polymorphous adenocarcinoma is considered the counterpart of salivary-gland "polymorphous low-grade adenocarcinomas", and only three cases had been reported to date.
Methods: A 70-year old female was submitted to a screening mammography, which identified a 2.0 cm spiculated nodule in the upper-outer quadrant of the right breast, considered as undetermined for malignancy.
Results: Histologic sections demonstrated a well-differentiated neoplasm infiltrating the stroma and adipose tissue, composed of epithelial cells with enlarged nuclei, small nucleoli and scant cytoplasm organized in tubules and occasionally as foci of isolated cells. The immunohistochemical study showed that the tumour cells were positive for Cytokeratin 7 and E-Cadherin, but were negative for GATA3, BRST2, Oestrogen receptor (ER), Progesterone receptor (PR) and HER2. Furthermore, there was focal positivity for p63 in rare areas of the neoplasm, but no staining for the myoepithelial markers CD10, SMA and Cytokeratin 5. The tumour cells also exhibited focal positivity for CD117, diffuse positivity for BCL2, and the proliferative index assessed with Ki67 was 60%.
Conclusion: Herein we describe a case of Polymorphous adenocarcinoma of the breast, a rare tumour characterized by diverse morphology, negativity for ER, PR and HER2, absence of a biphasic cellular pattern and diffuse positivity for BCL2. This diagnosis should be suspected in carcinomas with apparent discrepancy of a triple-negative immunoprofile and a well-differentiated histology, and without the typical dual cell population of other salivary gland-like neoplasms of the breast.

E-PS-02-014
Solitary cylindroma (dermal analogue tumour) of the breast: 20-year follow-up
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Background & objectives: Solitary Cylindroma (SC) of the breast are very uncommon lesions and can be diagnostically challenging. Little is known about the behaviour of SC of the breast. We present a case of SC with a radiological 20-year follow-up.
Methods: A 69-year old Caucasian female presenting with a 15 mm suspicious spiculate nodule in the upper quadrant of the left breast was seen in screening mammography. The needle core biopsy was diagnosed as a radial scar. Due of its size over 1 cm, the lesion was completely excised. Histologically, the epithelial proliferation was confirmed to be centred in breast.
Results: The tumour was composed of ducts and solid islands of two type of cells, the outer layer of basaloid cells and the inner row of luminal cells in a "jigsaw pattern". Immunohistochemistry showed no expression of HR and HER-2. Solitary Cylindroma (SC) of the breast was diagnosed. The rest of the screening mammographies was reviewed. We could observe that the lesion was noted from 1997.
Conclusion: Solitary Cylindroma (SC) or Dermal analogue tumours of the breast was first described in 2001.
SC was composed of a dual population, luminal (CEA, CK 7, C-Kit and EMA positive) and outer myoepithelial layer (p63 positive), surrounded by basal membrane (Actin, IV Collagen).
Even if the clinical behaviour of Solitary Cylindroma (SC) remains to be defined, the case we present here confirm the indolent nature of this disease, confirmed after 20 years of follow up.

E-PS-02-015
Evaluation of HER2 scoring algorithms for identification of HER2-low breast cancer
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Background & objectives: Her2-low is a novel biomarker for a Her2-antibody-drug conjugate currently trialled in breast cancer and assessed by Her2 IHC using a unique scoring algorithm. We determined prevalence of Her2-low and concordance with conventional Her2 algorithm.

Methods: We assessed a retrospective cohort representing all breast cancer diagnoses from a single institution in a calendar year (2019). The cohort included both screening and symptomatic cases. Her2 had been assessed previously using IHC and ISH. Cases were re-scored using the new Her2-low algorithm and results compared with previous diagnoses obtained using the conventional Her2 algorithm.
Results: Her2-low cannot be identified robustly using exiting Her-2 data derived using the conventional scoring algorithm and retrospective cases will require reassessment with the new algorithm. At present, prevalence of Her-2 low in the breast cancer patient population is uncertain and this study is an attempt to identify its prevalence and its association with tumour type and grade, age at presentation, type of presentation (screening or symptomatic) and Er status. In addition, we show data on concordance between individual pathologists after specific training in the new Her2-low scoring system and we compare scoring obtained on glass slides with digital pathology (DP) slides.
Conclusion: Conventional Her-2 scoring algorithm are designed to identify patients with Her2 overexpressing/HER2 amplified breast cancer. A new drug for Her2-low requires a unique Her2-low category for which there is a new algorithm. We show that the conventional scoring system has poor specificity to identify Her2-low and historical cases will require re-scoring. Pathologists will need training in this new biomarker. An assessment programme to monitor diagnostic concordance could use DP effectively.

E-PS-02-016
Recognising Magtrace in a sentinel lymph node biopsy – a case report
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Background & objectives: A 40-year old female had a wide local excision and sentinel lymph node biopsy for a grade three invasive ductal carcinoma NST post neoadjuvant chemotherapy. Morphologically both nodes were negative for metastatic carcinoma and a response to neoadjuvant therapy.
Methods: On examination, both nodes contained an abundance of pigment laden macrophages within the sinuses and a prominence of eosinophils. The patient had no significant past medical history including skin conditions or tattoos. Both nodes were negative for AE1/AE3. However, a Perls' stain was strongly positive. On further questioning it became apparent that Magtrace had been used during surgery.
Results: The changes identified were iron deposition due to the use of Magtrace. The Magtrace and Sentimag Localisation System is a magnetic system used to guide sentinel node biopsies in patients undergoing surgery for breast carcinoma. Magtrace comprises of iron nanoparticles which is injected into the breast. The Sentimag probe then uses magnetism to detect the particles and identify the sentinel node by producing an audible signal and brown stain.
Conclusion: It is important for histopathologists to be made aware of the changes associated with Magtrace because it is predicted that in the future Magtrace will be used more frequently as clinical studies have shown it to be just as effective as traditional techniques as well as being easy to use and flexible whilst avoiding radiation exposure.

E-PS-02-018
Molecular classification of breast cancer among Egyptian patients: a single institute experience
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Background & objectives: Breast cancer is classified into molecular subtypes to predict clinical outcomes independent of other prognostic indicators. The aim of this study is to investigate the distribution of breast cancer molecular subtypes among Egyptian females in correlation with clinicopathological parameters.
Methods: This retrospective study included a cohort of 1072 breast cancer cases from archives of Pathology laboratory at Ain Shams University hospital, Egypt, between 2015 and 2019. Molecular subtypes (luminal A, luminal B, Her2-enriched, and triple-negative) were determined based upon immunohistochemical analysis of ER, PR, Her2, Ki-67, plus SISH for Her2. These data was correlated with the clinicopathological and prognostic indicators.
Results: The mean age of the patients was 51.4 (±12.4) years. The most prevalent subtype was luminal A in 463 cases (43.2%), followed by luminal B in 430 cases (40.1%), Her2-enriched in 91 cases (8.5%), and then triple negative in 88 cases (8.2%). Invasive ductal carcinoma was the most common histological type (91.1%) then lobular carcinoma (6.5%) and the other types accounted for (2.4%). Most of the tumours were grade-II (85%). The triple-negative patients' mean age was 48 years; the lowest among the other subtypes (p=0.02). Both HER2-enriched and triple-negative cases had the highest percentage of T3 stage tumours. HER2 subtype was associated with highest nodal (p=0.02) and distant metastasis (p=0.03).
Conclusion: Luminal A and luminal B subtypes are the most common among Egyptian breast cancer patients. Her2-enriched subtype correlates with aggressive clinical behaviour having the highest tendency for metastasis, and triple-negative subtype is more frequent among the younger age group.

E-PS-02-020
Neuroendocrine mammary carcinoma with long-interval adrenal metastasis: a case report
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Background & objectives: Neuroendocrine mammary carcinoma (NEMC) is a rare neoplasm comprising about 1 % of breast malignancies.
Methods: We report a case of patient who had NEMC four years ago, now presenting with right adrenal mass. A right adrenalectomy was done and the current mass was examined along with the previous case.
Results: Reviewing the histology revealed identical morphological and immunohistochemical features in both specimens. A tumour with neuroendocrine-like cells is seen. Tumour cells expressed diffuse GATA3, E-cadherin, BCL-2, ER (2+ in 80% of tumour cells), PR (2+ in 2% of tumour cells), Synaptophysin, CK AE1/AE3 and focal CK 7 and Chromogranin .Ki-67 proliferative index was 30%. Inhibin A, P53, EMA, Melan-A, Vimentin, GCDFP-15, Mammoglobin, WT-1, S100 and Calretinin were all negative. A diagnosis of metastatic NEMC was made.
Conclusion: NEMC is a rare mammary neoplasm with scarce literature regarding its course, metastatic potential and therapy. A few authors reported metastasis to various sites, in some cases years after initial diagnosis.

E-PS-02-021
Double trouble: artifactual epithelial displacement mimics invasion in a papilloma with extensive usual duct hyperplasia mimicking a solid papillary carcinoma
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Background & objectives: Mammary solid papillary carcinoma (SPC) and usual duct hyperplasia (UDH) of the breast are morphological look-alikes, characterized by cellular streaming, solid growth and a lack of high-grade nuclear atypia. Immunohistochemistry is helpful to distinguish these entities from one another.
Methods: A 48-years-old woman presented with a palpable lump at three o'clock in the left breast. Medical imaging revealed a slightly irregular

10 mm mass. A core needle biopsy showed a solid papillary proliferation of epithelial cells with oval to round overlapping nuclei, surrounded by a sclerotic stroma. This distorted lesion contained peripheral clefts and cellular streaming, without high-grade nuclear atypia.
Results: Immunohistochemistry for oestrogen receptor (ER), cytokeratin-5 (CK-5), chromogranin and synaptophysin distinguished this sclerosing papilloma with extensive UDH from an SPC. Immunohistochemistry is helpful to distinguish both entities from one another, since UDH shows no immunoreactivity for chromogranin and synaptophysin, and presents with a mosaic-type expression pattern of ER and CK-5.
The lumpectomy specimen revealed a second challenge: multiple epithelial islets without surrounding myoepithelial cells were observed near the papilloma in three consecutive tissue blocks, mimicking an invasive carcinoma. However, they were surrounded by steatonecrosis and reactive fibroblasts, indicating a location within the biopsy needle tract, resembling a comet's tail.
Conclusion: A sclerosing papilloma with extensive UDH is a morphologically mimic of an SPC. Diagnosis is confirmed by immunohistochemistry. Displaced epithelial islets in the biopsy tract mimicked in invasive carcinoma. Breast pathologists should be aware of this uncommon double pitfall.

E-PS-02-023
How many cells should we count in digital assessment of the proliferation marker Ki67 in breast cancer?
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Background & objectives: Recent studies suggest that downgrading of Ki67 levels occurs when >2-300 cells are counted in breast cancer (BC) sections. To investigate this, we used digital image analysis (DIA) to count Ki67-positive cells in digitally identified hot-spots.
Methods: Sections from 200 BC cases, stained for Ki67, were assessed using QuPath software. The percentage Ki67-positive cells was recorded in five 100-cell groups in digitally identified hot-spots. Then increments of 100 cells up to 500 cells, were compared. The number of positive cases at each of three clinically relevant cut-off levels (15%, 20%, 30%) was calculated in each group.
Results: At all three cut-off levels the percentage positive cases were lowest when counting 500 cells and highest when counting 1-200 cells. At the 15% cut-off level, 172 and 184 cases were positive at the 500- and 100-cell increments respectively, implying that 12 cases were downgraded with increasing number of cells assessed. At the 20% and 30% cut-offs, 30 and 25 cases respectively were similarly downgraded. The differences in the number of Ki67-positive cases between all five 100-cell increments were higher at the 20%- and 30% cut-off levels compared to the 15% cut-off level.
Conclusion: In this study, the percentage of Ki67-positive cells was diluted with increasing number of cells counted, leading to downgrading of the proliferation status of some tumours. When using DIA, the highest Ki67 levels may be achieved by counting 1-200 cells.

E-PS-02-024
Pathological assessment of breast carcinoma specimens undergoing neoadjuvant chemotherapy
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Background & objectives: Breast Carcinoma (BC) is the frequent type of diagnosed cancers in females. In this study, Miller Payne system of classification was used for the pathological assessment of breast tumour in patients going through neoadjuvant chemotherapy.
Methods: Representative segments of local wide excision and mastectomies were taken and were fixed in 10% formalin. Hematoxylin and eosin staining was done on the representative sections to observe the pathological changes that occurred after a minimum of 4 cycles of neoadjuvant chemotherapy. Miller Payne system for classification was used for reporting the chemotherapeutic effects of neoadjuvant therapy.
Results: Out of 40 cases, mostly having histological grades 3 and 2. pCR was observed in 17.5% patients according to Miller Payne Classification (grade 5). Incomplete response is observed, out of which 12.5% cases showed Miller Payne Classification grade 4, 20% cases showed grade 3, 42.5.5% belongs to grade 2 and 7.5% cases showed Miller Payne chemotherapy effect grade 1. Only one case with pCR reported ductal carcinoma in situ.
Conclusion: Conclusions: Neoadjuvant therapy is now becoming the standard of care and is a treatment modality that is often used for breast cancer patients. Pathologic assessment as a prognostic marker is still a gold standard for patient's adjuvant for research and clinical trials.
Keywords: Breast carcinoma, Complete pathological response (pCR), Miller classification, Neoadjuvant therapy, Prognostic marker

E-PS-02-026
Prediction of response to neoadjuvant chemotherapy in Egyptian patients with locally advanced breast cancer: the evolving role of tumour infiltrating lymphocytes (TILs)
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Background & objectives: Presence of TILs in breast cancer indicates better therapeutic responses to neoadjuvant-chemotherapy (NAC), increased pCR and improved outcome. We aim at evaluation of TILs in breast cancer biopsies in correlation with pathological response after NAC in locally advanced breast cancer
Methods: This study was conducted at Ain Shams university hospital and Maadi Military hospital in Egypt. 45 female patients with locally advanced breast cancer were treated with NAC, pathological response was assessed. Tumours were categorized into: luminal A, luminal B, Her2 enriched and TNBC. Assessment of TILs (CD4 and CD8 lymphocytes) was based on Immuno-Oncology Biomarker Working Group guidelines
Results: Tumours were classified into high and low TIL groups using the interquartile range cut-off (29%). High CD4 group showed increased pCR ($p = 0.003$) and smaller residual tumours ($p= 0.04$). High CD8 group showed a significant association with smaller residual tumours ($p=0.003$). At follow-up of 24-months, CD4 and CD8 high groups showed significantly higher 2-years DFS. The difference between CD4 high and low groups was significant in regards to oestrogen receptor status, showing higher levels in hormone-negative tumours ($p= 0.029$). Patients with Her2 subtype showed higher CD4 ($p= 0.007$) and CD8 expression ($p=0.018$). In CD4 & CD8 low groups, more patients developed local recurrence and distant metastasis ($P= 0.025$).
Conclusion: We concluded that TILs may predict response to NAC and overall prognosis of breast cancer. The evaluation of TILs in correlation with morphological or genomics-based parameters helps to stratify patients of breast cancer.

E-PS-02-027
Cytological evaluation of breast lesion in patients presenting at Machakos level 5 hospital, Kenya: a retrospective study
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Background & objectives: Fine needle aspiration cytology (FNAC) has gained popularity due to its fast and easy approach, being inexpensive,

and can be performed with little complications. It has become popular as a valuable tool in preoperative assessment of breast masses.
Methods: Medical records of 90 patients presenting to Machakos Cancer Care and Research Centre in Machakos Level 5 Hospital, Kenya between August 2019 and January 2020 were evaluated retrospectively.
Results: Of the 90 diagnosed breast lesions, 89% (n = 89) occurred in females, while 1 % (n = 1) occurred in males, giving rise to a female-to-male ratio of 89:1. Neoplastic breast lesions (n = 85) comprised 94.4 %, while non-neoplastic breast lesions (n = 5) comprised 5.5 % of all diagnosed breast lesions. The neoplastic lesions were classified as 23.5% (n = 20) benign and 76.4% (n = 65) malignant, resulting in a benign-to-malignant ratio of 3.25:1.
Conclusion: Neoplastic and non-neoplastic breast lesions were effectively diagnosed using breast cytology.

E-PS-02-028
Breast metastasis of oesophageal carcinoma: a rare case report
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Background & objectives: Metastatic breast carcinomas from extramammarian malignancies are very rare and breast metastasis of oesophageal carcinoma is even rarer.
Methods: 38-year-old female patient presented with a breast mass. On breast ultrasonography hypoechoic solid nodular lesion (BIRADS 5) was seen and the patient underwent core-needle biopsy.
Results: On microscopic evaluation, solid clusters was seen on low magnification view. On high power, poorly differentiated cells with scant cytoplasm and hyperchromatic nuclei was seen. The patient's history of oesophageal squamous cell carcinoma was known. Immunohistochemically, tumour cells were negative with Gata-3, ER and PR whereas positive with p63 and CK5/6. The case was evaluated as the metastasis of the oesophageal carcinoma to the breast.
Conclusion: Oesophageal carcinomas rarely metastasize to the breast. However, when a breast tumour is detected in a patient with oesophageal carcinoma metastatic tumour should be kept in mind.

E-PS-02-029
Radiation associated angiosarcoma two years after primary breast cancer: a case report
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Background & objectives: Radiation-associated angiosarcomas (RAS) of the breast may arise in a previous radiation field of primary breast cancer. They occur rarely but confer a high probability of local recurrence and poor prognosis.
Methods: A 85-year-old woman with left breast invasive ductal carcinoma was treated with breast conserving surgery, sentinel lymph node excision, and standard radiation therapy to the breast two years ago. After two years, the patient applied with an erythematous oedematous lesion in the incision area. PET-CT revealed thickening of the breast skin and increased FDG uptake in the axillary lymph nodes.
Results: A punch biopsy was taken from this area and reported as angiosarcoma. The patient underwent mastectomy and axillary lymph node dissection. Macroscopically, an irregular tumoral lesion measured 28x23cm with ulceration which caused thickening of the skin was observed. Histopathologically, epithelioid and spindle cell areas and erythrocyte extravasations were seen. Necrosis and mitosis were common. Metastasis was observed in two lymph nodes. Immunohistochemically, tumour cells were diffuse and strongly positive with CD31, FLI1, and ERG, while ER, PR, and Gata-3 were negative.
Conclusion: We reported the case as a poorly differentiated angiosarcoma. RAS is defined by three characteristics: a sarcoma in the previous field of radiation, a latency period of at least 3 years and a histological distinction from the primary neoplasm. The reported median latency period between radiation and diagnosis of RAS is 6–7 years. However, secondary angiosarcoma in our case occurred only two years after primary breast carcinoma.

E-PS-02-030
The role of HER2 gene copy number variations in immunohistochemistry-equivocal (2+) breast cancer
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Background & objectives: Due to tumour heterogeneity of breast cancers, HER2 amplified cells can be identified even in HER2 fluorescence in situ hybridization (FISH) negative/equivocal cases. We aimed to determine the prognostic significance of these copy number variations in HER2 negative breast cancers.
Methods: From the period of 2010-2015, HER2 immunohistochemistry-equivocal (IHC 2+) cases of female breast cancer (with primary, unilateral tumours without treatment before sampling) with negative/equivocal result of dual-colour FISH were collected from the database of our institute. Molecular subtypes were defined according to the St. Gallen 2013 consensus. The IHC and FISH analyses were performed based on the ASCO/CAP 2013 guidelines.
Results: The impact of the ratio of amplified cell population on distant metastases-free survival (DMFS) was analysed in breast cancers with less than 50% amplified cells (HER2 negative tumours). The median follow up of the153 patients was 43.48 months. Distant metastases were observed in 28.29% of the cases. Univariate analysis revealed significant positive correlation between the ratio of the HER2 amplified cells and the longer DMFS (p=0.014). By analysing the subtypes separately, this correlation remained significant only in the HER2 negative luminal B-like group (p=0.025), where by using multivariate analysis, the ratio of the amplified cells proved to be an independent prognostic factor from the Ki67 and progesterone receptor expression.
Conclusion: According to our results, within the 0-49% range, the higher HER2 amplified tumour cell ratio surprisingly might be a positive prognostic variable for the HER2 negative luminal B-like breast cancers. However, further validation of our results on larger cohorts is required.
This study was funded by the Start Up grant 11722 of Semmelweis University, Budapest.

E-PS-02-031
Negative conversion of biomarkers in liver metastatic breast cancer: a single centre study
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Background & objectives: Receptor conversion phenomenon involves changes in oestrogen receptor (ER), progesterone receptor (PR) or human epidermal growth factor 2 (HER2) in metastatic breast carcinoma. It is important to notice this discordance to modify therapy modalities.
Methods: Receptor conversion phenomenon was found relatively frequent in liver metastasis so we reviewed 16 liver metastatic breast carcinoma and compared their receptor status with their primary breast carcinoma and discussed the literature about the possible mechanisms of this situation and relation to the treatment, prognosis. Primary tumour HER2 amplification was assessed both by immunohistochemistry and dual in situ hybridization.
Results: The characteristics of the primary tumour are preserved in most of the metastatic patients. No positive conversion was found among them. Three of the metastases altered their HER2 expression to negative.

Possible mechanisms for this negative conversion was discussed. The sample size was too little to associate with prognosis.
Conclusion: The receptor conversion mechanisms in metastatic lesions are still unclear and debateful. It can be due to tumoral heterogeneity, genetic or epigenetic alterations or intervening therapies. HER2 negative conversion is mostly associated with chemotherapy and trastuzumab and is still considered as a bad prognostic factor. Awareness of this mechanisms is important to decide the best therapy options especially in metastatic lesions.

E-PS-02-032
The existence of calcifications in breast cancer tissue doesn't affect expression of HER2-neu protein
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Background & objectives: There is evidence that calcifications in breast cancer (BC) may have an active role in mitogenesis and upregulation of gene expression.
Aim. To investigate the effect of presence of microcalcifications in breast cancer tissue on Her2-neu expression.
Methods: In this study 468 tissue samples of BC were examined, 55 of which had microcalcifications, and 413 surgical biopsies showed no signs of calcification. The immunohistochemical study of Her2-neu expression and statistical analysis of the results (Chi-square test) was used in this work. Samples with strong expression of the Her2-neu protein were selected for the study.
Results: In the study of BC samples with calcifications, it was found that the proportion of Her2-neu-positive cases among them was 20,93%. In the control group of BC without calcification Her2-neu expression was detected in 16,71% (p>0,05).
Conclusion: The expression of Her2-neu protein in the groups of BC patients with the presence and absence of calcifications was not statistically different. Our study shows no association between the presence of calcifications in breast cancer tissue and Her2-neu receptor expression.

E-PS-02-033
Molecular and genetic factors of metastases to regional lymph nodes in breast cancer patients
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Background & objectives: Breast cancer is accompanied by metastatic lymph nodes in 40% of cases. To identify molecular and genetic predictive factors of metastases to regional lymph nodes in breast cancer patients based on the analysis of gene expression profile of the primary tumour.
Methods: The study included 200 patients with morphologically verified unicentric invasive breast cancer T1-4N0-3M0 in 2 groups: 100 cases with metastases in lymph nodes and 100 cases without it. The molecular genetic testing of tumour tissue was carried out using reverse transcription polymerase chain reaction (RT-PCR); the diagnostic panel consisted of 28 functional genes.
Results: The primary breast tumour in the group of patients with metastases to regional lymph nodes was characterized by increased proliferative activity based on expression of Ki-67 gene ($p = 0.03$), as well as an increased level of mRNA of genes NAT ($p = 0.04$) and CD68 ($p < 0.001$) and decreased expression of PTEN ($p < 0.001$) and gene ESR1 ($p = 0.04$). According to the results of discriminatory analysis, the predictive accuracy of presence or absence of metastases to regional lymph nodes based on molecular genetic testing of the primary tumour in 7 genes expression panel was 91.9% and 78.8%, respectively.
Conclusion: Molecular genetic testing of the primary breast cancer tissue using the panel of 7 genes (PTEN, CD68, CCNB1, MGB1, MYC, BCL2, ESR1) can become an additional diagnostic tool for predicting the presence of lymph node metastases when planning the volume of axillary surgery in breast cancer patients.
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E-PS-02-034
Changes of the luminal A subtype of breast cancer in local metastasis
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Background & objectives: Subtype discordance in primary and metastatic breast cancer (BC) is the possible reason of lower therapy effect. Objective of the study: to evaluate changes in the luminal A subtype of breast cancer in regional metastasis.
Methods: Samples of primary tumour and local metastasis obtained from 36 patients were stained immunohistochemically with antibodies to ER, PR, Her2/neu and Ki67. Primary tumour in all cases had the luminal A subtype (according to St. Gallen 2015 consensus). The frequency of changes in BC subtype in metastasis was evaluated, the detected frequencies were compared using a Fischer exact probability test.
Results: Regional metastasis had the discordant subtype in 11 cases (30.6%, 95%, 16.9-48.3%) and concordant (luminal A) subtype in 25 of the 36 cases (69.4%, 95%, 51.7-83.1%). In 10 cases the metastatic tumour had the luminal B subtype (27,8%, 95% DI 14,8-45,4%), in 1 case - triple negative subtype (2,8%, 95% DI 0.1-16.2%). The difference in the frequency of primary tumour and metastasis subtype concordance and discordance was statistically significant ($p=0.002$), as well as the difference in the frequency of occurrence of luminal B and triple negative subtypes of metastases ($p=0.006$).
Conclusion: Changes in the luminal A subtype of breast cancer in regional metastasis were observed in 30.6% of cases, while the frequency of cases with concordant subtype was significantly higher. Among cases with discordance of primary tumour and regional metastases subtypes, the luminal B subtype of the metastasis is more common (27.8%) than the triple negative subtype (2.8%).
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E-PS-02-035
Secretory breast carcinoma with poor prognosis - a case report
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Background & objectives: Secretory breast carcinoma (SBC) is a very rare disease; it accounts for less than 0.05%. The SBC is defined by a pattern of pathological, phenotypical and specific molecular features. Reports of death from distant metastasis are very rare.
Methods: A 37 year-old woman with a stage IIB tumour. Diagnosed on core-needle biopsy as a triple negative infiltrative carcinoma grade II of SBR. She received a neoadjuvant chemotherapy with six cycles of a combination of carboplatin AUC5 plus docetaxel for 3 cycles followed by 3 cycles of FAC. She underwent a radical mastectomy with lymph node dissection
Results: The patient had no response to chemotherapy, with an extensive residual disease (RCBIII) of a SBC with no axillary lymph node metastasis. The tumour cells showed a mild positivity for oestrogen receptor

(ER) score 5 of Allred and negative for progesterone receptor (PR), with no overexpression of HER2. GCDFP15, Mammaglobine and CK5/6 were positives. The fluorescence in situ hybridization showed a rearrangement of the ETV6 gene. She received chest wall radiotherapy. 18 months after the end of treatment the patient had a pleuro-pulmonary metastasis and died three months after.
Conclusion: The management of SBC is usually surgical with an indolent evolution. In our case the misdiagnosis on core-needle biopsy led us to treat it as a triple negative disease. The metastatic disease is extremely rare in SBC. The clinical course of SBC may be age dependant; our patient was over 20 years. Guidelines to manage these rare tumours are not available.

E-PS-02-036
An unusual presentation of paediatric malignant phyllodes tumour of the breast in a 13 year old girl with review of the literature
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Background & objectives: In June 2018, a premenarchal 13 year old girl presented with a 40 mm large lump in the central and lateral part of her right breast with brown nipple discharge. Ultrasound examination revealed a fibroadenoma-like lesion with code 3.
Methods: Fine needle aspiration cytology proved to be inconclusive. It showed inflammation containing mesenchymal cells and atypical epithelial cells with tendency to papillary fronds. It raised the suspicion of fibroadenoma, a cystic or papillary lesion. Core biopsy (14G) revealed only necrotic and haemorrhagic mass without viable epithelial or stromal cells.
Results: Excision biopsy was performed. Microscopical examination detected a 44 mm large malignant phyllodes tumour (MPT) with extensive necrotic/haemorrhagic changes. Leaf-like stromal fronds were present. The tumour border was focally infiltrative to the adjacent stroma. Atypia was observed in the epithelial part. The hypercellular stroma was dominated by an atypical spindle cell proliferation with stromal overgrowth and with a high number of mitoses (11-15 per 10 high power fields).
Conclusion: The final diagnosis of MFT came only from excision biopsy, followed by total mastectomy for a tumour free margin. The patient is recurrence free 1.5 years after the operation. Examination of pathology records revealed 39 MPT cases between 1982-2020 with only one paediatric case (46% of the patients were aged ≤ 50 years, the youngest eight patients were between 23-36 years of age). MPT constitutes <1% of all primary breast neoplasms, which can occur in adolescents and young adults.

E-PS-02-037
Analysis of clinicopathologic features of glycogen-rich clear cell carcinoma (GRCC) of the breast
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Background & objectives: Glycogen-rich clear cell carcinoma (GRCC) accounting for 1%-3%. This article aims to explore the clinicopathological features of GRCC of the breast in order to further deepen the understanding of the disease and improve the diagnostic level.
Methods: Six patients with pathologically diagnosed GRCC of the breast from January 2015 to December 2019 were collected, and their pathomorphological features, clinical pathological features, and immunophenotypic features were analysed.
Results: All 6 patients were female, and the age of onset was 46-57 years old, most common among middle-aged women. All 6 cases underwent pathological examination and found that triple negative breast cancer accounted for 50%, which indicates that the malignancy of GRCC is relatively high and the prognosis is poor.
Conclusion: GRCC of the breast is a rare type of breast cancer. Pathology is an important means of diagnosis. It depends not only on the morphological characteristics of the tumour tissue, but also on the expression of its specific immunohistochemical indicator period acid-Schiff (PAS). Differentiate other diseases to achieve the purpose of early diagnosis and early treatment.

E-PS-02-038
Breast cancer containing eggs of schistosoma
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Background & objectives: The presence of eggs of Schistosoma haematobium is commonly associated with squamous cell carcinoma of the urinary bladder. The finding of eggs in other tumours is rare. We describe one case of breast cancer in which eggs were also seen.
Methods: A 48-year-old female was seen at the Cancer Institute of Angola for swelling in the left breast, with heterogeneous calcifications on mammography. After a needle biopsy, a diagnosis of invasive breast carcinoma NST was made at the cT2N1 stage. Surgery was performed and the specimen was studied with HE and immunohistochemistry
Results: Neoplasia with 3.8cm was found, aside with 12 lymph nodes in the axilla, some with a metastatic pattern. Histological study confirms the diagnosis; invasive breast carcinoma NST, G3, with metastasis in 3 of 16 lymph nodes. In the middle of tumour frequent eggs of Schistosoma, many already calcified were seen.
On immunohistochemistry, ER and PR were positive in 10% of the neoplastic cells; HER2 was also positive (3+) in most of the neoplastic cells. Ki67 was strongly positive in 60 to 70% of cells.
Eggs of Schistosoma have a recognized carcinogenic effect on urothelium, being associated with squamous cell carcinoma of the bladder Their presence in breast cancer is occasional
Conclusion: The presence of eggs in neoplasias of other sites, namely in the breast that is a site where parasitic migration does not occur usually, has not been reported before. The case presented here is exceptional and, therefore, justifies its description.

E-PS-02-039
Breast cancer in Angola: new data with immunohystochemical contribution
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Background & objectives: Breast cancer is common in Angola. The report of new cases is important to strengthen data related to prevalence and to help the development of programs of screening and early diagnosis; training technical staff and improving survival rates.
Methods: 285 new cases diagnosed in Cancer Institute of Angola and Clinica Sagrada Esperança between January 2011 and February 2020 were included. 32 cases were withdrawn because the quality of the material was deficient. The tissue was studied by histology and immunohistochemistry using the following markers: ER, PR, HER2; Ki67; E cadherin; CK5/6; p63; PGFR.
Results: Age (years): average 48.2; min 24; max 84. Histological types: NST invasive breast carcinoma: 73.2%; invasive lobular carcinoma: 8.4%; mucinous carcinoma: 5.3%; invasive papillary carcinoma: 1.3%; metaplastic carcinoma: 1.2%; others: 10.6%. Grade - 1: 4.0%; 2: 57.0%; 3: 39%. Staging (%): DCIS 0; I: 0.8; IIa: 7.1; IIb: 14.2; IIIa: 24.5; IIIb: 29.6; IIIc: 7.9; IV: 15.9. Molecular types (%): luminal A: 23,7; luminal B: 27,3; HER2 pos: 12,7; triple negative: 29,2; Luminal B Her2 positive: 7,1; Triple negative: 74 cases (29,2%) distributed as follows: basal cells 53; medullar type 10; apocrine 6; metaplastic 3; adenoid cystic 1. Total of HER2 + : 51 (19.8%); total ER+: 151(59.7%);

Conclusion: Breast cancer in Angola is diagnosed at advanced stages. The percentage of triple-negative and luminal B cases is high. The data obtained are a good indicator of the modalities of screening and treatment to be developed.

E-PS-02-040

Primary well-differentiated breast angiosarcoma with cutaneous affectation: an unusual clinical finding

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Background & objectives: Angiosarcomas are the most frequent primary sarcomas of the breast, though they are still very uncommon (<0.05% of breast malignancies). They may arise spontaneously (primary angiosarcoma) or following radiation therapy for breast cancer (secondary angiosarcoma).
Methods: A 42-year-old female, with a right breast primary well-differentiated angiosarcoma, diagnosed in January 2016. Three years after quadrantectomy, follow up imaging studies revealed several systemic infiltrative nodules at both breasts, left lung, liver, bones and skin. Clinically, the patient was initially asymptomatic, though clinical progression was early evident by interspersed cutaneous papules. A biopsy of an skin lesion was performed.
Results: Histologic examination showed a notorious small and medium-sized vessels proliferation, with dilated or collapsed spaces, covered by a bland-appearance endothelium. Immunohistochemical study revealed positivity for CD31 and CD34, focal c-myc expression, and actin stain partial positivity. HHV 8, CD138, ER and D2-40 were negative and endothelial cells exhibited focal increased proliferative activity (Ki-67). A definite diagnosis of metastatic low-grade angiosarcoma with cutaneous extension was made.
Conclusion: Primary breast angiosarcomas typically occur in young women with no history of previous cancer and without other risk factors. Despite histological grading was previously considered predictive, recent data have indicated that angiosarcoma grade has no prognostic value. Low-grade lesions usually can metastasize, being cutaneous affectation quite rare.

E-PS-02-041

Morphological evaluation of vasculogenous mimicry as an alternative method of tumour blood supply

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Background & objectives: Vasculogenic mimicry(VM) is an alternative method of blood supply to the tumour, realized through the formation of channels limited by the basement membrane (BM) and formed without the participation of endothelial cells (ECs).
Methods: Light microscopy was used, immunohistochemical and histochemical studies were carried out using CD34, CD31 "Dako", E-cadherin, vimentin, and PAS reaction. 18 cases of CMM (10 men and 8 women) and 26 cases of breast invasive carcinoma of no special type (IC NST) were retrospectively studied.
Results: A large part of the tumour cell population (84%) of breast cancer in the central regions of the tumour node and invasive growth zone in the thickness of the anaplastic component during double staining with PAS and CD34 reagents was CD34- / PAS+ phenotypically and participated in the formation of vasculogenic channels. In the remaining 16% of the cells, expression of both PAS and CD34 - CD34+/ PAS+ tumour cells was detected.
Conclusion: Despite various points of view regarding the true genesis of vasculogenic channels, it is currently believed that their appearance among TCs contributes to the appearance of malignant invasive and metastatic properties of the tumour.

E-PS-02-042

Malignant phyllodes tumour with osteoclastic giant cells in a young female, a very rare histology

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Background & objectives: Phyllodes Tumour is a fibroepithelial neoplasm accounting for 0.3-1% of primary breast neoplasms. The presence of giant cells in malignant phyllodes tumour (MPT) is rare and much rarer is the occurrence of osteoclastic giant cells in MPT.
Methods: Here, we present the case of a 39 year old woman who had history of cystic left breast swelling since 3 years. Grossly, it was a partly skin covered breast tissue. Cut surface showed a solid cum cystic and haemorrhagic lesion that measured 13 x 10 x 4 cm.
Results: Microscopy revealed breast tissue exhibiting cleft like areas showing compressed breast ducts and spindly stroma with transition to high grade tumour composed of small fascicles of spindle shaped cells with vesicular nuclei, conspicuous nucleoli and moderate eosinophilic cytoplasm interspersed with scattered uniform distribution of osteoclast giant cells. Approximately 20 mitosis were identified. Immunohistochemical epithelial markers were negative in osteoclastic giant cells and showed CD68 expression. Spindle cells were positive for SATB2. Based on these morphological and immunohistochemical, it was diagnosed as MPT with osteoclastic giant cells.
Conclusion: MPT with osteoclastic giant cells is very rare. This can be confused for metaplastic carcinoma and undifferentiated pleomorphic sarcoma (UPS). MPT is usually associated with fibrosarcomatous type of stromal differentiation but very rarely UPS like differentiation may occur giving rise to a diagnostic dilemma. A definite distinction is imperative considering the better prognostic implications of malignant phyllodes tumour than UPS and metaplastic carcinoma and different management options available.

E-PS-02-043

Interest of CD10 immunostaining in grading of phyllodes tumours of the breast

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Background & objectives: Phyllodes tumours (PT) of the breast are classified as benign, borderline, and malignant according to histological features which still unclear to discriminate between different grades. This study aims to highlight the interest of CD10 immunostaining in grading of these tumours.
Methods: This study included 64 PT (47 benign, 9 borderline, and 8 malignant) collected over 14 years (2006-2019). The expression of CD10 was studied in using immunohistochemistry to evaluate whether differences in expression correlated with tumour grade of the WHO grading system.
Results: Patients ages ranged from 19 to 65 years (mean, 42). Three of the 47 cases of benign PT cases stained positively for CD10 in the stromal cells. Six of the nine borderline PT cases were positive and seven of the eight malignant PT cases were positive. These results showed highly significant correlation between CD10 expression and the tumour grade ($P<0.0001$) between benign and borderline tumours. But these correlation was statically insignificant ($p=0.33$) between borderline and malignant tumours.
Conclusion: There is a strong correlation between CD10 expression and tumour grade (benign/borderline) which could be an important

observation that may have both diagnostic and prognostic implications as well as promising potential target for development of novel therapies.

E-PS-02-044

Myoepithelial carcinoma arising within an adenomyoepithelioma of the breast - case report with a short review of the current literature

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Background & objectives: Adenomyoepithelioma of the breast is a rare tumour characterized by biphasic proliferation of both epithelial and myoepithelial cells. A myoepithelial carcinoma arising within an adenomyoepithelioma is even more unusual.
Methods: A 100-year-old woman presented with a tumour of the left breast. Gross examination showed a tumour, measuring 5x2cm. Microscopic examination showed a tumour composed of oval, spindle and a few clear cells with foci of necrosis and glandular-like structures. Three mitoses were counted in 10 HPF. Tumour cells were positive for SMA, S-100,CK5/6, CK903, CK7,CK8-18, and negative for ER, PR, Desmin,CD34.
Results: The diagnosis of myoepithelial carcinoma arising within an adenomyoepithelioma was given.
Conclusion: Malignant myoepithelial tumours are either pure myoepithelial carcinoma or an adenomyoepithelioma with a component of myoepithelial carcinoma. The definitive diagnosis of myoepithelial carcinoma is based on histological and immunohistochemical findings. The treatment of choice is surgical, namely wide tumour excision or mastectomy with regional lymph node excision. Adjuvant radiotherapy or chemoradiation are often administered in order to minimize local recurrence. Myoepithelial carcinoma has an aggressive course, with locally invasive and widespread metastatic potential to several organs.

E-PS-02-045

Granular cell tumour of the breast: a case report

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Background & objectives: Granular cell tumour (GCT) is a soft tissue neoplasm mainly found in the skin, oral cavity or digestive tract. A GCT involving the breast parenchyma is rare and is seen approximately 1 in 1000 breast cancers.
Methods: A 62-year-old woman presented with a 3-month history of lump in left breast. Mammography revealed a heterogeneous, irregular mass, strongly suspicious for malignancy.
Grossly, a piece of unremarkable greyish yellow fibro-fatty tissue, measuring 35mm x 27mm x, 15mm was received. Sections were studied with H&E, and IHC markers S100, CD56, Inhibin and CD68 and were reported digitally using Aperio Imagescope.
Results: Representative sections of the right breast lesion showed irregular stellate configuration of fibro collagenous tissue, surrounded by adipose element, scattered within which large cells with bright eosinophilic, granular cytoplasm ,and vesicular nuclei with occasional prominent nucleoli within were observed.
These large cells were seen insinuating and interspersed within the fibrocollagenous framework in trabecular, anastomosing, and nest-like pattern without any well-defined capsule. Occasional foci of lymphoid aggregates toward the periphery with germinal centres were noted.
Scattered granular cells throughout showed strong expression for S100, CD68, Inhibin and for CD56.
Immunohistochemistry studies confirmed benign granular cell tumour of the breast.
Conclusion: Although, GCT is one of the rare tumours of the breast, it should be considered in the differential diagnosis of benign and malignant lesions of breast. Mammographically and clinically it can mimic carcinoma of breast. Large granular cells should not be mistaken for malignant cells and reported as malignancy. Wide local excision is the treatment of choice for these lesions.

E-PS-02-046

Primary angiosarcoma of the breast: a case report of an unusual malignancy

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Background & objectives: Primary angiosarcoma, a malignant neoplasm of breast without clear aetiology and not associated with history of radiation exposure, is the most frequent sarcoma of the breast but still very uncommon. We report this unusual case with emphasis on histological features.
Methods: We report the case of a 57-year-old woman with no known history of radiation exposure, who present, in screening programme, a well-circumscribed 20-mm-diameter tumour at the upper outer quadrant of left breast. After core-needle biopsy, a wide local excision with sufficient margins was performed.
Results: On gross evaluation, breast sample showed a well-circumscribed haemorrhagic mass, measuring 25 mm, without areas of cystic degeneration. On microscopic examination, the lesion showed low-grade features, with well-formed interanastomosing vascular spaces that dissected through mammary stroma and adipose tissue, lined by hyperchromatic endothelial cells, with focal papillary formations. Mitoses were scant and necrosis as well as foci of stromal haemorrhage were not observed.
Conclusion: Primary angiosarcoma of the breast is an uncommon neoplasm with worrisome prognosis. It is important to evaluate histological features as well as size, but recent studies showed that grade does not correlate with prognosis, because morphologically well-differentiated lesions can metastasise.

E-PS-02-047

Breast carcinosarcomas: a case series from the cancer registry

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Background & objectives: Breast carcinosarcomas (BCS) are rare biphasic malignant tumours. They are often encountered within metaplastic breast cancer entity. Results from some studies show that epithelial-mesenchymal transition may be one of possible mechanisms of BCS development.
Methods: Data on BCS cases were automatically extracted from the Belarusian Cancer Registry (search criteria "ICD-O code of histology: 8490/3" and "ICD-10 code C50" and retrospectively analysed. 25 cases of BCS were registered during 1995 – 2019 years.
Results: Mean age at diagnosis was 57 (range 28 – 82) years. Right breast was affected in 9 (36%) cases, left in 16 (64%). Most often the tumour was located in upper external quadrant (n=10, 40%), followed by lower external and internal (both n=2, 10%) and upper internal (n=1, 5%), central part was involved in 2 (10%) cases, in 9 (39.1%) tumour involved several parts. The disease was diagnosed in stage I in 5 cases (20%), II – 13 (52%), III – 4 (16%). Metastases to regional lymph nodes were present in 9 (36%) cases. No data on histological components of the tumours were available in the records.
Conclusion: Here we presented an analysis of BCS incidence and clinicopathologic characteristics based on the data from population registry.

BCS are rare tumours, mostly affecting women in 6-7 decades of life, with clinical characteristics at presentation similar to those of breast carcinomas. Histological examination of tumour biopsy or surgical specimen is the only method for correct diagnosis.

E-PS-02-048

Comparison of GATA3, gross cystic disease fluid protein-15 and mammaglobin in primary, metastatic and triple negative breast carcinomas

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Background & objectives: Mammaglobin and GCDFP-1 are traditional IHC markers utilized to recognize metastasis of breast carcinoma in an unknown primary. This study was done to evaluate and compare GATA3 with GCDFP-15 and Mammaglobin in invasive primary, metastatic and triple negative breast carcinomas.
Methods: IHC for GATA3, GCDFP-15 and Mammaglobin was applied on 100 cases of primary breast carcinomas, including 20 triple negative cases and 30 cases of metastatic breast carcinomas. Staining scores were given for each marker by multiplying the percentage of positive tumour cells by the intensity of staining (1+, 2+ or 3+), with scores ranging from 0 to 300.
Results: GATA3-3 was expressed in 92% of primary, 80% of metastatic and 60% of triple negative breast carcinomas, with an average staining score of 270. Mammaglobin was expressed in 68% of primary, 56.7% of metastatic and 25% of triple negative breast carcinomas, with an average staining score of 180. GCDFP-15 was expressed in 48% of primary, 26.7% of metastatic and 05% of breast carcinomas, with an average staining score of 60.
Conclusion: GATA3 has a higher sensitivity and increased staining scores in primary breast carcinomas, metastatic breast carcinomas as well as in triple negative breast carcinomas.
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E-PS-02-049

Demographic and histopathologic characteristics of breast lesions at a district hospital in Nigeria

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Background & objectives: Breast cancer is the most common cancer and a leading cause of cancer deaths in women globally. Consequently, breast lumps cause anxiety, necessitating evaluation of its nature. This audit describes the histopathological spectrum of breast lumps in a district hospital.
Methods: This was a retrospective study of all histologically diagnosed breast lesions seen at a pathology laboratory over a 5-year period. Laboratory request forms and duplicate copies of histopathology reports of all cases were retrieved, and relevant clinical information was extracted. The corresponding slides were also retrieved and reviewed. The tumours were classified according to WHO International Classification of breast tumours
Results: 839 breast tumours were diagnosed during the study period, females and benign tumours accounted for 98.3% and 70% respectively. The age range is 10-96 years with a mean age of 33.3 years. Fibroadenoma (50.9%) and fibrocystic change (27.3%) were the most common benign tumours. Malignant tumour incidence peaked in the 40-49 and 30-39 years age groups. The most common malignant tumours were invasive ductal carcinoma (84.5%), and invasive mucinous carcinoma.
Conclusion: The study showed that breast tumours are common, with benign tumours being more than twice as common as malignant tumours. Benign tumours are common in females of reproductive age group, with fibroadenoma being the most common type in this study followed by fibrocystic change. There is a declined in mean age of patients with malignant breast tumours in our study, with invasive ductal carcinoma (NST) being the most common type followed by invasive mucinous carcinoma and invasive lobular carcinoma.

E-PS-02-050

Paget's disease of the breast: differential diagnosis using additional immunohistochemical panels

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Background & objectives: Paget's disease in most cases is associated with one or more tumours. Currently, there is a tendency towards overdiagnosis of Paget's disease of breast in the world. The aim of study is to find additional differential diagnostic IHC-markers of Paget's Breast disease.
Methods: We studied surgical material that was obtained from 10 women aged 28-63 years with a confirmed diagnosis: Paget's breast disease. The average age of patients is 43 years. In addition to the primary diagnostic antibodies, such as: HER2, CEA, ER, PR, the following antibodies were used: CK7, CD138, E-cadherin, MUC1, GATA3
Results: In the presented samples was observed: Intense, broad cytoplasmic expression of CK7, broad but less intense membranous expression of CD138 and E-cadherin, Intense, but less broad nuclear expression of GATA3, Low cytoplasmic expression of MUC1
Conclusion: CD138 can be used as the primary differential diagnostic marker between Paget`s cells and Toker`s cells. Toker`s cells have low CD138 expression.CK7 can be used as an additional IHC marker of Paget's disease of the breast due to high sensitivity. It cannot be used as the primary marker due to its low specificity.GATA3,MUC1 and E-cadherin can be used as additional markers of Paget`s disease of the breast.

E-PS-02-051

Assessment of tumour-infiltrating lymphocytes presence in biopsies with different biological subtypes of breast cancer

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Background & objectives: Tumour-infiltrating lymphocytes(TIL) are a manifestation of the antitumor activity of the immune system. TIL considered as a prognostic biomarker of the effectiveness of immunotherapy. The aim of this study was to correlate the TIL variety with different immunohistochemical(IHC) subtypes of BC.
Methods: 100 breast biopsies from patients with BC were divided into following groups:1-(luminal A)-20;2-(luminal B,HER2 positive)-20;group 3(luminal B,HER2-negative)- 20; group 4(HER2- positive) -20; group 5(triple negative)- 20 cases. H&E slides were studied microscopically. IHC analyses were carried out with the help of monoclonal mouse antibodies: to ER, PgR, HER2, Ki67.Relations between parameters were assessed by Spearman's rank correlation coefficient.
Results: Analysis of the volume fraction of TIL presence in the tumours' stroma revealed variations of parameters in different IHC subtypes of BC. The values of indicators in the groups were as following: group 1 – 6.5 ±5.26%, group 2-28.05±10.95%, group 3-15.35±10.44%, group 4-28.90 ±5.73%, group 5-46.85±8.66% of a tissue with TIL presence' volume fraction. The study of multiple correlations between groups revealed a positive correlation between the values of r=0.71986.
Conclusion: BCs characterized with high heterogeneity. Molecular subtypes of BC identified by immunohistochemical study are used in clinicomorphological practice. All subtypes have different reaction to chemotherapy. Histological study of TIL presence in BC biopsies discussed in

the aspect of prognostic biomarker and potentially predictive parameters, which can help in stratifying patients with possible clinical progression results. Further study of the tumour stroma' immune response will contribute to improve the prognosis of BC patients.

E-PS-02-052

Desmoid fibromatosis of the breast: report of a rare entity with a challenging diagnosis

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Background & objectives: Desmoid fibromatosis (DF) accounts for 0.2% of all breast tumours. It has a high rate of local recurrence without metastatic potential. We report a case of a breast-DF to emphasize its clinico-histological features and to discuss its differential diagnoses.
Methods: We present a case of DF of the breast in a 33-year-old woman who presented with a single lump of the left breast measuring 15 mm.
Results: Ultrasound showed a hypoechogenic spiculated mass suggesting an invasive carcinoma. Biopsy revealed a spindle cell proliferation of fibroblasts and myofibroblasts without atypia or mitoses. There was no epithelial component. Immunohistochemical analysis showed negativity for keratin and CD34 and was inconclusive for β-catenin and Desmin. Wide local excision was completed and revealed the same proliferation with infiltration of the adjacent breast tissue. All surgical margins were free from tumour. Immunohistochemistry led to the diagnosis of DF confirmed by positive nuclear staining for β-catenin. Tumour cells were also positive focally for SMA and negative for Desmin. The patient is followed now for 4 months with no apparent recurrence.
Conclusion: The breast is an unusual site of DF. Biopsy is not always successful to make the exact diagnosis. Differential diagnoses include phyllodes tumour, fibromatosis-like metaplastic carcinoma and myofibroblastoma. Wide local excision with clean margins is considered as the standard treatment.

E-PS-02-054

Number of tumour-involved sentinel nodes as a predictor of axillary lymph node metastases in breast cancer: single institution study

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Background & objectives: The axillary lymph node status is one of the strongest prognostic factors in breast cancer. Modifications in management of breast cancer based on biology of the tumour, raised questions about axillary dissection necessity for patients with sentinel lymph node metastases.
Methods: We observed pathohistological data of 1976 patients (mean age 58 years) who underwent intraoperative lymphatic mapping and sentinel lymph node dissection of potentially curable breast cancer at our institution between January 2014 and June 2019.We assessed the relation between number of sentinel node metastases and tumour grade, tumour size, hormone receptors, HER-2-expression as well as number of positive non-sentinel nodes.
Results: 455 (23,05%) of examined sentinel nodes had macro- (87,5%) and micrometastases (12,5%). 81,53% of sentinel nodes had 1 tumour-involved lymph node. 57,8% of examined axillar lymph nodes were positive. The incidence of non-sentinel node metastases increased with the number of sentinel node macrometastases and micrometastases ($p< 0,05$). In patients with T1 and T2 lesions, the incidence of 1 sentinel node involvement was 54,33%. Patients with T1 or T2, hormon-receptor positive tumours and 1 sentinel node metastasis had a low incidence of nonsentinel node metastases ($p<0,05$).
Conclusion: Number of tumour-involved sentinel lymph nodes may be a strong predictor of axillary lymph node metastases. Axillary lymph node dissection may not be necessary in patients with T1/T2 stage and hormone receptor positive tumours with detected 1 sentinel node metastasis.

E-PS-02-056

Fibroadenoma of left axillary ectopic breast tissue, a clinical mimicker of tuberculous lymphadenitis: a case report

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Background & objectives: A fibroadenoma left axillary ectopic tissue is such a rare entity in literature. A first case is hereby reported.
The objectives
1) describe the single first case in our clinical settings
2) inform clinicians about this diagnosis among other differentials
Methods: case report, a descriptive study in which we reviewed the clinical profile of the patient and the cytological diagnosis with histopathological diagnosis confirmation
Results: A fine needle aspiration onto two nodules favoured fibroadenoma left axillary ectopic breast tissue which was definitely confirmed by histopathological analysis of the excisional biopsy
Conclusion: Though rare is fibroadenoma left axillary ectopic breast tissue, it should be always mentioned into differentials diagnoses of axillary masses.

E-PS-02-057

Tall cell variant of papillary breast carcinoma. A case report of a very rare tumour entity

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Background & objectives: Tall cell variant of papillary breast carcinoma (TCVPBC) is a subtype of papillary carcinoma of the breast resembling the tall cell variant of papillary thyroid carcinoma. We describe an additional case of TCVPBC and the problems correlating with its diagnosis.
Methods: A circumscribed nodule of 0,9cm, in the UOQ of the right breast, of a 71 year-old woman, was discovered incidentally during a mammographic examination. A hook was placed and the lesion was excised for diagnostic evaluation. Sentinel lymph node biopsy (SLNB) was also performed.
Results: Microscopically, the majority of the tumour consisted of solid circumscribed nodules of epithelial cells with a focal papillary and trabecular arrangement of cuboidal or tall columnar cells with eosinophilic cytoplasm and round to oval nuclei with reverse nuclear polarity and occasional grooves. Myoepithelial markers, TTF-1, thyroglobulin, hormone receptors and c-erb-B2, were negative. The diagnosis was of an invasive tumour with features consistent with tall cell papillary breast carcinoma.
Conclusion: TCVPBC is a recently described, rare, special histologic subtype of invasive breast carcinoma with specific morphologic, immunohistochemical and molecular features, with overall favourable prognosis, which has to be differentiated from other papillary lesions of the breast and metastatic thyroid carcinoma. Wide excision is the treatment of choice with lack of evidence for SLNB.

E-PS-02-058

Frequency of triple-positive breast cancer, according to pathomorphological laboratory

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Background & objectives: Immunophenotypic heterogeneity in BC determines a different prognosis and response to therapy. HER2-expression

leads to a worse prognosis. Expression of hormonal receptors together with the expression of HER2 (triple-positive breast cancer) leads to a worse response to therapy.
Methods: We analysed pathological reports in our laboratory during the period 2011-2019 y.y. All cases were stained with antibodies to hormone receptors, HER2 protein and Ki-67.We examined only patients who were not treated before surgery. In all cases, the degree of differentiation (grade), the presence or absence of metastases, and the stage were assessed. The comparison group selected ER + BC.
Results: In total over the period of 2011-2019 years, 3182 cases were operated for BC without neoadjuvant therapy. The proportion of TPBC was 5.2% of their number. Most TPBCs were grade 3 (58%), only 2 cases were grade 1. Ki-67 index ranged from 5 to 90%, the average value was 28.4%, median 25%, mode 40%. Among TPBC 35.9% of tumours had metastases in regional lymph nodes according to the pathological report, although the clinical stage before surgery was N0.
Conclusion: According to Patrizia Vici et al., TPBC accounts for up to 50% of HER2 + BC, 5-15% of all BC. We have similar data. TPBC have a higher grade and Ki-67 index compared to other ER + tumours. The N+ status is higher than in the general population of ER + breast tumours. These data confirm the thesis that TPBCs have worse prognosis and more aggressive behaviour.

E-PS-02-059
Distinguishing features of solid papillary carcinoma in breast needle core biopsies
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Background & objectives: Papillary lesion of the breast is the most challenging diagnosis that causes frequent reason of referral. Solid papillary carcinoma (SPC) is one of the papillary lesion with distinct entity that should not be missed including in needle core biopsy samples.
Methods: Presenting to you two cases of SPC diagnosed in biopsies and confirmed by excised samples. Both cases are from women at 60s with painless breast lump without nipple discharge. Breast ultrasound shows lobulated hypoechoic lesion and mammogram shows features of highly suspicious of malignancy with BIRADS V.
Results: Microscopically, the lesion exhibits solid tumour arranged in sheets, displaying streaming pattern resemblance florid usual ductal hyperplasia, but with arborizing papillae, fibrovascular cores and hyaline collagen. Another key feature includes perivascular pseudorosettes formation and the presence of extracellular mucin. The cells are monotonous, polygonal in shape with low nuclear grade. Mitotic figures are occasionally seen. No myoepithelial cells observed within the lesion or outer nodules. Immunohistochemical staining shows diffuse positivity for ER, PR and synaptophysin but negative for HER-2, P63 and CK5/6. The presence of invasive foci, absence of myoepithelial cells at the periphery and the jigsaw pattern render a diagnosis of invasive SPC.
Conclusion: Both cases were subjected for wide local excision with axillary clearance. One case positive for sentinel lymph node, the other one was negative. To conclude, there are distinct features of SPC that enable pathologist to suggest a diagnosis in biopsy sample and not to overcall as invasive carcinoma of no special type.

E-PS-02-060
Malign adenomyoepithelioma of breast
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Background & objectives: Breast adenomyoepithelioma is an unusual benign neoplasm characterized by biphasic proliferation of epithelial and myoepithelial cells. Although most tumours are benign, rarely malign transformation of the myoepithelial cells, ductal epithelial cells or both may occur.
Methods: We discuss a case of 75 year old women who had a pain and discharge in her left breast with a grand mass. Breast ultrasound showed 7x6 cm, solid and hypoechoic lesion in the superior half of the left breast. This lesion was reported as BIRADS5 category.
Results: Modified radical mastectomy and ipsilateral axillary lymph node dissection were performed. Microscopic examination revealed adenomyoepithelioma consisting of tubular epithelial and spindle myoepithelial component. Malignancy in the current case was evidenced by the presence of infiltrating growth pattern, high mitotic index, cytological aytipi and necrosis. There were no metastasis in lymph nodes. Immunostains were used to show epithelial and myoepithelial components.
Conclusion: Malign adenomyoepithelioma is a rare neoplasm. It should be considered in the differential diagnosis of other solid breast lesions. Recognition of the cellular elements and the characteristic architecture in combination with immunohistochemistry are essential for correct diagnosis.

E-PS-02-062
PD-L1 status of triple negative breast cancer in Russia
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Background & objectives: The purpose of the study was to evaluate the features of PD-L1 expression in triple negative breast cancer (TNBC) in the Russian population.
Methods: We determined the PD-L1 status of 81 patients with TNBC as part of a scientific study of the RUSSCO. In each case, an immunohistochemical study was performed using Ventana Bench Mark Ultra automatic stainer according to a closed protocol with rabbit monoclonal antibodies Ventana PD-L1 SP142, Opti View DAB IHC Detection Kit with Opti View Amplification Kit.
Results: Positive PD-L1 status was detected in 38.27% of TNBC cases. Almost all tumours had an expression level up to 10%. Only 3.70% of cases showed ligand expression on tumour cells.
Conclusion: According to the results of the experience of testing PD-L1 in TNBC in Russia, we obtained data comparable to those of large international studies. RUSSCO's information and logistic support allows making this analysis available to all citizens of the country.

E-PS-03 Cardiovascular Pathology

E-PS-03-001
Allopurinol and drug induced myocarditis
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Background & objectives: Myocarditis is an inflammatory disease and an important cause of acute heart failure, sudden death, and dilated cardiomyopathy. Viruses account for most cases of myocarditis, but other etiologic agents include drugs, toxic substances, or autoimmune conditions.
Methods: A 49 year-old male presented to the emergency department with fever and limb myalgia. His past history included episodes of microcrystalline pyrophosphate oligoarthritis for which he was receiving allopurinol. Laboratory workup showed neutrophilia and increased CRP. Patient was admitted with fever of unknown origin. Transoesophageal echocardiography revealed a left atrial wall thickening, and a nodular area in right atrial wall.

Results: Histological findings (myocyte necrosis and inflammation) were consistent with the diagnosis of myocarditis in left and right atrium. There were no findings suggestive of neoplasia. The patient was still on allopurinol, which can affect the myocardium in a late (type IV) hypersensitivity reaction, even in the absence of systemic inflammation. Thus, allopurinol was stopped and patient significantly improved his clinical condition. After 1 month, MRI didn't show inflammation.

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a multiorgan hypersensitivity reaction mostly caused by drugs in patients with a genetic predisposition. Polymorphisms in HLA alleles, such as HLA-B*58:01, explain the increased risk for the development of allopurinol-induced DRESS syndrome.

Conclusion: Although allopurinol has ability to induce hypersensibility reactions, myocardium is not the most common site of involvement.

Advances in cardiac non-invasive techniques have been useful in diagnostic setting, but toxic, infectious-inflammatory, infiltrative, or autoimmune processes may need endomyocardial biopsy to establish the right aetiology.

This case highlights the importance of a correlation between endomyocardial biopsy and clinical history, since early diagnosis and prompt discontinuation of the drug is essential.

E-PS-03-002

Fulminant eosinophilic myocarditis

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Background & objectives: Eosinophilic granulomatosis with polyangiitis is one of the most common systemic vasculitides to affect the heart. Cardiac involvement is associated with eosinophilia, and includes myocarditis, coronary vasculitis, myocardial infarction, arrhythmias and sudden death. Definite diagnosis is exclusively established by histology.

Methods: A 22-year-old male presented to the emergency department with chest discomfort. Patient had history of asthma and allergic rhinitis. Laboratory workup showed marked eosinophilia, high levels of LDH, troponin and NT-proBNP. Echocardiogram revealed severe left ventricular systolic dysfunction. Patient had a rapid clinical deterioration, with acute heart failure, respiratory failure and acute kidney injury. It was performed endomyocardial biopsy (EMB).

Results: Histology showed severe myocardial necrosis, myocyte damage and diffuse eosinophilic inflammatory infiltrate. Perivascular spaces had mixed inflammatory infiltrate, with abundant eosinophils.

The diagnosis of eosinophilic granulomatosis with polyangiitis was confirmed, as four out six criteria were present: asthma, eosinophilia >10%, extravascular eosinophils on EMB and paranasal sinusitis (showed by maxillary and ethmoidal sinus opacifications in paranasal sinus CT).

Eosinophilic granulomatosis with polyangiitis, also known as Churg–Strauss syndrome, is a rare systemic necrotizing vasculitis involving small-to-medium-sized vessels, associated with asthma and blood and tissue eosinophilia. According to the American College of Rheumatology, the presence of four or more out of the criteria establishes the diagnosis (sensitivity of 85%; specificity of 99.7%).

Conclusion: Eosinophilic granulomatosis with polyangiitis has an extremely low incidence (0.5 to 6.8 new cases per million patients/ year). Myocarditis is one of the most common cardiac manifestations of the disease, and literature suggests that younger patients have higher risk in its development.

This was a rare case of rapidly progressing vasculitis, presenting with fulminant myocarditis, where EMB had a high diagnostic value for diagnosis and treatment decision.

E-PS-03-003

Autoimmune myocarditis: a case report in relation to MHC class I polypeptide-related sequence A, NKG2D, and CD4+ lymphocytes

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Background & objectives: Autoimmune myocarditis is an uncommon situation that has been associated with different types of stressors. The relationship between the immune system and the myocardiocytes en surrounding endothelium is a topic of great debate.

Methods: H&E stain, Immunohistochemistry (CD68, CD4), and immunofluorescence MHC class-I polypeptide-related sequence A -MICA, NKG2D, dendritic cell, C4, IgG).

Results: We present a case report of a 48 years old male who underwent autoimmune myocarditis that led to a cardiac transplant, dying a month after the surgery. Specific tests were performed to filiate the disease, observing an interesting interaction between myocardiocytes, antigen-presenting cells, and lymphocytes. Immunofluorescence showed MICA expression in dendritic and endothelial cells and its interaction with NKG2D+ CD4+ T cells.

NKG2D ligands are stress-induced proteins, with a restricted tissue distribution in the intestinal epithelium and can be enhanced under stress conditions such as viral/bacterial infections or malignant transformation. In this way, NKG2DLs act as danger signals to activate NK cells and CD8+ T lymphocytes upon NKG2D receptor engagement.

Conclusion: The cross-talk between MICA expressing cells and cytotoxic NKG2D+ T cells could lead to endothelial damage mediated by activation of complement via C4, although the underlying mechanisms are not yet fully understood and need further investigations.

E-PS-03-004

Situs inversus totalis and adult sudden cardiac death

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Background & objectives: Situs Inversus Totalis (SIT) is a rare congenital condition, appearing, in vivo or at autopsy, as an incidental finding or with clinical manifestations. It may include organ malformations, namely cardiovascular. The authors draw attention to this entity in post-mortem settings.

Methods: A retrospective study to 7890 autopsies with anatomopathological examination was performed, searching for SIT cases and their outcomes. The literature was reviewed.

Results: One (n=1, 0.01%) case was found: a 64 year-old male that died sudden and unexpectedly on a road, despite resuscitation manœuvers. Toxicology results were not relevant. Post-mortem external habitus was not noteworthy (apart a thoracic scar). Internal habitus exposed the Situs Inversus Totalis, with cardiomegaly. Macro and microscopic evaluation of the heart and organ samples disclosed Congenitally Corrected Transposition of the Great Arteries (ccTGA) with Atrial Mirror Image. Upon this congenital malformation, valvular degenerative pathology, bi-atrial dilation and bi-ventricular hypertrophy were documented. Patent foramen ovale was present. Atherosclerotic lesions were observed.

Conclusion: Congenitally Corrected Transposition of the Great Arteries (ccTGA) with Atrial Mirror Image is reported in Dextrocardia, Situs Inversus and Situs Inversus Totalis. Sudden and unexpected death may supervene due to rhythm disturbances, valvular pathology, ventricular disfunction and/or heart failure.

E-PS-03-006
Borrelia-associated chronic myocarditis - case report
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Background & objectives: Most myocarditis are caused by viruses. Rare pathogen of myocarditis is Borrelia. Heart damage occurs in 1-10% of all cases borreliosis.
Methods: Case report of endomyocardial biopsy of 62-years-old forester who contacts with acarusis. Patient admitted with terminal symptoms of heart failure. Coronary artery disease wasn't revealed by examination. Obtained samples were stained by hematoxylin and eosin, picrofuxin to Van Gison, silver-stain for reveal of Borrelia and IHC-research.
Results: Lymphocytic infiltrates (more than 14 lymphocytes in the 10 fields of vision), hypertrophy of cardiomyocytes and empty cardiomyocytes were observed in samples stained to hematoxylin and eosin. Diffuse perimuscular and perivascular sclerosis is revealed by picrofuxyn to Van Gison. Positive expression CD3 (more than 14 lymphocytes in 10 fields of vision) and CD45 (more than 7 macrophages in 10 fields of vision) proved active phase of chronic myocarditis. Selective stain by silver confirms Borrelia.
Conclusion: Patient obtained anti-spirochetosis therapy with effect. Our data of morphological research describe chronic myocarditis caused by Borrelia.

E-PS-03-007
Hamartoma on the tricuspid valve in a new-born
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Background & objectives: We describe a hamartoma on the tricuspid valve with unique histologic structure that meets the criteria for true hamartoma. Few cases of a hamartoma on the heart valve have been described, but none of them is parallel to our finding.
Methods: A new-born with atrial septal defect and dysplastic tricuspid valve with a pendant formation flying in the right atrium was indicated for surgery. A canvas-like tissue with fibrous/adipose appearance, bound by fibrous tendrils to annulus of the tricuspid valve was removed.
The surgical specimen was routinely processed and stained with special stains and examined immunohistochemically.
Results: The specimen was composed of finger-like projections made of fibrous, focally myxomatous tissue with presence of elastic fibres and diffuse vascular network. The tissue contained bands of cross-striated muscle arranged longitudinally with the shape of the tissue portion.
Conclusion: Hamartomas, according to classical definition, consist of disorganized tissue that is normally present in the given place. However, the term "hamartoma" is used variably for several benign tumours and tumour-like lesions in the literature.
In our case, the specimen was composed of tissue types that are found in the atrioventricular valves and the myocardium. These characteristics meet the criteria for diagnosis of a true hamartoma on the tricuspid valve.

E-PS-03-009
Mesothelial/monocytic incidental cardiac excrescence (MICE) in a patient with suspected acute rheumatic heart disease: a case report
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Background & objectives: Rheumatic heart disease (RHD) manifests as a pan-carditis resulting from altered immune response to Streptococcal pharyngitis. The acute phase is seldom seen in surgical pathology practice. Mesothelial/monocytic incidental cardiac excrescence (MICE) is a rare benign incidental finding in cardiothoracic surgery.
Methods: We present a case of MICE associated with suspected acute RHD. A 17-year-old male was found to have a pansystolic murmur on pre-enlistment medical examination. Transthoracic echocardiography revealed mitral valve prolapse with severe mitral regurgitation. During surgery for mitral valve replacement, the surgeon reported thickened mitral valve and possible pericarditis. A 2.5cm anterior mediastinal lymph node was also excised.
Results: Microscopic examination showed mitral valve endocarditis. Aggregates of activated macrophages were seen with focal peripheral palisading surrounding central fibrinous areas, reminiscent of the Aschoff nodules. The "mediastinal lymph node" included two small reactive lymph nodes and a loose nodular fragment comprising sheets of histiocytes admixed with rare islands of mesothelial cells. There were also entrapped adipocytes, fibrin and mixed inflammatory infiltrate. The histiocytes were positive for CD68 and CD31, and negative for S100 and CD1a. Diagnosis of MICE and possible acute RHD was made. Retrospectively, the patient admitted that he had two to three days of sore throat before his enlistment check-up.
Conclusion: MICE is believed to be part of the entity "histiocytosis with raisinoid nuclei". A reactive or iatrogenic aetiology has been proposed. About 15% of MICE are associated with RHD. Diagnosis requires close clinico-pathological correlation.

E-PS-03-010
Leiomyosarcoma of the descendent aorta, a case report
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Background & objectives: Leiomyosarcoma (LMS) of the descendent thoracic aorta is extremely rare and described in few reports. The vast majority are diagnosed post-mortem. We report a case of aortic LMS underlining the difficulty of in vivo diagnosis.
Methods: A 75 years old male, presented for precordial pain, dyspnoea, feeling of chest constriction, dysphagia; thorax CT raised a lung cancer suspicion. Positive pathology diagnosis was reached employing a series of minimally invasive procedures. The patient underwent imagistic assays, toracocenthesis and ultrasound guided transthoracic biopsy, followed by histopathological examination through routine staining and immunohistochemistry.
Results: Thoracic CT scan showed a mass abutting descending aorta. As bronchoscopic and pleural fluid cytology were inconclusive, the hypothesis of thrombosed aortic aneurism was put forward but unsubstantiated. Ultrasound guided transthoracic biopsy followed by histopathological exam revealed a highly cellular proliferation containing spindle cells with positivity for caldesmon and SMA and negativity for desmin, p63, TTF1, S100, CD34, MDM2, EMA, CK7 and CK cocktail, supporting a diagnosis of aortic LMS. Proliferation factor was positive in 30-40% of the tumour cells. Patient was referred to oncology services, declined specific therapy and survived 2 months after diagnosis.
Conclusion: Imagistic approaches are usually not enough to establish a clear diagnosis of aortic LMS. Minimally invasive bioptic approaches have a good safety profile and adequate efficacy, still cytological examination may not always reach diagnosis despite the advanced stage of tumour.

E-PS-03-011
Cardiac sarcoidosis or arrhythmogenic right ventricular cardiomyopathy?: a diagnostic challenge
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Background & objectives: Arrhythmogenic cardiomyopathy (AC) and cardiac sarcoid can be identified in explanted heart specimens. Both are

morphologically and histopathologically distinct but studies have shown histological overlap between so-called "burnt-out" sarcoid and AC. This case highlights the diagnostic challenge for the histopathologist.
Methods: A middle-aged male with no past medical history, presented with syncope and complete atrioventricular block and underwent dual-chamber pacemaker insertion. Imaging showed biventricular dilatation, late gadolinium enhancement and possible FDG avidity within hilar lymph nodes. However, the study quality was poor. Despite immunosuppression therapy for suspected sarcoid, the patient rapidly deteriorated into severe biventricular failure, necessitating cardiac transplantation.
Results: Macroscopic examination of the explanted heart showed right ventricular wall atrophy and fibrofatty replacement. The left ventricle was largely normal.
Microscopy showed extensive fibrosis and fatty replacement of the myocardium in the right ventricle, with extension into the posterior left ventricle, with focal areas of lymphocytic inflammation but the inflammatory cells did not appear to be associated with myocyte damage. There was a single giant cell present but no well-formed granulomas were identified.
Conclusion: The distribution of fibrofatty replacement without granulomas suggests AC. Genetic confirmation is awaited. Following cardiac transplantation the patient shows no evidence of recurrent sarcoidosis. Histological features of cardiac sarcoid can mimic AC, thus posing a diagnostic difficulty for histopathologists.

E-PS-03-012
Investigation of the presence of neutrophils and macrophages in the tissues of calcified aorta affected by atherosclerosis
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Background & objectives: The presence of aortic calcification causes severe tissue overstretching. Neutrophils and macrophages promote experimental abdominal aortic aneurysm formation.
Aim: to compare the number of neutrophils and macrophages in the tissue of the atherosclerotic aorta with calcification and without it.
Methods: We examined 30 samples of aorta with calcification (group I) and 10 samples of aorta wall tissue without biomineralization (group II), which were considered as control group. All samples were examined by histology and immunohistochemistry. Samples were fixed, embedded in paraffin and analysed for neutrophils and macrophages accumulation with anti-MPO and anti-CD68 antibodies.
Results: MPO expression was increased in aortic tissues with calcifications (42.08±2.85 cells per 1 mm2) in comparison to those without them (33.3±2.23, $p<0.05$, Student's t-test). Both groups I and II had 48.31 ± 3.53 and 32.1 ± 2.69 macrophages per 1 mm2 respectively ($p<0.01$).
Conclusion: Thus, calcified aortic tissue has a higher number of neutrophils and macrophages, which may affect the risk of aortic wall rupture.

E-PS-03-014
What histologic differences exists between primary or secondary dilative cardiomyopathy?
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Background & objectives: Dilative cardiomyopathy (DCM) represents a myocardial structural disorders associated with mechanical dysfunctions and rhythm disturbances that causes enlargement of both ventricles. More than 50% of primary DCM are familial diseases and identifying those forms is essential for discovering asymptomatic patients.
Methods: We included in our study 353 dead patients with DCM for a period of 3 years. We eliminated all secondary known cases of DCM. At autopsy, the heart was measured and trimmed by four-chamber view or short axis (bread loafing) slicing technique. Histology assessments were made using paraffin embedding and slides were stained routinely and with special enzymes.
Results: Primary DCM was suspected in 55 patients and those family members were advised to have regular cardiologic examinations and genetic assays. At autopsy, patient's heart with DCM has an increased weight with globular shape and decreased tonus. In endocardium fibrous thickening starts mainly in the septum of left ventricle affecting trabecular muscles. Histology revealed different degrees of myocyte enlargement, "box-car" nuclei and protruding collagenous fibres arranged diffuse or perivascular. Majority of myocytes exhibit degenerative brown pigment (lipofuscin) and in interstitial space we found moderate cellularity represented by fibroblasts, fibrocytes and lymphocytes. Comparing slides form patients with primary and secondary DCM there were insufficient data useful for distinguish these two entities.
Conclusion: Primary DCM is proposed to be included in "cytoskeletopathies" and without cardio-pulmonary transplant, these patients have an ominous prognosis with reduced 5-year survival rate. A good correlation was found between clinical or functional status and the extent of microscopic lesions (expressed mainly by interstitial fibrosis). An early detection of DCM and proper treatment can improve quality of life in these patients. Histology alone is not useful for differential diagnosis.

E-PS-04 Cytopathology

E-PS-04-001
Diagnostic accuracy of rapid onsite evaluation of retroperitoneal masses
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Background & objectives: Various mass lesions can arise in retroperitoneum. ROSE determines adequacy of material obtained for cytological analysis on site and can provide insight into the nature of mass. Aim of this study is to determine diagnostic accuracy of ROSE of retroperitoneal masses.
Methods: A cross sectional study was conducted in King Edward Medical University/ Mayo Hospital, Lahore, Pakistan. 77 patients with retroperitoneal masses were subjected to ROSE and histopathology of radiologically guided biopsy. Adequacy of cellularity of material obtained for cytology was analysed and reported by pathologist in the radiology suite. Keeping histopathological diagnoses as gold standard, diagnostic accuracy of ROSE was established.
Results: Overall diagnostic accuracy of rapid onsite evaluation technique was found to be 75 % in our setup. Majority of lesions were positive for malignant cells and most of these were of lymphoid origin. Remaining cases were benign and of variable morphology.
Conclusion: ROSE of retroperitoneal masses will help in improving the adequacy rate, diagnostic yield and accuracy of procedure thus saving time and resources of both patients and physicians. A preliminary diagnosis made on the basis of ROSE may help physicians.

E-PS-04-002
Positive peritoneal cytology in endometrial cancer: report of a case presenting with ascites
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Background & objectives: Endometrial cancer (EC) is the most common gynaecologic malignancy. Patients' symptoms may vary from

abnormal uterine bleeding to abdominal pain or change in bowel/ bladder function in advanced stages.
Methods: Ascites is a rare initial presentation and, to the best of our knowledge, only a few isolated cases have been reported in the literature. Our patient, a 70-year-old woman, presented with ascites. MRI examination revealed a mass in uterine cavity and numerous omental implants. Fine needle aspiration of peritoneal fluid and endometrial biopsy with a Pipelle aspiration catheter were performed.
Results: Peritoneal smears showed the presence of neoplastic cells with cytological and immunocytochemical (CK7+, ER+, Vimentin+, CEA-) features consistent with metastatic endometrial carcinoma.
Histological evaluation of the tissue samples revealed high grade serous endometrial carcinoma. In the differential diagnosis, carcinosarcoma should be included because of areas with solid/diffuse patterns.
Our patient received chemotherapy and remains alive, 6 months after initial diagnosis.
Positive peritoneal cytology (PPC) is associated with EC characterized by deep myometrial invasion, cervical stromal invasion, large tumour size, non-endometrioid histologic type, and lymphatic metastasis. Moreover, the incidence of PPC in patients with early stage EC has been reported to range from 5% - 10%.
Conclusion: PPC constitutes a controversial issue in EC in terms of its prognostic value. Although the International Federation of Gynaecology and Obstetrics (FIGO) removed the presence of PPC from the staging criteria in 2009, compared to FIGO 1988, PPC has to be reported separately.

E-PS-04-003
Cytological and immunocytological features of solid-pseudopapillary neoplasm: a series of cases
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Background & objectives: Solid-pseudopapillary neoplasm (SPN) is a low-grade malignancy primary pancreatic epithelial neoplasm accounting for 1% of all exocrine pancreatic tumours. SPN occurs predominantly in young women and occasionally in men. Cytological diagnosis is crucial for patient management.
Methods: We reviewed all cytological cases obtained by ecoendoscopy in a referral centre between 2009 and 2020. Smears were studied with Papanicolaou and Diff-Quick stains. Immunocytochemistry for CD10, synaptophysin, Cyclin-D1 and beta-catenin was performed on Papanicolaou or cell blocks. In one case histological material was available.
Results: Four cases of SPN with cytological material were found, 3 males and 1 female from 27 to 84 years-old. Characteristically, smears usually were highly cellular. Cells were uniform with round to oval nuclei, dispersed or granular chromatin and small indistinct nucleoli. Nuclear grooves were frequently found and cytoplasm size ranged from scant to moderate. Neoplastic cells were arranged singly, in cohesive clusters or branching papillary structures. Fibrovascular core stroma appeared myxoid and metachromatic. Hyaline globules were occasionally present. Inmunocytochemical studies showed positive stain for neuroendocrine markers (synaptophysin or cromogranin), oestrogen receptor (in female patients), CD10 and beta-catenin. Differential diagnosis were established with neuroendocrine tumours and acinar cell carcinoma.
Conclusion: Cytology and immunocytochemistry are essential to SPN diagnosis. Beta-catenin is one of the most reliable marker in the diagnosis of this entity. Although SPN usually affects female patients, our series showed a male preponderance.

E-PS-04-004
Mucinous breast lesions: fine needle aspiration diagnosis and pitfalls
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Background & objectives: Mucinous breast lesions (MBL) are uncommon and range from benign to malignant conditions. Fine needle aspiration (FNA) is one of the techniques for evaluating breast masses. This study aims to correlate between cytologic and histologic findings in mucinous spectrum.
Methods: A search for mucin, mucocele-like lesion (MLL), and mucinous carcinoma (MC) from Chiang Mai University Hospital cytologic electronical database between 2017-2019 was performed. All cytologic slides were reviewed to determine cytomorphological characteristics that specific for benign or malignant MBL, including background, cellularity, arrangements, and nuclear with cytoplasmic details.
Results: 16 FNA diagnoses from females aged 34-84 years were 2 (12.5%) proliferative lesions with atypia (PLA), and 14 (87.5%) malignancy. Correlation with histology, two PLA were 1 fibroadenoma with myxoid stroma (FAM) and 1 MC. 14 malignant cases were 9 (64.3%) MC, 2 (14.3%) mixed MC and invasive ductal carcinoma (IDC), NOS, and 1 (7.1%) for each ductal carcinoma in situ with mucin content, MLL, and metastatic lung adenocarcinoma. Our study showed MC can be accurately diagnosed. However, the cytologic findings cannot entirely distinguish between benign and malignant tumours. Benign lesions, particularly FAM and MLL, can be missed diagnosed as MC. IDC, NOS and metastatic adenocarcinoma can mimic breast MC.
Conclusion: FNA is useful to detect MBL. Awareness for the possible differential diagnoses, correlation with clinical and radiologic findings as well as history of other primary cancer are crucial for accurate diagnosis.

E-PS-04-005
Potential misdiagnosis of reactive mesothelium as metastatic carcinoma based on Ber-EP4 staining
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Background & objectives: The distinction between reactive mesothelium and carcinoma in serous effusions can be difficult. Immunocytochemistry (ICC) is widely used to improve body fluid cytology accuracy, and several markers have been proposed. Ber-EP4 has shown high sensitivity and specificity in previous studies.
Methods: We here report two cases of pericardial effusions misdiagnosed as metastatic carcinoma, based on Ber-EP4 staining. Pericardial fluid was processed by centrifugation and ICC markers were performed. In the second case, a pericardial biopsy was also obtained and immunostained. Literature was reviewed and all studies describing Ber-EP4 staining in cytological samples have been summarized.
Results: Our first case was a 41 year old man who consulted on thoracic pain. Imaging studies showed a large pericardial effusion. Cytology revealed atypical tridimensional groups. Ber-EP4 showed strong membranous staining, and it stained most cells of several cell groups (40%). A pericardial biopsy was performed and also showed patchy intense membranous Ber-EP4 positivity in 40-50% of mesothelial cells. The second case was a 82 year old man with history of ischemic cardiomyopathy who consulted on abdominal pain. Pericardial fluid showed tridimensional cell clusters. Ber-EP4 strongly stained most cell groups, and percentage of cells stained varied between groups (10-100%). Both patients were evaluated (PET-CT, endoscopy) and no malignancy was found.

Conclusion: Most cases of Ber-EP4 positivity in mesothelium show weak/patchy staining, but intense staining may be seen both in cytological and histological specimens. ICC should always be interpreted cautiously and correlated with clinical tests, other ICC markers and patient's previous history.

E-PS-04-006

Melanoma and breast cancer metastases in our cytopathology teaching collection: comparing tasks and tools from a quarter century ago with today

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Background & objectives: To compare the possibilities and impacts of diagnosis of metastases of two aggressive malignancies a quarter of a century ago and now.
Methods: A Cytological educational collection has been built up with histological correlates of more than 450 cases over 25 years. Metastases are included for their differential diagnostic difficulty.
Results: Three selected cases from the beginning of the collection had limited possibilities of confirmation of the primary at the cytological level using special methods. Comparative morphology was the most powerful tool. It does not lose its role at present, but the use of immunocytochemical procedures has become the rule and accurate confirmation has become the primary goal. In the recent cases, more frequently a positive tumour history in a longer time interval was observed.
Conclusion: The exact diagnosis of melanoma and breast cancer metastases in today's cytodiagnostic practice differs by:
- A real chance to influence the treatment process.
- Diagnostic procedures and detection reagents have progressed.
- Current therapeutic possibilities justify increased demands on accurate diagnostics.

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E-PS-04-009

The prevalence and distribution trends of cervical abnormalities on Pap test according to the Bethesda system 2014: a study from Pakistan

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Background & objectives: To evaluate the trends and distribution of cervical pathologies based on
Papanicolaou (Pap) smear results, in a local population in Pakistan, reclassified
according to The Bethesda System 2014(TBS).
Methods: A retrospective analysis of Pap smear (PS) test reports received in the Histopathology Department of Foundation University Islamabad (FUI) was done from January, 2011 to December, 2015 and they were reviewed according to The Bethesda 2014.The abnormalities were also correlated according to age distribution.
Results: Of the 2272 cases reviewed in women aged between 20-80 years, 32 showed epithelial cell abnormalities which constituted 1.40% of the total smears screened. Negative for intraepithelial lesion or malignancy (NILM), Atypical squamous cells of undetermined significance (ASC-US), Low-grade squamous intraepithelial lesion (LSIL), High-grade squamous intraepithelial lesion (HSIL) and Squamous cell carcinoma(SCC)were detected in 98.6%, 0.35%, 0.52%, 0.35% and 0.17% of the Pap smears respectively. The rate of positive specimens increased from 0.47%in 2011, to 1.23%in 2012, 1.71% in 2013, 2.01% in 2014, and 1.01% in 2015.In our study, 69.1% of the epithelial abnormalities were in the age group 60 and above.
Conclusion: This study highlights the need for implementation of an education and awareness program regarding the risk factors and possible preventive measures for cervical cancer

E-PS-04-010

Metastatic breast cancer to the parotid gland - a case report

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Background & objectives: We present a case of metastasis to the parotid gland, in a 76-year old female patient, with a history of breast ductal carcinoma, who was admitted to our hospital to investigate a painful, hard mass in her right parotid region.
Methods: Fine needle aspiration of the mass and examination of Smears and thin prep slides.
Results: In the smears, multiple large malignant cells were seen, isolated and in loose groups, with large hyperchromatic nuclei, conspicuous nucleoli and sparse cytoplasm.
The tumour cells were ER(+), PR(+), Ca 15/3(+), e-cadherin(+) and Her2(+2). The Ki76 index was low.
In combination with the patients history, the final diagnosis was metastatic ductal carcinoma.
The cytological diagnosis was later confirmed with a biopsy and the patient was treated with hormone therapy.
Conclusion: Metastatic ductal carcinoma to the parotid gland is rather unusual, with only 24 cases reported in the literature. Further research is required as to this day, there is no optimal protocol for treating a breast metastasis to the parotid and the prognosis is generally low.

E-PS-04-011

Total cell count in cerebrospinal fluid Giemsa staining cytological specimen by computer-assisted image analysis

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Background & objectives: We counted total cell number in cerebrospinal fluid (CSF) Giemsa staining (Giemsa) stained cytological specimens by computer-assisted image analysis (CAIA).
Methods: We analysed total 35 cases including clinically and cytologically negative (Negative), non-haematological tumour cytologically positive (Non-HT positive), and haematological tumour cytologically positive (HT positive); 10, 12, and 13 cases, collected in Gunma University hospital from 2001 to 2011. Whole area of specimens was captured by virtual slide scanner, analysed total cells by CAIA. P-values < 0.05 were considered statistically significant.
Results: The average of total cell number of Negative, Non-HT positive, HT positive group were 25165±46563、15477±26778、53978±106176 respectively. There was no significant difference in total cell number between Negative and Non-HT positive group (p=0.5887). HT positive group tended to have many cells compared with Negative group (p=0.1069), and HT positive had significantly more total cell number than Non-HT positive group (p=0.0167). Our results suggested that cell number on the specimens was increased in haematological tumour cases. While, in Non-haematological tumour cases, the cell number did not increase in comparison to Non-tumour cases.
Conclusion: When screening CSF cytological specimens, increased cell number would indicate existence of haematological tumour cells. However, in non-haematological tumour cases, it is important not to miss atypical cells because cell number does not change.

E-PS-04-012

Pericardial effusions: a one-year single institution analysis with reclassification according to the new international system for reporting serous fluid cytopathology

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Background & objectives: Our study aimed to compare our spectrum of samples with the data in the literature, correlate it to the clinical history, and apply the new International System for Reporting Serous Fluid Cytopathology.
Methods: The pericardial fluid (PF) specimens of a one year period (2018) were retrieved. Clinical history and cytological diagnosis were recorded. All specimens were re-classified according to the new International System for Reporting Serous Fluid Cytopathology.
Results: 87 PF specimens were obtained from 70 patients (36 males and 34 females). Of these, one (1,1%) was Non-diagnostic (ND), 62 (71,2%) were categorized as Negative for Malignancy (NFM), and 24 (27,6%) were classified as Malignant (MAL). The benign PF specimens were most frequently related to malignancy (18/29%), followed by unknown/unclear cause (15/24,2%), infection (9/14,5%), cardiac disorder (9/14,5%), rheumatic disease (6/9,7%), and other (5/8%). In males, the most common tumour producing malignant PF was lung carcinoma (7/11); other malignancies were rare (oesophageal, bladder, AML, Adenocarcinoma NOS). In women, the leading neoplasm was breast cancer (7/13), followed by lung carcinoma (3/13). Single cases revealed ovarian cancer, plasmablastic lymphoma, and neuroendocrine carcinoma.
Conclusion: Our findings are well comparable with the results of previous studies. Most benign pericardial effusions are related to malignancy (29%). The vast majority of PFs can be related to clinical history or a specific disease (75,8%). By far, metastatic carcinoma was the most common cause of malignant PF (22/24; 91,7%) with the top differential diagnoses of lung and breast carcinoma. However, malignant mesothelioma involving the pericardium was not present.

E-PS-04-014

International telecytology diagnosis using whole slide images (WSI)

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Background & objectives: Cytology specimens are difficult to apply for digital pathology. Our university opened a Japan-style health check facility in Ho-Chi-Minh city in 2018 and asked to make telecytology diagnosis for uterine cervical specimens.
Methods: We use NanoZoomer S210 as WSI scanner. We used Liqui-PREP LBC system for preparation. Slides were scanned by 40x mode with 3 layer Z-stack with 2 μm thickness. Vietnamese pathologists who learned Japanese style cytology diagnosis in Mita hospital make primary diagnosis using conventional microscope in Vietnam, then we observe WSI images and make secondary telecytology diagnosis from Japan.
Results: The Papanicolaou staining showed different colour between Japan and Vietnam. We need to condition our eyes to the Vietnamese colour. Until the end of December 2019, almost 14 months, we performed 600 tele cytology diagnosis. The WSI quality and the concordance rate of diagnosis was fairly good between Vietnamese and Japanese pathologists. The ratio of NILM in cervical cytology was about 98% which is almost similar to Japan.
Conclusion: Good LBC preparation, 40x mode scanning, and good staining are essential for digital cytology.

E-PS-04-015

EUS-FNA of pancreas: an initial 3-year Malaysian study in private laboratory

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Background & objectives: Endoscopic ultrasound (EUS)-guided fine-needle aspiration (FNA) is being increasingly used in the diagnosis and management of pancreatic mass. Gastroenterologists in Malaysia have been increasingly using EUS FNA, owing to its increasing precision, and relative safety of the procedure.
Methods: This is a cross sectional study conducted on clinical and cytological characteristics on all the EUS-FNA cytology samples of pancreas received in Clinipath Laboratory from 2017 to 2019. Data collected included patient demographics (gender, age and mass lesion location) and tumour characteristics. 679 cases of EUS-FNA were received and reported as per the new guidelines of Papanicolaou Society of Cytopathology.
Results: Pancreatic adenocarcinoma ranging from well-differentiated to poorly differentiated was confirmed in 506 cases. Mucinous cystic neoplasms, neuroendocrine tumours, lymphomas, spindle cell tumours and small blue round cell tumours constituted 36 cases. Benign lesions and chronic pancreatitis were 62 in number. The rest of the samples showed pauci-cellularity or complete absence of epithelial cells to arrive at any conclusion. In very occasional cases, atypical cells that were suspicious of an underlying malignancy but not affirmative were also reported. Correlation with clinical picture and CT scan findings were undertaken in all cases.
Conclusion: EUS-FNA is emerging to be the most useful technology in the diagnosis of pancreatic lesions In Malaysia. The precision of the procedure and accuracy of the results of EUS-FNA samples have dramatically increased over the past few years. This initial study carried out for the first time in Malaysia is to document the increasing diagnostic capability of EUS-FNA in the management of pancreatic lesions in a private set up.

E-PS-04-019

Basal cell adenoma of parotid: a cytological diagnosis confirmed by histology

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Background & objectives: Basal cell adenomas of the parotid are benign tumours resembling pleomorphic adenoma , accounting approximately 2% of epithelial tumours of salivary glands, affecting usually adults, mostly females, being more common in the mid- to late sixth decade of life.
Methods: We report a 46-year old male patient with a tumour of the right parotid, who underwent Fine Needle Aspiration (FNA) and subsequently surgical resection of the tumour. The FNA specimen was sent to our Department of Cytology, where it was stained using conventional (Papanicolaou) and liquid-based methods. The surgical specimen was sent to out Department of Pathology for histological examination.
Results: The cytological examination revealed aggregates, sheets or syncytial fragments of uniform oval epithelial cells with ill defined cytoplasm, round-to-oval nuclei, surrounded by a bright hyaline bands. The diagnosis of a basal cell adenoma was set and surgical resection of the tumour followed. Multiple sections from the tumour for histology confirmed the cytological diagnosis, revealing a well-circumscribed, encapsulated tumour presenting solid, trabecular, tubular and membranous architecture, composed of cells with two cell morphologies: Basaloid cells with peripheral palisading, positive for Vimentin and Actin and larger central (ductal) cells from the bulk of the nodules, angular in shape with

more cytoplasm and pale round nuclei, positive for cytokeratin and S100a.
Conclusion: Basal cell adenomas of the salivary glands have a low recurrence rate and they rarely demonstrate malignant transformation. FNA is usually followed by surgery, in order to assure the complete resection and to minimize the chances for recurrence.

E-PS-04-020
Outcome of thyroid nodules diagnosed as atypia or follicular lesion of undetermined significance: a 10-year single institutional experience
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Background & objectives: Determine the outcomes of patients seen at a single university based-institution who were initially diagnosed with AUS/FLUS as to the rate of malignancy, management protocol, result of repeat cytology, and final histopathologic diagnoses.
Methods: This is a retrospective correlation study includes patients who has at least one FNA diagnosed as AUS/FLUS, and with follow up data such as repeat FNA or surgery. The rate of malignancy after surgery, correlation with age and sex after initial diagnosis of AUS/FLUS were identified. Data are tabulated using Microsoft Excel® and analysed using SPSS® (Chicago, IL, USA).
Results: Most of the patients underwent immediate surgery after initial FNAB diagnosis of AUS/FLUS compared to repeat FNAB recommended by The Bethesda System (TBS). Majority of the lesions are benign; the calculated malignancy rate was between 33.33% to 37.29% which was higher compared to TBS's 10% to 15%. Papillary thyroid carcinoma was the most common malignancy, while adenomatous colloid goiter was the most common benign lesion. There was no significant association between age and gender, with the risk of having a benign or malignant pathology.
Conclusion: AUS/FLUS is associated with higher risk of malignancy. Recommendation of TBS of repeat aspiration after initial diagnosis of AUS/FLUS should be reconsidered. Further refinement of this category and its associated clinical outcomes is desired to establish appropriate case-based management.

E-PS-04-021
Ultrasound guided fine needle aspiration biopsy of superficial lymph nodes performed by pathologist
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Background & objectives: Ultrasound plays a prominent role in the diagnosis of lymphadenopathies due to its versatility, low cost, and absence of side effects. Properly trained interventional pathologists perform ultrasound-guided FNA biopsy procedures with a methodology which has proven to be very efficient.
Methods: For two years, the cases of ultrasound guided FNA biopsy of superficial lymph nodes performed by a pathologist were counted in our institutions. In situ microscopic assessment was done in all the cases. The following variables were taken into account: clinical data, lymph node characteristics, number of passes, need for ancillary techniques and cytological diagnosis.
Results: There were 363 cases. 96.42% were representative samples. Only one pass was necessary in 40% of cases, and on average less than 2 passes were performed. Overall, insufficient samples represented 3.58%, and specifically 8.18% in lymph nodes smaller than 11mm in diameter (n=110), and 1.57% in lymph nodes larger than 10mm (n=253). Of the 13 insufficient samples, the average lymph node size was 9.9mm.
Conclusion: During ultrasound guided FNA biopsy of superficial lymph nodes, real-time decision making is determined by rapid on site evaluation. Determining the minimum number of passes required to reach diagnosis (and reducing time and cost) is only possible when it is immediately assessed for adequacy.
In Spain, ultrasound guided FNA biopsy performed by pathologists has been well established in two hospital centre for 5 years.

E-PS-04-022
Cytology of inflammatory myofibroblastic tumour of the lung: a case report
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Background & objectives: Inflammatory myofibroblastic tumour (IMT) of the lung is a rare condition that may mimic cancer. In adults, it occurs in less than 1 % of all lung tumours(WHO 2015). To date there have been few reports on cytology of IMT of the lung.
Methods: Here we report the case of an asymptomatic 30-year-old man who presented an abnormal shadow in his left lung at his annual health check in his institution.
Results: CT scan of the chest demonstrated an intrabronchial mass in the left B3 bronchus. A bronchoscopy for airway inspection found an endobronchial tumour obstructing the left B3 bronchus. A transbronchial biopsy(TBB) and brush cytology with bronchial washing were performed. Cytology disclosed abundant spindle-shaped atypical cells seen in various-sized clusters and singly intermixed with prominent mature plasma cells and lymphocytes. Histology of the TBB specimen by immunohistochemistry suggested IMT. Segmentectomy(upper segment of left upper lobe) specimen with immunohistochemistry and FISH examination of ALK gene rearrangement confirmed IMT, namely a mesenchymal tumour with spindle cells(myofibroblastic nature) and abundant inflammatory cells.
Conclusion: The cytologic diagnosis of pulmonary IMT is challenging due to its rarity. However highly cellular cytological specimens with myofibroblastic spindle cells, plasma cells and lymphocytes could be a clue for differential diagnosis of IMT.

E-PS-04-023
Cyto-histological analysis of salivary gland tumours in central Kazakhstan
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Background & objectives: Salivary gland tumours make up 4% to 25% of all human body tumours. The choice of treatment tactics for salivary gland tumours depends on the histology of the biopsies, which is why the study of their pathomorphology is relevant.
Methods: The purpose of the study is to study the cyto-histological characteristics of common tumours of the salivary glands in the Central Kazakhstan.64 preparations with salivary gland tumours were studied. Cytological (Romanovsky-Gimza staining) and histological studies (hematoxylin-eosin staining) were performed to verify the tumours.
Results: During the verification of preparations, red blood cells, single white blood cells, flat epithelium without atypia were found in 16 cases, which indicates that the process is benign, in 10-proliferating cubic epithelium, in 6 – polymorphic adenoma, in 3 – cylindroma, in 1 – lymphosarcoma. In malignant tumours-in 8 cases, a picture of carcinoma was found, in 8 – red blood cells, proliferating cubic epithelium, in 6-cylindroma, in 6 – adenocarcinoma. Histological analysis revealed the

presence of pleomorphic adenoma in 31 cases, monomorphic adenoma in 4,and adenolymphoma only in 1case. In malignant variants of both the cylindroma and the adenocarcinoma were identified in 12 cases.
Conclusion: Benign tumours of the salivary glands are more often represented by polymorphic adenoma. In malignant tumours of the salivary glands, the predominant tumours are cylindroma and adenocarcinoma, morphologically, the tumours are similar.

E-PS-05 Dermatopathology

E-PS-05-001
Chondroid syringoma with extensive mature bone and cartilage formation: a case report and review of the literature
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Background & objectives: Chondroid syringoma is a rare, skin adnexal tumour, mostly involves the head and neck region. It is usually present as a skin painless nodule. We present a rare case of chondroid syringoma with extensive mature bone and cartilage formation.
Methods: Chondroid syringoma is a rare, skin adnexal tumour, mostly involves the head and neck region. It is usually present as a skin painless nodule. The histopathological are usually composed of variable mixture of epithelial and myoepithelial structures on a background of chondromyxoid and fibrous stroma. It rarely shows mature bone or cartilage formation.
Results: To the best of our knowledge, only several cases of chondroid syringoma with bone formation and few cases of chondroid syringoma with cartilage formation have been reported in published studies up to date. Here, we report a case of chondroid syringoma with extensive mature bone and cartilage formation which is probably the first reported case showing this mixture of appearances.
Conclusion: Histopathologically, the presence of tumour with extensive mature bone and cartilage formation may cause diagnostic difficulties and wide differential diagnosis. Therefore, awareness of this rare entity can be helpful to avoid future diagnostic pitfalls, particularly when the appearances are unusual.

E-PS-05-002
Primary cutaneous amyloidoma: a case report
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Background & objectives: Amyloidoma is defined as solitary, localized, tumour-like deposit of amyloid in any organs without systemic amyloidosis.
Methods: Here we report the case of a 66 year old female patient with a tumoral mass located on the left upper lip with ulcerated. The mass measuring 1×1 cm had grown in size over the past 2 years.
Results: Histologic examination revealed dense amorphous material stained with Congo red and Cristal violet in whole dermis. The amyloid type was determined immunohistochemically as ALκ amyloid. Systemic amyloidosis was not detected on systemic examination. The mass was removed surgically, recurrence have not been found.
Conclusion: Although amyloidoma has been reported in many different anatomic regions such as respiratory, genitourinary and gastrointestinal tracts, nervous system, breast and soft tissue, the skin involvement is a very rare condition, and only a few cases have been described in the literature so far.
So we reported our case with solitary, cutaneous amyloidoma, because of rarity.

E-PS-05-003
Cutaneous lymphadenoma: a case report of a rare entity
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Background & objectives: We report a case of cutaneous lymphadenoma in the left pre-auricular region of a 35 year old man. Although a rare entity, cutaneous lymphadenoma is recognised as a benign lesion and surgical excision is curative.
Methods: A nodule measuring 6x6x4mm was excised from the preauricular region of a 35 year old man with no significant medical history. Microscopic examination reveals within the dermis an epithelial tumour composed of sheets and nests of loosely cohesive epithelioid cells, without retraction artefact, surrounded by a single layer of small basaloid cells. Admixed with the epithelial cells are numerous bland lymphocytes.
Results: The immunohistochemistry panel performed shows that the epithelial cells exhibit strong diffuse expression of Cytokeratin(AE1/AE3), CK5/6 and bcl-2, and the majority of cells express p63.BerEP4 highlights the epithelial cells at the periphery of the nests and sheets. Only a minority of cells express EMA and CEA is negative. Interspersed there are S100 protein positive intralobular dendritic cells. The presence of small bland lymphocytes infiltrating the epithelial component is confirmed by LCA immunoexpression.
Conclusion: Cutaneous lymphadenoma is a rare neoplasm with 56 cases reported in the English literature as at 2014.It usually presents as a slow-growing nodule, most commonly on the head and it is clinically mistaken for dermatofibroma, sebaceous hyperplasia or basal cell carcinoma. Cutaneous lymphadenoma may be readily misdiagnosed due to its resemblance to the more common basal cell carcinoma. Although a rare entity, an accurate diagnosis can be achieved on close examination of morphologic features and hence ensure appropriate surgical treatment.

E-PS-05-004
Don't forget about perianal hidradenoma papilliferum!
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Background & objectives: Hidradenoma papilliferum (HP) is a rare benign tumour of the apocrine sweat glands. It occurs mostly in women, being more frequent in the vulvar area and uncommon in the perianal region.
Methods: We describe a case of HP from a 37-year-old woman who presented to the Surgery Department with a progressively increased perianal nodule, accompanied by small bleeding after bowel movement. She has first noticed the lesion approximately 3 months before. Her past history was unremarkable and she denied any other symptoms.
Results: Examination of the perianal region revealed a well-defined, erythematous nodule, measuring 7x6 mm and being localized within the right posterolateral quadrant of the anal margin. The tumour was excised with 3 mm surgical margin.
Gross examination showed a nodular, skin-covered lesion measuring 7 mm in diameter, with grey-white cut surface. Histological analysis revealed tubular and cystic structures along with papillary folds, lined by a dual population of columnar to cuboidal cells with apocrine differentiation and pale nuclei. Tumour exhibit reduced fibrous stroma with scanty plasmocytes. The pathologic diagnosis was hidradenoma papilliferum.
No postoperative complications were observed. The patient recovered well and showed no evidence of recurrence after 24 months follow-up.
Conclusion: Becoming aware of the existence of HP is essential for differential diagnosis of ano-genital lesions. Even though it is hard to diagnose, HP seems to have a favourable prognosis and preferred treatment option is surgical excision.

E-PS-05-005

DRESS syndrome that resembles graft versus host reaction after chemotherapy in a paediatric patient: a case report

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Background & objectives: DRESS syndrome is a potentially life threating adverse drug-induced reaction that can mimic other diseases. The aim of this article is to describe a case of DRESS syndrome associated with chemotherapy, whose histopathological presentation was similar to graft-versus-host-disease.
Methods: We present the case of a 4-year-old male patient who started chemotherapy with Vincristine, Cytarabine and Etoposide. The first clinical signs consisted in fever, hemodynamic instability and itchy erythema on the inner thigh with irregular plaques. Those lesions began to affect the whole body surface. He also presented non-blanchable violaceous macules and papules, which did not involve the oral mucosa.
Results: Biopsies of skin lesions were taken and hyperkeratosis, local parakeratosis, acanthosis with slight spongiosis and intraepithelial dyskeratotic cells were observed. There was perivascular lymphoid infiltrate with abundant eosinophils in the dermis. Additionally, permeation of the eosinophils to the acrosyringium and the epithelium were found.
Conclusion: DRESS syndrome is a drug-induced reaction that share histopathological findings in skin to those seen in graft-versus-host-disease. The key to differentiate between these two diseases is by observation of the least amount of apoptosis and the greater amount of eosinophils presented, that guide the diagnosis towards DRESS syndrome. Despite the histological findings are not pathognomonic they were characteristic enough to be of importance in differential diagnosis.

E-PS-05-006

Severe psoriasis associated with advanced liver fibrosis: a case report

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Background & objectives: Psoriasis is a chronic inflammatory skin disease and a risk factor for development of metabolic syndrome and related comorbidities such as hepatic failure. The aim of this article is to describe a case of cirrhosis that was associated with psoriasis.
Methods: We present the case of a 62-years-old female patient with medical history of obesity and liver cirrhosis secondary to non-alcoholic steatohepatitis. The first clinical signs were the appearance of erythematous plaques in the trunk and the scalp, which soon developed crusts. Those lesions were not painful or itchy. For its study, biopsies of the skin were taken
Results: The histopathologic study showed marked hyperkeratosis and parakeratosis of the epidermis associated to foci of mononuclear cell infiltration as well as neutrophils forming Munro's microabscesses. Besides, there were psoriasiform hyperplasia of the epithelium with telangiectasias in the dermal papillae and slight perivascular lymphoid infiltrate. Because of these findings, diagnosis of psoriasis was made.
Conclusion: Patients with psoriasis are at high risk of developing hepatic disease. Previous studies have shown that proinflammatory cytokines via interleukin 17 signalling can led to advanced liver fibrosis.

E-PS-05-007

Giant verrucous carcinoma of the lower extremity in a sub-Saharan

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Background & objectives: Verrucous carcinoma is an unusual variant of well-differentiated verrucous carcinoma, with slow-growing but locally invasive. Most of them are non painful exophytic white plaques in the oral cavity of middle-aged men. Its presentation in extremities is rare.
Methods: 53 years old Sub-Saharan male with ulcerovegetating lesion of 13 years of evolution located in the anterolateral region of left ankle and foot. In 2014, Primary Care suspected a vascular origin, advising sporadic local cures. In 2018, Dermatology took an incisional biopsy of a purulent lesion with raised borders, fibrin plaques and central necrosis. Magnetic resonance ruled out muscular invasion.
Results: The diagnosis was verrucous carcinoma. The patient rejected amputation. In 2019, he consulted because of pain and fetid smell due to an infection of the skin and soft tissues. He accepted infracondileal amputation. The lesion of 27 cm was yellowish white, well-defined and unctuous diagnosing exophytic verrucous carcinoma with some mitosis, perineural invasion, expansive growth, and Breslow thickness of 1´9 cm and with the proximal margin greater than 4´5 cm.
Conclusion: Verrucous carcinoma is a low grade tumour associated to VPH infection, repeated traumatism or tobacco and alcohol intake. Histopathological diagnosis in small biopsies is controversial, so clinic-pathological correlation is determining. The treatment of choice is surgery with large resection margins due to high risk of local recurrence. It rarely metastasises to regional ganglia. The significance of this case resides in its clinical context and rare location, taking longer to treat.

E-PS-05-008

Syringocystadenocarcinoma papilliferum

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Background & objectives: Syringocystadenocarcinoma papilliferum (SCACP) is a rare adnexal tumour of the skin, derived from sweat glands, with apocrine differentiation, the malignant variant of Syringocystadenoma papilliferum (SCAP). Until the present day, there are less than 50 cases reported in the literature.
Methods: A 74 years old woman clinically presented with a solitary tumour located on the face, under the left infra-orbital margin. The lesion developed slowly over the past 7 years. On clinical examination, the tumour was poorly demarcated, painful, ulcerated, indurated, with purulent discharge, measuring 2/2/1 cm. A split-thickness technique was used for excision.
Results: The lesion presented as an ulcerated 1.6/1.4 cm nodule, with grey-brownish cut surface. Histologically, an exophytic and endophytic well circumscribed, non-encapsulated tumour, located in the dermis, with pushing invasion into the subcutaneous fat. Superficially, there were papillary structures lined by double layered cells (reminding of the benign counterpart of the lesion - SCAP) forming funnel-shaped structures, communicating with cystic spaces; epithelial lining had pleomorphic cells and increased mitotic activity. The deep component presented solid areas with squamoid features. Stroma was reduced, with plasma cell rich infiltrate and areas of necrosis and ulceration. The tumour cells were positive for EMA, CK7, weakly positive for BerEP4 and negative for SMA and S100.
Conclusion: SCACP is an extremely rare skin tumour, in this case with architectural features of SCAP and moderately differentiated squamous invasive component, showing us the importance of broad differential diagnosis and a correct diagnosis to provide the best possible patient care.

E-PS-05-009

Epstein-Barr Virus-associated hydroa vacciniforme, excellent response to antiviral treatment

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Background & objectives: A 16-year-old female patient is admitted to the dermatology clinic for vesicupapular rashes on the nose that have been repeated for 2 years in the spring-summer season. She had no known systemic disease and no history of drug use.
Methods: This year, the patient's complaints increased compared to the previous year. Her complaints, which started in April last year and

regressed in October, this year continued during the winter and lesions spread in the malar region and hand dorsum. In her systemic examination, there was no abnormal finding other than mobile 1 cm diameter submandibular lymphadenopathy.
Results: On the dermatological examination, vesicle and papules completely covering the nose and haemorrhagic overlying epidermis were seen. Also there were several hyperpigmented varioloform scars in the malar region and hand dorsum. Leishmania, fungi and mycobacterium were not detected in microbiological examination. On histopathological examination, intense inflammation (mostly lymphocytes) under the ulcerated epidermis was observed. Lymphocytes were stained in the reactive pattern with CD3,4,5,30 and nuclear positivity was detected with EBER. Direct immunofluorescence was negative. EBV-VCA Ig G and EBNA Ig G positivity shown in peripheral blood. Patient was diagnosed as EBV-associated hydroa vacciniforme with the clinical and histopathological findings.
Conclusion: Valaciclovir treatment was given to patient and her lesions regressed with post-inflammatory hyperpigmentation at 2-month follow-up. Systemic screening was performed due to the risk of developing lymphoproliferative syndrome, but there was no finding. The patient was followed up for periodic biopsies in terms of the risk of developing EBV-associated hydroa vacciniforme-like lymphoproliferative disease.

E-PS-05-010
PRAME: a marker of sebaceous differentiation
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Background & objectives: PRAME (PReferentially expressed Antigen in MElanoma) is a member of the CTA (cancer testis antigens) family originally identified as overexpressed in melanoma. We describe the use of PRAME in the diagnosis of sebaceous cutaneous lesions.
Methods: We observed expression of PRAME in normal sebaceous glands. The current panel of adjunctive stains (EMA, Adipophilin, AR and Oil Red-O) is of limited effectiveness. We present two cases of sebaceoma, both with a clinical diagnosis of basal cell carcinoma. We stained for PRAME and compared them to a number of skin tumours that may enter in the differential diagnosis.
Results: Both are well-circumscribed basaloid tumours lacking epidermal connection. One shows distinctive rippled, petaloid and labyrinthine architecture. Both have scattered cells showing cytoplasmic vacuolation and nuclear indentation lying singly or in small clusters, suggestive of sebaceous differentiation. PRAME-IHC confirms sebaceous differentiation in these cells and highlights numerous others more basaloid cells with less obvious sebaceous phenotype. One case is MMR deficient (MLH1 & PMS2). The other lesions are negative for PRAME.
Conclusion: The identification of cutaneous tumours with sebaceous differentiation is important because of their association with ds-DNA mismatch repair (MMR) syndromes (Lynch or Muir-Torre syndrome). Sebaceous cells are key to this diagnosis however they can be scant in sebaceoma (and sebaceous carcinoma). PRAME helps identify sebaceous differentiation even in cells with little cytoplasmic vacuolation and does not stain other clear cells. PRAME is a useful adjunctive stain to demonstrate sebaceous differentiation.

E-PS-05-011
Hyperkeratosis lenticularis perstans (Flegel disease) in an uncommon localisation
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Background & objectives: Hyperkeratosis lenticularis perstans (also known as Flegel´s disease) is a rare dermatosis first described in 1957, caused by an abnormal disorder of the keratinization, that usually has characteristic clinicopathologic features, typically affecting the dorsal feet and lower extremities.
Methods: We present a case from our hospital.
Results: A 79 year-old woman presented with a one-year history of small, orange, asymptomatic and hyperkeratotic papules on her back. Patient´s medical history was unremarkable. These lesions were interpreted as horn plugs, suggesting Darier´s or Grover´s disease.
Histopathologic findings revealed focal and compact hyperkeratosis overlying a flattened epidermis, a well-circumscribed band-like mononuclear infiltrate in the papillary dermis.
The infiltrate was predominantly of CD3-T cells (similar CD4 and CD8-positive cells).
Conclusion: In only one previous report, as far as we know, hyperkeratosis lenticularis perstans involved the back region, supporting the localized disorder of this disease.
It has been noted to be an autosomal dominant disease. However, our patient seems to be an sporadic case.
Despite typically involving feet and legs, we remark the importance of adding this entity to the differential when this kind of lesions occurs in thorax and back, meanwhile we review its specific histological findings.

E-PS-05-012
Two case reports of hamartomatous lesions of the hair follicle
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Background & objectives: We present two cases of rare hamartomatous lesions of the hair follicle in the skin.
Methods: The first case was a cystic lesion of the scalp. Microscopically, it consisted of a cystically dilated hair follicle, containing hair shaft fragments and communicating with the epidermis. It was lined by stratified squamous lesion with a granular cell layer and numerous hair follicles arising from the cystic wall. Thus, it was diagnosed as trichofolliculoma.
Results: In the second case we received a papule of the nose. Histologically, there was a central cystic cavity, with keratin pearls and without hair shafts, connected with numerous small sebaceous nodules. Each epithelial component was surrounded by a dense collagenous stroma. There were also small vessels, with perivascular fibroplasia. It was diagnosed as a folliculosebaceous cystic hamartoma (FSCH).
Conclusion: Due to the rarity of the lesion, some studies consider FSCH to be a very late stage of trichofolliculoma. However, the lack of communication with the surface, along with the stromal component is considered a distinct difference between the two entities. Moreover, a study of chronological changes in trichofolliculoma showed no features indicating the replacement of the regressing secondary hair follicles by any sebaceous elements.

E-PS-05-014
Primary anorectal melanoma – a diagnostic challenge of a mimicking neoplasm
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Background & objectives: Anal melanoma represents 0,5-2% of all anorectal neoplasias and less than 2% of all melanomas. It is the third most common melanoma after cutaneous and ocular melanoma, and it is the most common site of occurrence in the gastrointestinal tract.
Methods: We present a case report of a 69-year old woman admitted to our hospital with a history of mucus rectal discharge and rectorrhagia. A

colonoscopy was performed showing a 4,0 cm lesion in the anorectal transition. The patient was submitted to an excisional biopsy.
Results: Gross examination revealed two fragments, with 4x2.5x2.5cm and 2x1x0.5cm. The biggest showing one ulcerated lesion with 4x1.8x1.8cm, well defined, firm and whitish.
Histologically, we observed an expansive malignant melanocytic neoplasia, with lamina propria invasion and mucosa ulceration. The tumour exhibited a solid pattern, composed by epithelioid and fusiform cells, with an eosinophilic cytoplasm and pleomorphic nuclei with evident nucleoli, sometimes with multinucleation. Melanic pigment was present irregularly through the neoplasm. The stroma was fibrovascular with a slight lymphocytic permeation. Tumoral thickness was 19 mm with 2 mitosis/mm2, focally coincident with the deep surgical margin.
Conclusion: The patient was submitted to abdominoperineal amputation, that revealed lymph node metastasis. One year later, there was a relapse with multiple distant metastasis: lung, liver, left kidney, pancreas, stomach and subcutaneous tissue.
The prognosis is poor and distant metastasis are the main cause of morbidity and mortality among these patients.

E-PS-05-015
Intermediate proliferating pilar tumour, case report and review of literature
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Background & objectives: Proliferating pilar tumours (PPT) are rare entities arising from the outer root sheath of hair follicles; it is thought to arise from pre-existing pilar cysts. PPTs are usually benign however malignant transformation has been recorded in very rare cases.
Methods: Current literature categories PPT into 3 categories - benign, low grade malignant and high grade malignant. Low grade features include stromal invasion and mild cytopathological abnormalities. Infiltrative growth, marked atypia, high mitotic activity and geographic necrosis may indicate malignant transformation. The differential diagnosis includes squamous cell carcinoma and trichilemmal cysts.
Results: We report a case of a 70 year old gentleman with a 9 month history of a rapidly growing scalp mass. Radiology demonstrated a multi cystic lesion with bony erosions and small vessels connecting the lesion to the epidural space. Initial biopsy revealed mildly atypical squamous nests with evidence of trichilemmal keratinisation. A proliferating trichilemmal neoplasm was suspected however further characterisation could not be made. The excision was performed and showed features consistent with a low grade PPT. The tumour showed mild to moderate cytological atypia and focal infiltrative growth pattern. There was no evidence of tumour necrosis or abnormal mitotic figures.
Conclusion: The determination of malignant potential in a proliferating pilar tumour can be challenging given the small number of cases reported in current literature. A high level of clinical suspicion and a multidisciplinary approach is necessary to facilitate effective patient care.

E-PS-05-016
Pseudotumoral presentation of cutaneous Rosai-Dorfman disease
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Background & objectives: Cutaneous Rosai-Dorfman (CRD) disease is a rare entity characterized by a histiocytic proliferation in the skin. CRD diagnosis remains a challenge because of its often nonspecific histologic presentation.
Methods: We present the case of an 82 y/o male with an isolated lesion on the forehead, slowly growing over a period of more than 3 years, evolving from a plaque stage to a tumour-like lesion. Multiple biopsies were performed between 2015 and 2018.
Results: Biopsies showed a vaguely nodular histiocytic infiltrate in the upper dermis, increasing over time to occupy all of the dermis thickness. By immunohistochemistry, the histiocytes expressed CD68, S100, but not CD1a. This was accompanied by an intense polymorphous inflammatory infiltrate, composed predominantly of plasma cells with mild atypia, prominent nucleoli, but no light chain restriction. Initially the plasma cell infiltrate was periadnexal and interstitial, but eventually became diffuse. Neither peripheral blood alterations nor adenopathies or visceromegalias were noted. A broad spectrum of entities was considered, including malignant soft tissue tumours, but the special studies along with the histology and the emperipolesis in the last biopsy, allowed the diagnosis of CRD.
Conclusion: CRD exhibits varied and occasionally confounding histologic and clinical features, such as a pseudosarcomatous lesion, as in our case report. Systemic work-up should be performed to rule out extracutaneous involvement. Immunohistochemistry is particularly important to rule out other pathologies.

E-PS-05-017
Effects of platelet rich plasma in treatment of atopic dermatitis
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Background & objectives: Atopic Dermatitis is a chronic T cell mediated inflammatory disease. Steroids and other immunosuppressant therapies are used for its treatment. Platelet rich plasma (PRP) has been utilized as an alternative treatment option for various disorders. The aim of our study was to treat a patient of Atopic Dermatitis with PRP.
Methods: A 16 year old girl presented to Musavvir Stem Cell clinic, Karachi with itchy cutaneous lesions on both palms for past 7 months. She was a diagnosed case of Atopic Dermatitis. After explaining the procedure and obtaining consent, 15 cc blood sample was drawn. The base line lab tests including CBC, ESR, random blood sugar, C - reactive protein (CRP) & Ig E were performed. Rest of the blood sample was transferred to PRP kit. The collected PRP was placed in Adilight 2 for activation. The final product was transferred through cutaneous injections into both palms. Three panels of PRP were administered with a gap of 15 days each. We assessed the patient by examination and by laboratory parameters.
Results: Initially, raised levels of ESR, eosinophils, CRP and abnormal Ig E were noted. After the first panel, mild improvement was seen. However, after the second and third therapy, the patient reported marked control on the itchiness, disappearance of rash as well as improved ESR, CRP, normal eosinophils and IgE levels.
Conclusion: This study reports the beneficial effect of PRP therapy in a patient of Atopic Dermatitis. It proves to be a safe & cost effective alternative treatment option.

E-PS-05-018
Disseminated extrafacial rosacea- acne rosacea papulonecrotic type- a case report
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Background & objectives: Extrafacial rosacea is a rare form of chronic acneiform skin disorder. It may occur in middle-aged males on the head and neck, earlobes, arms and upper parts of thorax with diverse clinical manifestation, whether affecting face or not.

Methods: We present a 56-year-old male patient with untreated skin changes on the cheeks, scalp and chest in the form of dark erythematous and oedematous confluent plaques, domed nodules and individual pustules lasted for four months. Cauliflower-like appearance of plaques and small pustules were located on the both earlobes. Having done a skin biopsy, the accurate diagnosis was reached.
Results: The pathology analysis described an irregularly thickened, hyperkeratotic epidermis with ulceration and crust on the surface. Diffuse, mixed inflammatory infiltrate was sited in superficial and mid dermis invading hair follicles and forming adnexal pustules as well as extensive necrotic areas. Small groups of epithelioid cells were located within infiltrate. The causing agent Demodex was seen in pilosebaceous unit. Histopathological features of acne rosacea- papulonecrotic type confirmed the diagnosis.
Conclusion: Our report indicates an uncommon form of rosacea that may be misdiagnosed. In the lack of typical clinical characteristics, in order to differentiate from other skin disorders, such as folliculotropic mycosis fungoides, and determine the proper diagnosis, histopathology examination plays essential role.

E-PS-05-019
Superficial CD34 positive fibroblastic tumour: the first case with a targeted sequencing finding
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Background & objectives: Superficial CD34 positive fibroblastic tumour (SCPFT) is a recently described rare mesenchymal neoplasm of borderline malignancy with only 42 cases reported to date.
Methods: Herein, the authors describe the case of a 52-year-old male with a mass at the submandibular area.
Targeted sequencing of 93 cancer-related genes was performed on a tumour DNA in the absence of paired normal.
Results: The tumour is characterized by its superficial location and unique histologic features of striking pleomorphism, sparse mitotic figures, and diffuse CD34 immunoreactivity.
The sequencing result showed 3 single-nucleotide variants (SNVs) and their corresponding variant allele fraction (VAF) and dbSNP ID number: ATM M1321I (48.24%, rs35184530), BRAF D22N (43.18%, rs397507456), TERT promoter (47.12%, rs10462697). Two missense SNVs (ATM M1321I and BRAF D22N) were reported in COSMIC database, but, considering VAF, these 3 SNVs could be a heterozygous germline variants. Three genes belong to a group of 152 genes that contribute to cancer susceptibility based on literature review.
Conclusion: To the best of our knowledge, this report presents the first case of SCPFT with genetic findings. A combination of germline variants could lead to a higher susceptibility for tumorigenesis.

E-PS-05-020
New case paradoxical reactions under TNF-α blocking agents
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Background & objectives: Paradoxical psoriasis is a side effect caused by TNF-α blockade, independent of the specific drug and associated with increased activation of innate immunity. Paradoxical psoriasis is provoked by biological agents without identified predisposing factors.
Methods: Under the care there were 2 patients with a diagnosis "Psoriasis Vulgaris, psoriatic arthritis" received therapy with the certolizumab pegol.
Results: One of them a 41-year-old woman had an exacerbation of palmoplantar pustulosis psoriasis after the fifth course of certolizumab pegol in the dosing is 400 mg (given as 2 subcutaneous injections of 200 mg each). Another a 65-year-old man had an exacerbation of palmoplantar pustulosis and plaque psoriasis after the third course of certolizumab pegol in the same dose. The histology of a skin biopsy from the affected areas was in keeping with palmoplantar pustular psoriasis: histology of the skin biopsy revealed confluent parakeratosis, acanthosis, neutrophils in stratum corneum and a dermal infiltrate of lymphocytes.
Conclusion: There are different theories that have been proposed to explain PAEs, the most realistic hypothesis is an imbalance in cytokine production, which can contribute to the development of new pathological pathways and cause PAEs.
The onset of PAEs close surveillance of newly available biological drugs is necessary in order to detect the occurrence of new and/or undescribed PAEs.

E-PS-05-021
Chemotherapy-induced ulcerative necrotic skin lesions: clinical cases of pyoderma gangrenosum on the background of targeted therapy for haematologic disorders
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Background & objectives: Multiple ulcerative necrotic lesions of the extremities in patients with oncohaematological diseases reduce the quality of life, provoking reduction or cancellation of chemotherapy. Analysis of development mechanisms optimizes complex therapy increasing the effectiveness of treatment.
Methods: Two cases of pyoderma gangrenosum (PG) in patients receiving targeted therapy. The first patient with multiple myeloma received inhibitor of proinflammatory cytokines (lenalidomide), the second patient with chronic B-cell lymphocytic leukaemia received a tyrosine kinase inhibitor (ibrutinib).
Results: Histological examination of skin samples demonstrate: in 1 case - the dense neutrophilic infiltrate in the dermis with the formation of subepithelial microabscesses, necrosis of individual collagen fibres, in 2 case - profuse neutrophilic infiltration of the dermis and hypodermis without signs of leukocytoclastic vasculitis, which confirmed the diagnosis of PG. With a break in the specific treatment of oncohaematological disorders, rashes regressed.
Conclusion: Multiple PG ulcers are regarded as a consequence of an imbalance of cytokines and a decrease in the regulation of the TNF-dependent apoptosis pathway provoked by biological drugs.

E-PS-05-022
Primary cutaneous eccrine carcinoma with pagetoid spread: a case report and review of literature
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Background & objectives: Primary eccrine carcinoma is an extremely rare cutaneous malignant tumour arising from the eccrine glands. The aim is to discuss the complex classification of these tumours and the role of immuno-profile to differentiate between primary eccrine adenocarcinoma and metastatic adenocarcinoma.
Methods: We report an 89-year-old white man who presented with a one year history of indurated scaly plaque on the right cheek , clinically suspected as squamous cell carcinoma. The patient has a past history of multiple basal cell carcinoma affecting the head and neck. There was no lymph node involvement.
Results: Histopathological examination showed epidermal infiltration by monoclonal malignant cells, which were highlighted by CK7 and CEA staining. The dermal component composed of nests of malignant epithelial cells with evidence of ductal differentiation. The tumour extended to

the eccrine ducts in intraductal carcinoma (DCIS) like pattern. Perineural invasion is identified. Immunohistochemistry and clinical assessment excluded extra-cutaneous adenocarcinoma. The patient was treated with wide local excision with three- year follow up without evidence of local recurrence or distant metastasis.
Conclusion: Primary eccrine carcinoma is a locally aggressive with a high rate of recurrence or distant metastasis. It mimics cutaneous metastatic adenocarcinoma from breast, lung or colon. Clinical exclusion of extra-cutaneous adenocarcinoma and immunohistochemistry are essential to exclude cutaneous metastatic adenocarcinoma.

E-PS-05-023
Lymphoepithelioma-like carcinoma of the skin: a case report
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Background & objectives: Lymphoepithelioma-like carcinoma is defined as a rare and poorly differentiated variant of squamous cell carcinoma, with prominent reactive inflammatory infiltrate mimicking undifferentiated nasopharyngeal carcinoma and has uncertain origin.
Methods: We present a case of a 59-year-old woman with a noose papule, measuring 1,2cm in diameter. The lesion was excised with a clinical hypothesis of basal cell carcinoma.
Results: Microscopically, the tumour is composed of irregular nests of malignant epithelial cells in a background of reactive lymphoid cells including mature plasma cells in dermis. The tumour cells were mainly polygonal in shape with an eosinophilic cytoplasm, containing vesicular nuclei, prominent atypia, numerous mitoses, diffuse lymphoplasmacytic infiltrate surrounding the epithelial nests and an infiltrating tumour margin. Immunohistochemistry revealed cytokeratin-positive cells (AE1/AE3) and p63 protein, indicating epithelial histogenesis and squamous differentiation. The tumour cells were negative for CK7, CK20, S100 and BerEp4. Lymphoid infiltrate was positive for CD3 and CD20. Indirect nasolaryngoscopy and Epstein-Barr virus immunoperoxidase staining excluded metastasis from a nasopharyngeal carcinoma.
Conclusion: According to literature review, the histogenesis of lymphoepitheliomalike carcinomas remains controversial between an adnexal origin and an infiltrated squamous cell carcinoma. In spite of the high-grade histologic features of LELCS, patients have a good prognosis, without recurrences or metastases.

E-PS-05-025
Plaque-like cutaneous mucinosis: an unusual disorder at an unusual age
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Background & objectives: Plaque-like cutaneous mucinosis (PCM) is a rare and heterogenous group of skin disorders related by mucin accumulation in the dermis, of which there are 15 cases reported. It affects more women in the third and fifth decade.
Methods: A healthy 11-year-old boy with a midline back lesion with progressive growth in the last 6 months. It is a well-defined, raised, soft plate, with several yellowish papules on its surface. Imaging studies only revealed lesion at the level of the dermis and superficial subcutaneous tissue. The diagnostic impression was of smooth muscle hamartoma. A biopsy was performed.
Results: Microscopically, the most striking finding is dermal mucin, arranged interstitially and perianexially (Azul-Alcian PAS positive), but not intrafollicular, without striking increase in fibroblasts or other alterations in collagen or elastic tissue. There is also present an slight chronic inflammatory infiltrate in a follicle and epidermis with reactive changes. The clinical presentation and the histological signs found, suggest the diagnosis of plaque-like cutaneous mucinosis (PCM).
Conclusion: The onset of PCM in childhood is even more infrequent, and it can suppose a diagnostic challenge to differentiate from other cutaneous connective tissue diseases or systemic inflammatory dermatoses.

E-PS-05-026
Idiopathic cutaneous angiosarcoma: about two cases
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Background & objectives: Angiosarcoma represents 5% of all malignant skin tumours. It is an aggressive neoplasia showing blood or lymphatic vessel differentiation. The head and neck are the most common sites.
We aimed to delineate the clinical and histopathological features of the cutaneous angiosarcoma.
Methods: We report two cases of cutaneous angiosarcoma diagnosed in the year of 2019. The first patient was a 56-year-old man who presented erythematous infiltrated lesion centred by two purple keratotic papules in the nose. The second patient was a 74-year-old man who presented ulcerative lesion with infiltrated border of the scalp for 6 months.
Results: Both patients have had a skin biopsy. Histopathologic examination revealed irregular anastomosing vascular channels in the dermis, lined by endothelial cells with enlarged and hyperchromic nuclei, dissecting collagen bundles, and surrounding vascular structures and eccrine ducts. Initially, for the second case, a melanoma of the scalp was strongly suspected. An immunohistochemical study, for both patients, was done. It was positive for CD31 and ERG and negative for CD34 , HHV-8 and HMB-45. The diagnosis of cutaneous angiosarcoma was retained. A granulomatous rosacea was associated to the angiosarcoma of the nose.
Conclusion: Cutaneous angiosarcoma is a rare malignant vascular tumour and predominantly seen in the white-skinned people. In most cases, its aetiology is unknown. its location at the head and the neck of the elderly is a great mimicker with many clinical presentations.

E-PS-05-030
Trichoblastic carcinosarcoma in the pre-sternal region: a case report
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Background & objectives: Trichoblastic carcinosarcoma is a rare case because it is a biphasic tumour. Second polyclonal theory in which two or more strains of multipotent cells generate epithelial or mesenchymal components.
Methods: CRS, female, 93 years old, Brazilian. He sought outpatient care an ulcerated nodular lesion, which was painless and had evolved for 9 months. On examination, the tumour lesion measured about five centimetres in diameter and had a vegetating ulcerative aspect in the presternal region. Underwent surgery for excision of the lesion, after being referred to the pathology service.
Results: The result of the anatomopathological examination was biphasic neoplasia consisting of epithelial and stromal components with a high mitotic index. Immunohistochemical examination reveals biphasic malignant cutaneous neoplasia consisting of a basaloid cell component of eosinophilic cytoplasm, a high nucleus-cytoplasm ratio, and evident nucleoli, forming infiltrative beams with important mitotic activity and follicular differentiation. There is a distinct and intermixed component to the epithelial blocks, consisting of atypical spindle cells and with mitotic activity a myxoid stroma. The immunoassay panel shows positivity for p63 protein in the

epithelial component, with a high proliferative index in both components. The set of findings favours low-grade trichoblastic carcinosarcoma.
Conclusion: Trichoblastic carcinosarcoma is a recently recognized adnexal neoplasm in the WHO classification of skin. The rarity of this tumour may be due to under-recognition and under-reporting. This case represents the ninth reported trichoblastic carcinosarcoma in the world.

E-PS-05-031
Spitz-type melanocytic tumours with the same morphological diagnosis and different genetic alterations: 3 case report series
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Background & objectives: Atypical Spitz tumour (AST) is a diagnostically challenging group of melanocytic lesions that share features of benign Spitz nevi (SN) and Spitz melanoma. Biological behaviour and clinical course of AST remains largely unknown. Nevertheless, ancillary diagnostic techniques offer new opportunities.
Methods: We present three clinical cases of skin lesions for female patients of 17, 6 and 44 years old. Local excision was performed and AST diagnosis was established with recommendations to obtain sentinel lymph node (SLN) biopsy. Positive SLN were detected in two cases. Immunohistochemical (IHC) and molecular testing was performed to present more relevant diagnosis.
Results: Intrinsic pattern was observed in IHC reactions with p16 and p21, aberrations at typical chromosomal loci were detected in FISH, and no mutations were identified after HRAS/BRAF genetic testing for a 17 years old patient. No chromosomal aberrations were identified for a second patient after comparative genomic hybridization. Significant cytological atypia, strong positive IHC reaction with HMB-45 and Ki-67 activity 10% were observed in metastatic cells of adult patient's SLN.
Conclusion: AST diagnosis remained just for a 17 years old patient, meanwhile SN and a Spitzoid melanoma diagnoses were established in the other two cases, respectively. Discussed cases of Spitz lineage tumours represent a diagnostic testing position towards stepwise implementation of ancillary diagnostic techniques assisting to improve accuracy of challenging ambiguous Spitzoid neoplasms diagnosis, and understand that routine histological testing alone may not be considered as a clinically reliable method for the accurate validation.

E-PS-05-032
Diffuse multiple syringomas of the scalp in scarring alopecia: guilt by association?
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Background & objectives: Syringomas and syringoma-like eccrine sweat duct proliferations may occur in association with alopecia. Some of these proliferations are focal incidental findings and not the primary cause of the alopecia.
Methods: A 57-year old woman, skin type V, presented with multiple ill-defined patches of alopecia in absence of erythema, scale, tufting or follicular plugging. The patient was otherwise fit and well with no relevant past medical history.
Results: Histopathology from the scalp biopsy revealed diffuse loss of hair follicles and multiple cystic structures with 'tadpole' appearance lined by ductal epithelium within a hyalinised stroma in the superficial dermis. Rare miniaturised hair follicles and follicular scars were present. Inflammation was minimal. A diagnosis of scarring alopecia with diffuse multiple syringomas was made.
Mehregan & Mehregan described syringoma-like eccrine sweat duct proliferations in scarring and non-scarring alopecia; they felt that eccrine duct hyperplasia was an incidental finding and did not play a major role in causing alopecia. Conversely, other authors believe that these proliferations are true syringomas causing scarring alopecia.
Conclusion: Whilst this finding may be incidental, in this instance we believe it may be a relevant cofactor in the pathogenesis of scarring alopecia. Our case underscores the value of clinicopathological correlation and biopsy in the setting of scarring alopecia.

E-PS-05-033
Double-hit primary cutaneous large B-cell lymphoma
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Background & objectives: Double-hit lymphoma (DHL) is defined as a high grade B-cell lymphoma (BCL) with MYC translocation combined with an additional translocation involving BCL2 and/or BCL6. The most common type is MYC/BCL2 DHL, whereas MYC/BCL6 is rare.
Methods: An 83 year old woman presented with a nodular well demarcated reddish lesion with smooth surface in right popliteal fossa.
Her past medical history war remarkable for melanoma.
Results: Histology showed a non-epidermotropic, dense and diffuse dermal and subcutaneous infiltrate separated from the epidermis by a Grenz zone and composed of sheets of large, fairly uniform, atypical lymphoid cells with prominent nucleoli. No germinal centre formation was seen. Ulceration was absent.
By immunohistochemistry, tumour cells showed an activated B-cell phenotype (CD20, CD79, PAX5, MUM1, BCL2 and BCL6 positive) with negative staining for CD3, CD10, CD30 and EBER. Diffuse weak positivity for CD5 was noted. The proliferation index was high.
Staging including a PET scan was negative.
Fluorescence in situ hybridisation showed MYC and BCL6 rearrangement, in keeping with a double-hit primary cutaneous diffuse large B-cell lymphoma.
Conclusion: The classification of primary cutaneous BCL displaying diffuse pattern and predominantly large cell morphology can be challenging. Correlation with clinical presentation, staging, histological features, immunohistochemistry and molecular analysis is crucial to reach the diagnosis that will allow prognostication and therapy.

E-PS-05-034
Nilotinib-induced alopecia: a clinicopathologic challenge
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Background & objectives: Nilotinib is a tyrosine kinase inhibitor used in the therapy for chronic myeloid leukaemia. Dermatological reactions (keratosis pilaris, pruritus, dry skin, alopecia) are its most common non-haematological adverse effects. Their management is challenging, in the absence of alternative anticancer agents.
Methods: A 49 year old woman presented with a 10 year history of hair thinning and hair loss in the fronto-temporal area with no discrete patches, focal perifollicular scale and mild erythema. Her past medical history was remarkable for chronic myeloid leukaemia treated with Nilotinib.
Results: Histopathology from the scalp biopsies showed an increased number of telogen hair follicles and an increased number of fibrous tracts in the subcutaneous tissue. Interface changes were seen at the infundibulum, with perifollicular lymphocytic infiltrate and fibrosis. Partial loss of the sebaceous gland was also present.
Although clinically non-scarring, a histopathological diagnosis of scarring alopecia consistent with early lichen planopilaris on a background of female pattern hair loss was made. In view of the clinical history, the findings were interpreted as secondary to Nilotinib therapy.

Conclusion: The mechanism of adverse reactions to tyrosine kinase inhibitors is not well understood. As the treatment of alopecia can be challenging, further investigation into the underlying mechanism involved in these effects may provide potential therapeutic target. Furthermore, our case highlights that the identification of one pathology in alopecia specimens does not exclude other concomitant aetiologies and pathologists should be aware of that.

E-PS-05-035

A rare case of cutaneous lymphoepithelial - like carcinoma

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Background & objectives: Poorly differentiated variant of cutaneous squamous cell carcinoma – lymphoepithelial carcinoma (lymphoepithelioma – like carcinoma) is an uncommon entity. The morphology and immunohistochemistry (IHC) are crucial for the diagnostic process.
Methods: From the database of our pathology department, we extracted the case of a 83-year old male patient that presented in the plastic surgery department with a painless cutaneous nodular tumour, with imprecise borders, ulcerated and inflamed, measuring 2/1.5 cm, localized in the temporal area. Regarding the surgical specimen, routine paraffin embedding, haematoxylin&eosin staining and immunohistochemistry was performed.
Results: Microscopically, the malignant epithelial proliferation had solid and lobular patterns, showing a dense inflammatory infiltrate (predominantly plasmocytic). The tumour was composed from 2 cell populations: the majority of the malignant cells had vesicular nuclei with nucleoli and eosinophil cytoplasm, the other cells having chromophobe cytoplasm (adipocyte-like). The tumour cells were positive for panCK (AE1/AE3), EMA, p63, CK8/18 and negative for S100, Melan-A and sinaptophysin.
Conclusion: The morphology of cutaneous lymphoepithelial carcinoma is often misleading and needs to be correlated with immunohistochemical studies. The IHC profile allowed us to eliminate metastatic undifferentiated nasopharyngeal carcinoma (lymphoepithelioma), Merkel cell carcinoma, lymphoma and melanoma from the differential diagnosis list.

E-PS-05-036

An uncommon and rare coexistence of basal cell carcinoma with molluscum contagiosum

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Background & objectives: Basal cell carcinoma (BCC) is the commonest skin cancer worldwide. Molluscum contagiosum on the other hand is a skin infection caused by a double stranded DNA virus, pox virus.
Methods: The coexistence of BCC and molluscum contagiosum has only been reported once in the literature to the best of our knowledge and there is no known documented case in the UK. We present an 80-year old man who was referred to the plastic surgery department by a dermatologist for excision of possible BCC on the helical root of the left ear
Results: The only past medical history was atrial fibrillation for which they were taking Rivaroxaban. He had no history to suggest immunosuppression. He underwent excision of the clinically convincing BCC along with the underlying cartilage.
Histologically, the skin excision revealed two different lesions. The first lesion showed basaloid proliferation with artefactual retraction consistent with nodular type basal cell carcinoma. In another separate focus was a cup crater filled with large cells that have eosinophilic cytoplasmic inclusions in keeping with Molluscum contagiosum. The margins were completely excised. BCC in skin excisions are part of the routine fairly straight forward cases
Conclusion: commonly diagnosed by a general pathologists. There have been documented association of BCC with several other skin lesions. It is also important to bear in mind the possibility of a co-existence with MC irrespective of the immune status.

E-PS-05-037

Renal cell carcinoma cutaneous metastasis: two cases of atypical metastatic presentation

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Background & objectives: RCC can metastasize to all organs, but most frequently to lung, bone, brain and liver. The skin and especially the scalp is a very unusual site. We present two cases of cutaneous metastatic clear cell RCC to the skin.
Methods: A 74-year-old male patient presented with multiple nodular masses on the scalp. He was diagnosed as clear cell renal cell carcinoma a year ago, and
a 63-year-old male patient with no medical or surgical history presented with nodular masses on the buccal mucosa and neck. Excisional biopsy was performed in both.
Results: On microscopic examination of both, the tumours were arranged in a diffuse, sheet-like pattern interrupted by small, thin walled vascular structure in dermis. Tumour cells had uniform, hyperchromatic nuclei and large, clear cytoplasm. The immunoprofile of these tumours showed diffuse staining for PAX8,CD10,vimentin,and negative staining for SOX10,HMB45,Melan A,CD68,CK 7,and CK20. Therefore, considering the morphological findings and immunohistochemistry results of these neoplasms, the patients were diagnosed with RCC metastatic to the skin.
Conclusion: The skin and particularly the scalp is a rare site of RCC metastatic involvement. Metastases to the skin should be kept in mind due to similarity of primary skin tumours. The morphological findings and immunohistochemistry results may be able to distinguish between primary and secondary neoplasms. Despite poor prognosis, diagnosis and surgical excision are crucial and may improve the survival.

E-PS-05-039

Cutaneous metastasis from hepatocellular carcinoma: a case report

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Background & objectives: Hepatocellular carcinoma(HCC) is a tumour with increasing incidence in the recent decade. The most frequent sites of extrahepatic metastasis of HCC are the lungs, bones, adrenal glands; the skin is a very rare site for metastasis. We report a case of cutaneous metastasis of HCC.
Methods: We present the case of a 67-year-old man who was diagnosed with HCC six years ago and presented with a 1-month history of an enlarging skin lesion at the left malar region. Clinically, it appeared as a reddish nodule with red/blue lacunas visible on dermoscopy. As the appearance was suggestive of a haemangiomatous lesion, it was sampled as punch biopsy.
Results: Histopathological evaluation of biopsy specimen showed that the lesion consisted of trabeculae of polygonal cells with eosinophilic cytoplasm and prominent nucleoli. The tumour cells were positive for hepatocyte antigen and negative for EMA and PANCK, confirming the diagnosis to be metastatic HCC.
Conclusion: Metastases of HCC should be included in the differential diagnosis of growing lesions on unusual localizations. Biopsy is essential to confirm the diagnosis. The diagnosis of HCC from a cutaneous lesion is very uncommon and is associated with poor prognosis.

E-PS-05-040

Cellular neurothekoma: A potential pitfall in cutaneous neoplasms

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Background & objectives: Cellular neurothekoma is a rare, benign, cutaneous neoplasm which frequently causes diagnostic difficulty. Recent studies have shown that cellular neurothekoma is unrelated to classical neurothekoma and is more likely of histiocytic lineage.
Methods: A twelve year-old female patient represented with a rapidly growing, painless nodular lesion on the back. The creamy coloured lesion was 0,8cm in diameter, localised in the subcutaneous tissue. In the dermis, clusters of mostly epithelioid, and rarely spindled cells with vesicular nuclei forming groups, sometimes micronodular; separated by dense collagenous stroma are seen on a myxoid background. The lesion contains approximately 12-13/10HPF mitoses.
Results: Fibrohystiocytic tumours, muscle derived lesions and neural lesions such as nerve sheath myxoma were considered in differential diagnosis. Immunohistochemical studies showed strong positive staining with vimentin, MITF and NSE. Negative staining of PanCK and EMA and strong positive staining with vimentin supported lesion's mesenchymal origin. While S100 and SOX10 negativity excluded neural sheath tumours and classical neurothekoma, negative staining of desmin and MyoD1 excluded muscle derived tumours. CD34 negativity excluded dermatofibrosarcoma protuberans. GFAP was performed due to lesion's resemblance of cutaneous meningioma and came out negative. In order to exclude atypical fibroxanthoma CD99 negativity was used. Histopathological and immunohistochemical findings were consistent with cellular neurothekoma.
Conclusion: This uncommon benign neoplasm should be included in the differential diagnosis of dermal nodules in children as they can be mistaken for malignancy due to high mitosis rates and cause unnecessary treatment.

E-PS-05-041

A case report: histopathological study of an acneiform eruption viz chloracne

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Background & objectives: Chloracne, a rare variant of acne caused by systemic over-exposure to halogenated aromatic compounds (chloracnegen) either occupational or environmental. These are acneiform eruptions commonly affecting the face in males and should be considered a differential diagnosis in similar presentations.
Methods: This study is about a 28-year-old-male working at a chemical industry, who presented with multiple hyperpigmented papules and comedones on face and upper limbs. We examined the histopathological aspects of the disease and correlated clinically.
Results: Histopathology revealed skin tissue lined by keratinized stratified squamous epithelium showing dilated infundibulum filled with keratotic plug composed of orthokeratotic basket-weave basophilic corneocytes. Other dilated infundibulum containing eosinophilic laminated or granular sebum were also seen. Few mature sebaceous glands were noted. Hyperpigmentation of the lesions resulted from presence of abundant melanin along the basal layer of the epidermis and epithelium of the infundibular plugs. A diagnosis of Chloracne was confirmed.
Conclusion: Though rare, chloracne is still prevalent and should be familiar to all practitioners to be considered a differential diagnosis in case of acneiform eruptions with relevant history of exposure to the chloracnegens and further confirmed on histopathology.

E-PS-05-042

A case report: histopathological study of an unusual presentation of lupus vulgaris

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Background & objectives: In practice, some cases of cutaneous tuberculosis do not readily fit into any clinical or histological categories. This case is one of those rarity and we illustrate the challenges faced in reaching up to the diagnosis.
Methods: A 65-year-old-male, presenting with single ill-defined erythematous plaque with dirty-yellow crusting over the back was biopsied. The histopathological aspects were assessed. Few other investigations were performed and clinical correlation done.
Results: Multiple histopathological sections revealed skin tissue lined by hyperkeratotic stratified squamous epithelium comprising small foci of inflammatory cell collection. The upper dermis showed infiltration of lymphocytes. Non-necrotizing granulomas composed of epithelioid cells, Langhans type giant cells with characteristic peripheral arrangement of the nuclei along with foreign body type giant cells and numerous lymphocytes were noted in the dermis. Other investigations were performed and correlated.
Conclusion: After a detailed histopathological examination along with consideration of differentials, a diagnosis of Lupus Vulgaris was confirmed.

E-PS-05-043

Porocarcinoma of skin – report of a rare case

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Background & objectives: Eccrine porocarcinoma (EP) is a rare type of skin cancer (from 0.005 to 0.01%) that forms from the sweat glands which difficult to diagnosis, because tumour have many common structures.
Methods: A case analysis of a postoperative skin biopsy obtained from a 39-year-old patient with a diagnosis of porocarcinoma of the right upper limb(hand projection)was carried out.
Results: The patient underwent 2 relapses. The debut of the second relapse was the tumour invasion into the soft tissues and bones of the forearm and distant lung metastases. The stump of the upper limb was amputated at the level of the upper third of the shoulder. Light microscopy shows elongated epidermis composed of interconnection strands of atypical epithelial poroid tumour cells, Solid aggregates of tumour cells and duct structures, and cystic epithelial cell nests aggregates. Prominent mitotic figures and atypical mitoses often observed. IHC study shows diffusely positive cytoplasmic staining for pancytokeratin AE1 / AE3, CK6 and CK7. Prominent cytoplasmic expression of CEA and EMA was observed only in Ductal and cystic structures.
Conclusion: This case broadens our understanding of the nature, physiology, and pathology of porocarcinomas. This gives hope for the timely and adequate diagnosis of these tumours with subsequent treatment.

E-PS-05-044

A misleading heavily pigmented melanocytic tumour

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Background & objectives: The differential diagnosis of heavily pigmented melanocytic neoplasms is wide including melanoma, blue nevus, pigmented epithelioid melanocytoma (PEM), deep penetrating

nevus and pigmented Spitzoid lesions. We report a case of a pigmented melanocytic tumour that posed a diagnostic challenge.
Methods: We report a case of a 43-year-old man who presented with a 4-year history of a scalp nodule that had enlarged slowly in the last 4 months.
Results: Physical examination revealed a blue dome-shaped mass, sized 1.7 cm. A marginal excision was performed. Histological examination revealed an epithelioid and spindle-shaped proliferation in the dermis, composed of mildly atypical melanocytes with heavy pigmentation. Nuclei were vesicular with prominent nucleoli and rare mitoses (1/10HPF). No tumour necrosis was observed. An additional junctional dendritic component was associated. Immunohistochemical staining showed expression of HMB45 and a low proliferation index (Ki67<1%). From the above findings, the proposed diagnosis was PEM. The case was sent to a referent centre of dermatopathology in France. Immunohistochemistry showed positivity for PRKAR1A and molecular testing revealed a mutation for GNAQ and no mutation of BRAF, NRAS and CKIT.
Conclusion: Compound blue nevus (CBN) is a rare variant in the vast clinical and morphological spectrum of blue melanocytic proliferations. CBN is a distinctive histopathologic variant of blue nevus with a challenging diagnosis. In fact, these lesions can be misdiagnosed as combined blue nevus, PEM and melanoma. Molecular analysis is necessary to make the right diagnosis and avoid unnecessary invasive procedures.

E-PS-05-045
ALK-positive histiocytosis: rare disease with tremendous implications - case report
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Background & objectives: ALK-positive histiocytosis is a newly described non-Langerhanscell tumour. It mainly affects children or adolescents and can be localized or systemic with involvement of many organs such as skin, liver, spleen, bone marrow. In disseminated cases can even lead to death.
Methods: We report a case of a 2 years old girl with a small vulvar lesion, clinically described as a cyst. There was no medical history. The lesion was excised and sent for histopathological investigation.
Results: The microscopy showed a non-circumscribed dermal lesion consistent of round to spindle cells with minimal cytomorphologic atypia. There were scattered mitotic figures. No necrosis.
Immunohistochemistry showed positivity of the cells for CD68 without S100 expression. These cells were also diffusely and strongly ALK-positive. Further molecular analysis with NGS revealed a KIF5B-ALK gene fusion. The diagnosis of an ALK-positive histiocytosis was then suggested.
The patient underwent computed tomography, ultrasonography and blood sampling, which demonstrated hepatosplenomegaly and slight elevated level of eosinophils in the blood. Liver and bone marrow biopsies showed no signs of disease. Our patient showed no relapse 10 months after the initial diagnosis.
Conclusion: Only limited cases of ALK-positive histiocytosis are reported in the English literature. Given its rarity, there is limited information about the possible therapeutic options and the prognosis. Awareness of the entity would help in better recording of the disease.

E-PS-05-046
Clinicopathological features of cornu cutaneum: a tertiary centre experience
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Background & objectives: Cornu cutaneum (CC) or cutaneous horn is a clinical term that describes conical protruding hyperkeratosis. This study aims to focus on the experience of a tertiary centre encountered throughout 11 years of surgical pathology and dermatopathology practise.
Methods: Medical reports of patients who had clinical diagnosis and underwent surgical excisions of CC lesions and also that had their respective histopathologic reports during the period from 2008 to 2019 at Istanbul Medeniyet University Goztepe Training and Research Hospital were analysed. A total of 137 patients with CC were detected from the pathology archive.
Results: Majority of the lesions were located on the head and neck(n=86, 63.2%). Twenty-one patients had a lesion on the upper limbs(15.4%), fifteen patients had a lesion on the lower limbs(11%), fourteen patients had a lesion on the trunk(10.3%). Base of the lesions were diagnosed as actinic keratosis in twenty-seven patients, verruca vulgaris in five patients, seborrheic keratosis in four patients, microinvasive squamous cell carcinoma in one patient, squamous papilloma in one patient.
Conclusion: Cutaneous horns are generally benign entities; however possibility of approximately one third of them harbouring premalignant or malignant skin lesions should be kept in mind.

E-PS-05-047
A five-year retrospective analysis of basal cell carcinoma: a monocentric study
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Background & objectives: This study aimed to define the histopathological subtypes, body site distribution, and single or multiple incidence rate(s) of BCC patients in Istanbul, Turkey, which has a population comprised of millions of people from many different areas of the country.
Methods: We retrospectively analysed data concerning 896 cases of BCC treated at Istanbul Medeniyet University Goztepe Training and Research Hospital between 2014 and 2018.
Results: Our univariate analysis showed age, tumour size, and tumour multicentricity to all be significantly related to gender($p = 0.011$, $p = 0.001$, and $p = 0.021$, respectively). Further, age, male gender, and tumour size were all significantly related to tumour multicentricity($p = 0.003$, $p = 0.021$, and $p = 0.001$, respectively).BCC was found to be most common in men, and the diameters of the BCC tumours were also larger in male patients. Multiple BCC was more frequently seen in older and in male patients, and the tumours again had larger diameters in these groups. The nodular type of BCC was the most frequently seen type in all the age groups.
Conclusion: As our study is the first BCC study that has the most number of cases in Turkey and as Istanbul reflects the population of Turkey, it is important for the data of BCC cases in Turkey.

E-PS-05-048
Cutaneous metastasis of bladder urothelial carcinoma: a case report
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Background & objectives: Cutaneous metastasis from transitional cell bladder carcinoma is a rare clinical entity associated with poor prognosis. We present a case of cutaneous metastasis arising from an urothelial bladder carcinoma in a male patient who had undergone a radical cystectomy 17-months previously.
Methods: A 86-year-old male presented with a 20-day history of an ulcerated nodule in his upper lip. His past medical history included a radical cystectomy that he had undergone 17 months previously, due to a high-grade urothelial bladder carcinoma(pT3). Punch biopsy was performed to the patient with suspicion of skin tumour.
Results: Microscopic view of biopsy showed subcutaneous infiltration of tumour. The infiltrative neoplastic cells were arranged haphazardly with

the loss of polarity. The nuclei were hyperchromatic and, prominent nucleoli were present. Immunohistochemical staining showed strong diffuse positive staining for PanCK, p63 and Gata-3. With these findings, the histopathological report was summarized as an invasive poorly differentiated bladder carcinoma metastasis.
Conclusion: We presented a rare case of cutaneous metastasis of urothelial carcinoma of the bladder. Metastatic disease should always be in the differential in any patient who presents with cutaneous lesions. Skin biopsy should be performed for histochemical analysis to prevent misdiagnosis.

E-PS-05-049
Basal cell carcinoma with intravascular invasion: an unusual finding of uncertain significance
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Background & objectives: Risk factors for aggressive behaviour in basal cell carcinoma (BCC) include histological type, the presence of a squamous component, perineural invasion, and the distance to the nearest margin. Yet, lymphovascular invasion is very rarely reported and its relevance remains unknown.
Methods: A 85-year-old woman consulted for a slowly-growing lesion in her nose. Personal medical history included no previous skin diseases. Clinical examination revealed a 9 mm, erythematous, indurated, lesion on the tip of her nose. Actinic damage was noted as well as two actinic keratosis. The lesion on the nose was removed with the clinical diagnosis of BCC.
Results: Histopathological examination revealed a conventional BCC, with infiltrative pattern. In the section corresponding to one of specimen tips, neoplastic intravascular invasion was noted. Immunohistochemical study confirmed the lymphatic nature of the vessels, which stained with antibodies for CD31 and D2-40. Intravascular neoplastic cells were positive for Ber-EP4 but not for Cytokeratin 20, Chromogranin-A, Synaptophysin or TTF-1.
Given the advanced age of the patient, close follow-up was considered the safest option and no additional treatment was done. The patient is free of disease 4 months after surgery.
Conclusion: Contrarily to perineural invasion, intravascular invasionin BCC is exceedingly rare, and its clinical significance remains unknown. No guidelines currently exist for adjuvant treatment or diagnostic measures in patients with this condition.

E-PS-05-050
A rare case of metastatic cutaneous cholangiocarcinoma
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Background & objectives: Cutaneous metastases from internal malignancies are uncommon. In cholangiocarcinomas the occurrence of cutaneous metastases is extremely rare.
Methods: A 52 year old woman was presented to Dermatology department with a skin lesion on the upper lip and another on the scalp. A CT scan revealed a 8 cm mass located in the hilar of the liver, one month ago with the diagnosis of cholangiocarcinoma. Skin biopsies were performed with the clinical diagnosis of herpes zoster, folliculitis or metastases.
Results: The histopathology revealed neoplastic cells in the papillary and reticular dermis of the skin with immunohistochemical features (CK19+, CK17+, VHL+) consistent with metastases from intrahepatic cholangiocarcinoma according to the clinical findings. The patient treated with chemotherapy but the disease progressed resulting in the death of the patients 4 months later.
Conclusion: The most common tumours that metastasize to the skin are breast, lung, colorectal, oral mucosa, gastric, hepatocellular and oesophageal. Cutaneous metastases is a rare manifestation of visceral tumours and represent advanced stages and are associated with poor prognosis.

E-PS-05-051
Aberrant epidermal hyperplasia in a case of spitzoid melanoma - a diagnostic pitfall
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Background & objectives: Squamoid epidermal hyperplasia is a poorly described and rarely reported lesion associated with underlaying dermal tumours. The histopathologic appearance is sometimes worrisome and may be misleading, raising the suspicion of a synchronous in situ or malignant epithelial overgrowth.
Methods: The aim of our study is to gain further insight into the epidermal hyperplasia associated with a spitzoid melanoma. Emphasis is placed on the importance of immunohistochemistry for establishing the correct diagnosis, as well as on the differential diagnosis with other entities. Similar to basaloid hyperplasia and Borst-Jadassohn phenomenon, the true nature of squamoid epidermal induction is poorly understood.
Results: We present a case of a 42 year old female diagnosed with spitzoid melanoma with peculiar epidermal hyperplasia. On standard examination the tumour exibits characteristic features of a malignant spitzoid lesion with marked atypical epidermal hyperplasia initially considered a synchronous squamous cell carcinoma. Ancillary test were used to document these lesions. In this way the diagnosis of squamous cell carcinoma was ruled out, and the epidermal changes are considered benign.
Conclusion: Sometimes melanoma is associated with pseudoepitheliomatous epidermal hyperplasia. The presence of prominent epidermal changes may make the clinical recognition difficult and lead to confusion with a collision scenario of squamous cell carcinoma and melanoma. Furthermore, a pathologist focusing on the epidermal changes may consider a squamous cell carcinoma and fail to recognize the melanoma if, for example, a superficial biopsy in performed. Immunohistochemistry is crucial for establishing the correct diagnosis for this type of lesion and for the differential diagnosis.

E-PS-05-052
Malignant proliferating trichilemmal tumour- a rare entity with aggressive pathological features
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Background & objectives: Malignant Proliferating Trichilemmal Tumour (MPTT) is an uncommon, controversial, appendageal skin tumour, usually developing on the scalp. Only hundreds of cases are reported, fewer than 50 being well-documented. We report a case of MPTT and discuss associated aggressive pathologic features.
Methods: A 47 –year old woman presented to the Hospital, with 3 large, firm, painless, subcutaneous nodules, in the occipital and vertex region, which have grown fast in recent months. The patient underwent surgery, the tissue fragments being referred to the Pathology Department. For histological examination we used HE stained slides and immunohistochemical staining for CD34, calretinin, EMA and Ki67 antibodies.
Results: Two of the lesions proved to be pilar cysts. The third tumour (occipital region), was a relatively well circumscribed 3.9x3.8x1.2cm nodule; histologically a subepidermal squamous infiltrative proliferation was identified, with multilobular architecture, solid and cystic areas. The cystic areas had centrally dense keratin and necrotic material, lined by squamous epithelium with trychilemmal keratinisation and cytological atypia. The solid lobules displayed marked atypia, epithelial pearls formation, frequent mitoses (7/HPF) and Ki67-90%.
Conclusion: Based on CD34 and calretinin intense positive immunoreactions in tumour cells, lacking connection to epidermis and cystic areas resembling proliferating pilar tumour, we made the

final diagnosis of MPTT. In short, we present a very rare case of MPTT, its particularity consisted of histological aggressive features: marked cytological atypia, numerous atypical mitotic figures and very high Ki67 index. Considering these characteristics, we believe that a more aggressive therapeutically management is needed (classically local wide excision being recommended).

E-PS-05-053

Primary mucinous eccrine adenocarcinoma of the scalp: a case report

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Background & objectives: Primary mucinous eccrine adenocarcinoma, a rare malignant neoplasm of the skin adnexa, usually occurs in the head and neck region. The most common sites for its occurrence are the eyelid, the peri-orbital region and the scalp.
Methods: A 75-year-old female patient presented with a palpable, non-tender nodule measuring 3x2 cm in the scalp, which was firm in consistency and at gross examination showed multiple, gelatinous tissue bits. The largest bit measured 2 x 1.5 cm and the cut surface was gelatinous.
Results: Microscopic examination showed large pools of mucin arranged in lobules, separated by collagenous septae. Epithelial tumour cells arranged in small clusters, tubules and cribriform patterns were floating in the pools of mucin. Individual tumour cells showed scant cytoplasm and hyperchromatic nuclei. Immunohistochemically, the tumour cells were positive for CK7, ER, PR and negative for CK20, CDX2, S100p, Chromogranin, Synaptophisin, as the Ki67 was very low.
Conclusion: Cutaneous mucinous carcinomas may present with a variety of clinical presentations. Metastatic deposits from undiagnosed visceral and breast adenocarcinoma are virtually indistinguishable microscopically from sweat gland carcinoma and must be considered before a diagnosis of sweat gland carcinoma is made.

E-PS-05-054

Eosinophilic cellulitis associated with LLC

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Background & objectives: Wells syndrome is an uncommon skin condition of unknown aetiology. Some authors believe it may be a local hypersensitivity reaction. It may occur associated with other diseases. However, first it should be ruled out an hematologic disease especially LLC.
Methods: We describe a cases of Wells' syndrome in a 67-year-old female with several episodes of recurrent pruritic eruptions of oedematous plaques on the during the process. The patient was diagnosed with B-cell chronic lymphocytic leukaemia which was revealed through the investigation of the cutaneous disease.
We do Histological examination of the skin and Direct immunofluorescence.
Results: The skin biopsy showed a prominent lymphohistiocytic cell infiltrate rich in eosinophils both interstitial and angiocentric in the superficial and deep dermis and in the subcutaneous tissue. flames figures were not found. Direct immunofluorescence showed no findings of immunobullous diseases
Conclusion: The patient was diagnosed as eosinophilic dermatosis of hematologic malignancy based on the medical history, recurrent skin lesions and histologic manifestation excluding other causes of tissue eosinophilia .The clinical and pathological correlation allowed the WS diagnosis, with complete resolution of the cutaneous clinical picture after chemotherapy for leukaemia treatment.

E-PS-05-055

Plasma cell granuloma of the skin

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Background & objectives: The plasma cell granuloma is included in the group of inflammatory pseudotumors, It is a rare benign lesion, of unknown cause. Only a few cases having been reported in the s
Methods: We perform histological examination and immunohistochemical evaluation, with kappa and lambda markers.
Results: The histological examination revealed a well-defined dermal nodule of plasmacytoid cells, without connection or infiltration of the epidermis. The epidermis cells showed signs of infection of VHS. At high power the polymorphous cellular infiltrate was constituted by lynfocites and dense infiltrate of plasma cells. Myofibroblatic cells were not found. On immunohistochemical evaluation, both kappa and lambda markers were positive and there was no light-chain restriction.
Conclusion: We believe that the term cutaneous inflammatory pseudotumors subsume lesions of diverse aetiology. Tumours with detectable myofibroblasts represent true cases of IMT while Cutaneous PCG is a disorder biologically distinct from conventional IMT representing a reaction pattern that is also found in vascular and infectious disorders like our present case.

E-PS-05-056

Porphyria cutanea tarda and bowenoid papulosis as primary presentation in a HIV infected patient - a rare association

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Background & objectives: Porphyria cutanea tarda (PCT) is a rare metabolic disease which can be hereditary or acquired. Association of PCT with HIV infection is poorly understood. Here we report a rare case of HIV infected patient with PCT and bowenoid papulosis (BP).
Methods: A 37 year male patient presented with fluid filled lesions over hands for the last 2 months. On examination multiple tense haemorrhagic bullae and crusted erosions were seen on the dorsa of the hands and over nose. Multiple hyperpigmented verrucous papules present over glans penis and prepuce were seen. Routine investigations and biopsies from hand and glans were done.
Results: Patient's baseline routine investigations were within normal limits. Serum was non-reactive for anti-HCV and HBV surface antigen. He was found positive for HIV testing. His skin biopsy from bulla over hands showed morphology of PCT, whereas biopsy form papule over glans showed features of bowenoid papulosis.
Conclusion: Dermatological symptoms can be the first manifestation of HIV infection. Bowenoid papulosis clinically resembles genital warts but the histopathology shows squamous cell carcinoma in situ. There can be a possibility of HIV infection causing increased susceptibility of patients to PCT. More large scale studies are required for the validation of this hypothesis.

E-PS-05-057

A case report of scrotal sebaceous carcinoma with carcinoma-in-situ

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Background & objectives: Sebaceous carcinoma is a malignant cutaneous neoplasm of sebaceous gland, commonly seen in the ocular area but extra ocular tumours are also seen. Carcinoma in-situ is usually seen in periocular lesions however these changes are not seen in extraocular sites.
Methods: Representative specimens were submitted for permanent paraffin sections from multiple sites of the patient viz. left arm,

right arm, lower abdomen, penile shaft and scrotum. Gross examination showed multiple hypopigmented lesions, then subsequent microscopic examination was performed.
Results: Sebaceous carcinoma with carcinoma- in-situ component was reported in scrotal tissue whereas, Sebaceous adenoma was diagnosed in specimens from right arm, left arm and lower abdomen and viral wart changes were identified in tissue from penile shaft.
Conclusion: We report a rare case of Sebaceous carcinoma with in-situ component in scrotum. The periocular lesions often show a pagetoid or carcinoma-in-situ change, such changes are usually not seen in extraocular cases. Hence, we conclude that Sebaceous carcinoma should be considered as a differential entity while examining adnexal lesions from the perineal area. Further case evidence and surveillance studies are required from around the world to ascertain the epidemiological significance.

E-PS-05-058
Features of the development of severe allergic reactions in oncohaematological diseases: a clinical case of toxic-allergic dermatitis in a patient with acute leukaemia
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Background & objectives: Oncohaematological diseases alter the immune-inflammatory response, which, when treated with conventional drugs, leads to cumulation with the development of allergies. Analysis of a case of toxic-allergic dermatitis in a patient in the regional phase of primary myelofibrosis provoked by furosemide.
Methods: A 62-year-old male with hepatosplenomegaly on the background of acute myelomonoblastic leukaemia, a permanent form of atrial fibrillation, pulmonary hypertension of the second art., chronic heart failure (CHF) of the first art., bilateral hydrothorax and hydropericardium. Against the background of adding furosemide 100-140mg per day to the complex therapy, blisters and erosions appeared during the day, accompanied by severe lymphorrhea.
Results: The results of the biopsy revealed necrosis with the formation of pustules, perivascular mixed infiltrate with a predominance of neutrophilic and eosinophilic granulocytes, destruction and infiltration of the vessel walls by granulocytes, and fibrin deposits in the vessel walls.
Conclusion: The appearance of severe toxic-allergic dermatitis is due to the reaction to the introduction of furosemide against the background of an altered immuno-inflammatory response, since the chemical structure of furosemide contains sulfone groups that give cross-allergic reactions.

E-PS-06 Digestive Diseases Pathology - GI

E-PS-06-002
Clear cell sarcoma-like tumour of the small intestine presenting as an intussusception in an adult patient: a case report
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Background & objectives: Small intestinal Clear Cell Sarcoma-Like Tumour (CCSLT) is a rare malignant neoplasm exhibiting melanocytic differentiation at a morphological, immunohistochemical and ultrastructural level with a distinct molecular profile. The clinical presentation of intussusception is uncommon with only one previous case described.
Methods: Clinical case review and review of the literature.
Results: We present a case of a 56 year old lady who presented with acute abdominal pain and tenderness. CT abdomen and pelvis showed an area of intussusception at the ileocaecal junction. The patient subsequently underwent a right hemicolectomy. Macroscopic examination confirmed the presence of intussusception within which a solid mass was identified. Microscopy showed a poorly differentiated neoplasm with solid growth pattern. The tumour was positive for S100, Sox 10 and CD56 on immunohistochemical analysis. A metastatic malignant melanoma was excluded clinically. Molecular testing confirmed the presence of EWSR1-CREB1 gene fusion, confirming the diagnosis of primary small intestinal clear cell sarcoma-like tumour.
Conclusion: Small intestinal clear cell sarcoma-like is a rare and aggressive neoplasm that affects young adults. Whilst uncommon, it needs to be considered as primary cause of intussusception in adults.

E-PS-06-003
Fatal outcome due to sarcina ventriculi infection in a case of emphysematous gastritis
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Background & objectives: Sarcina ventriculi is an extremely rare pathogen. These gram-positive cocci bacteria are rarely identified in gastric biopsies and usually described in the literature as an incidental finding, particularly in patients with delayed gastric emptying, gastroparesis, emphysematous gastritis or gastric perforation.
Methods: Fewer than 30 cases of human infection have been described in the literature so far, but rarely this microorganism is mentioned as a potential cause of death. We report the case of a 76-year-old patient with gastric perforation due to massive infection with Sarcina ventriculi. To date, this is the first report of human infection with Sarcina ventriculi in Romania.
Results: A 76-year-old male with severe abdominal pain was admitted for evaluation. CT scan showed a large pneumoperitoneum with parietal tear along the lesser curvature of the stomach. During the surgical procedure in which the perforation of the gastric wall was repaired, tissue samples were subsequently sent to the Pathology Department. Histopathological examination revealed marked acute inflammation, haemorrhagic areas and extensive necrosis of the fatty tissue. There was abundant bacterial overgrowth, including the presence of Sarcina microorganisms with characteristic microscopic features. Many such bacteria were present in the blood capillaries of the analysed fragments. Unfortunately, the patient died shortly after surgery, due to the complications induced by sepsis and multiorgan failure.
Conclusion: Although the pathogenesis of Sarcina spp. is well studied in veterinary literature, its role in human disease is not entirely understood and very few scientific studies identify this microorganism as a potential cause of death.

E-PS-06-004
Medullary carcinoma of the intestine in combination with intestinal lymphangiectasia leading to severe malabsorption syndrome
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Background & objectives: Clinical case of medullary carcinoma (MC) of the intestine in combination with intestinal lymphangiectasia at the 33-year patient accompanied by malabsorption syndrome during 10 years who died due to multi-organ failure.
Methods: Histological examination was made of the autopsy material. Immunohistochemistry was performed for the differential diagnosis

between low-grade adenocarcinoma, mesothelioma, T-cell and B-cell lymphomas, gastrointestinal stromal tumours.
Results: The diagnoses of lymphomas (CD45, CD20,CD3,CD8,CD30 negative), mesothelioma (Calretinin negative reactions), gastrointestinal tumour (DOG1, CD117 negative – non-specific staining in extra calls), neuroendocrine carcinoma (CD56, Chromogranine negative) were rejected. The tumour was positive to PDL1(+ve)/CK7(+ve)/CD10(+ve)/Vimentin(+ve)/CD10(+ve)/HgoD1(+ve)/PanMel(+ve)/MCK(+ve)/SATB2(+ve), that was typical for MC. The combination of MC of the intestine in combination with intestinal lymphangiectasia leaded to abnormality in absorption of food nutrients across the gastrointestinal tract and manifested as severe malabsorption syndrome
Conclusion: Taking into account the localization of the tumour, as well as its morpho-immunophenotypic characteristics, the neoplasm was verified as medullary carcinoma of the intestine. The tumour was characterized by a high malignant potential: clinically rapid progression and early metastasis to regional lymph nodes, histologically and immunohistochemically - a high proliferation index and mitotic index.

E-PS-06-005
The morphological changes of extraintestinal organs by the bacterial translocation in rats during of disruption of the mesenteric blood flow and reperfusion
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Background & objectives: The aim is studying morphology of internal organs by the bacterial translocation during of ischemia and reperfusion in rats.
Methods: 40 male rats were separated into 3 groups:1st(n=15)- 30/60min ischemia/reperfusion,2nd(n = 15)-30/120 min ischemia/reperfusion,3rd (n=10) –sham group. Mesentery ischemia was made by clamping mesenteric artery, Reperfusion was lead by removing clamps.BT was examined after injecting of fluorescent E.coli by microbiological method in organs. Morphological study (liver and lung) were observed by "Leica DM 1000" microscope. Significance of differences was determined by Fisher's exact test.
Results: in group 1 the positive BT was in 12(80%) of cases, mean a while histological frank full-blooded sign of liver central vein with saved structure with forming the lymphoid follicles in lungs were observed. In 2nd group with 2 hours of revascularization, BT was found in 11 (71%) of rats, morphologically the full-blooded sinusoids and veins in liver and lymphoid infiltration in lungs were revealed too. The aren't significance differences of BT frequency between 2 experimental groups (p>0,05). The organs of sham-operated rats were intact and BT was not detected.
Conclusion: Thus, the changes of morphological structure liver and lungs are similar and depend on fact of BT, but don't depend on length of ischemia-reperfusion period.

E-PS-06-006
Sprue-like enteropathy associated with Olmesartan
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Background & objectives: Sprue-like enteropathy associated with Olmesartan (Angiotensin II Receptor Blocker) was first described in 2012 and patients typically present with diarrhoea and sprue-like histopathologic findings, which can begin months or years after having started taking it.
Methods: A retrospective study of patients with olmesartan-induced enteropathy diagnosed in our hospital in the last two years was performed. Medical records and H&E stained slides were reviewed, paying special interest in GI symptoms, time from onset till first visit and duration of Olmesartan use before symptoms.
Results: Four cases were found, all of them had diarrhoea and weight loss; three also had vomiting. Gastroscopy displayed only mild gastritis in all cases.
Histologically duodenal villous atrophy and apoptosis were found in all cases and intraepithelial lymphocytes were increased in three cases.
The time from onset symptoms till first visit was 3-8 weeks and the duration of olmesartan use before symptoms was 4-8 years. The follow-up was 3-11 months.
Conclusion: Olmesartan-associated sprue-like enteropathy is a recently described entity clinically featured by severe diarrhoea and weight loss, and histopathologically by intestinal villous atrophy, variable intraepithelial lymphocytosis and inflammation of lamina propria. Our cases were also associated with chronic gastritis.
Cessation of olmesartan results in complete resolution of clinical and histologic features.

E-PS-06-007
14 cases of resected pancreatectomies after neoadjuvant treatment for primary unresectable ductal adenocarcinomas
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Background & objectives: Pancreatic adenocarcinoma is an aggressive malignancy whose only potentially curative treatment is surgery. Most cases are unresectable because of distant metastases or vascular invasion. Neoadjuvant therapy (NAT) is used as an effort to downstage locally advanced tumours, allowing surgical resection.
Methods: We present a retrospective study of patients diagnosed with locally advanced pancreatic carcinoma treated with NAT and subsequently operated from 2017 to 2019. Changes in radiological and pathological TNM stage and adjuvant treatment were reviewed, paying special interest in tumour regression degree (modified Ryan Scheme), presence of positive nodes, margins status and occurrence of relapses.
Results: Fourteen cases were found aged between 44 and 81. One case showed total response to treatment (GRT0); 10 cases, partial response (GRT2) and 3 cases, low response (GRT3). Nine cases showed positive nodes, 7 of which were not imaged detected previous to NAT. Surgical resection margins were negative in eleven cases. 6/12 cases that received post-adjuvant treatment developed posterior locoregional relapses or distant dissemination (average time to follow-up 10 month)
Conclusion: NAT allows a potentially curative surgical treatment of locally advanced pancreatic tumours, reduce tumour volume and allows negative resection margins. Accurate measurement of tumour size and consequently staging after NAT is difficult; therefore tumour regression grade becomes more relevant.
Imaging tests have limitation for the detection of nodes suspected of infiltration

E-PS-06-009
Collision tumour of the stomach: choriocarcinoma and adenocarcinoma in an elderly woman
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Background & objectives: Gastric choriocarcinoma accounts for less than 0.1% of gastric cancers, almost always showing admixed adenocarcinoma. We present a case of a 78 year-old woman with recurrent upper digestive tract haemorrhage and subsequent severe anaemia.

Methods: The patient underwent upper endoscopy which revealed a large tumour located in the proximal portion of the stomach. Biopsies were taken and showed moderately differentiated adenocarcinoma. The CT scan identified numerous enlarged perigastric lymph nodes, hepatic and peritoneal metastases. Beta hCG levels were not preoperatively determined. Palliative gastrectomy was performed, as the patient did not respond to conservative therapy.
Results: The specimen showed an 11 cm sessile, ulcerated tumour, located along the lesser curvature of the stomach, also involving the gastroesophageal junction. Microscopically, the tumour had two discrete components: the distal part of the tumour consisted of tubulopapillary adenocarcinoma, while the proximal portion of the mass was represented by choriocarcinoma. The latter showed cytotrophoblastic nests/sheets inconstantly rimmed by syncitiotrophoblast, with wide areas of haemorrhage and necrosis, and was vaguely reminiscent of squamous cell carcinoma, particularly because it also involved the oesophageal squamous mucosa. The choriocarcinomatous differentiation was confirmed by immunohistochemical stains, which revealed positivity for hCG, PLAP, CK7 and p63.
Conclusion: Gastric choriocarcinomas are aggressive, frequently haemorrhagic tumours. Thus, preoperative diagnosis is important and can be established through adequate bioptic samples and preoperative hCG levels. They may also mimic squamous cell carcinoma, but careful evaluation and immunohistochemical stains clarify this issue.

E-PS-06-010
Metastatic melanoma to an ileostomy reversal specimen – an incidental finding

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Background & objectives: A 57-year-old male patient with a known history of rectal adenocarcinoma, treated with neoadjuvant radiotherapy and low anterior resection, presented to our clinic for a programmed ileostomy reversal procedure.
Methods: The fixed ileal segment was examined. Two discrete indurated areas were found close to the resection margins. They showed focal haemorrhage on cut section and were entirely submitted. Microscopically, two intramural well-circumscribed deposits of 1 and 0,5 cm were found; sheets of pleomorphic epithelioid cells with cytoplasmic granular brown pigment and prominent nucleolated nuclei eroded the overlying mucosa.
Results: The morphology was consistent with metastatic melanoma. According to the clinician, a previous diagnosis of dysplastic nevus was made three years earlier in another unit. This cutaneous tumour, located on the anterior chest wall, was completely excised. Because no other radiologic or endoscopic abnormalities were found during admission, three-month follow-up was decided. Unfortunately, the patient presented shortly before with massive upper digestive haemorrhage. Similar deposits were found along the resected duodenal specimen and in a liver biopsy performed once the patient was stable.
Conclusion: Careful macroscopic examination of seemingly bland specimens is of paramount importance in daily practice, especially because complete patient history may sometimes be lacking at the time of processing. In our case, thorough sampling led to better patient care, with targeted therapy being considered at the moment by the multidisciplinary team. Additionally, closer dermatology follow-up should be considered in patients with dysplastic nevi.

E-PS-06-011
Unusual histopathological findings in cystic lymph node

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Background & objectives: The aim of this article is to report two cases of unusual histopathological findings in lymph nodes of the gallbladder due to fungal infection and metastatic colon primary tumour.
Methods: The first case is a 45-years-old female, who had a recent trip to North America and consulted for epigastric pain, paresthesias in the upper limbs and asthenia. The second case is a 60-years-old female, who had history of colorectal cancer and consulted for pain in the right hypochondrium of sudden onset that got worse when feeding.
Results: In the cystic lymph node of the first case were observed round fungal microorganisms that had spherules containing endospores. The histochemistry study showed that the microorganisms were PAS positive but were negative for Grocott's methenamine silver stain and mucicarmine. Because of these findings, diagnosis of coccidioidomycosis was made. In the cystic lymph node of the second case were observed epithelial tumour cells and lymphovascular invasion of soft tissues. Immunostaining for cytokeratin 20 and CDX2 were positive in contrast with cytokeratin 7 that was negative. Those findings suggested a metastasis of colorectal cancer.
Conclusion: Despite infectious and metastatic processes in lymph nodes of the gallbladder are very rare findings they should be considered when making differential diagnosis to ensure a prompt clinical intervention

E-PS-06-013
Incidental gallbladder tumours and pseudotumours in cholecystectomy specimens: a retrospective study of 40 cases

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Background & objectives: Gallbladder tumours display a wide range of histological subtypes. Gallbladder polyps are classified as benign or malignant. In this study, we investigated the characteristics of incidental benign and malignant gallbladder tumours in our institution.
Methods: We retrospectively reviewed all of the cholecystectomy specimens in the archives of the Pathology Department in the University Hospital Mongi Slim during a twelve-year period (January 2008-January 2020). The clinicopathological characteristics were extracted from the patients' clinical charts, which included symptoms, radiological findings, laboratory data, and surgical procedures as well as the outcome.
Results: There were 13 men and 27 women (sex-ratio M/F = 0,48) aged between 24 and 76 years (mean = 65 years). All patients underwent cholecystectomy (either open or laparoscopic). Histological examination of the surgical specimens established the diagnosis of adenoma in five cases, cholesterol polyps in six cases, intestinal-type adenocarcinoma in 26 cases, adenosquamous carcinoma in two cases and neuroendocrine carcinoma in one case.
Conclusion: Only 30% of gallbladder carcinomas are suspected preoperatively, and the remaining 70% are usually discovered incidentally by pathological examination during or after surgery. Gallbladder cancer has a poor prognosis because of its late diagnosis. Thorough sampling and careful attention on histological examination of all parts of cholecystectomy specimens allow the detection of early cancer with a better prognosis.

E-PS-06-014
A case report of indolent T-cell lymphoproliferative disorder of the gastrointestinal tract – a rare differential to consider in gastric biopsies

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Background & objectives: Indolent T-cell lymphoproliferative disorder (T-LPD) of the gastrointestinal tract is a rare provisional entity in the revised WHO classifications. It has a clonal nature and indolent behaviour, primarily affecting the small intestine and colon.
Methods: A 59-year-old African male, with HBV infection in the past, presented with nausea and weight loss, associated to long-standing postprandial fullness. Physical examination was unremarkable. An upper gastrointestinal endoscopy with biopsies was performed.
Results: Thickened gastric folds and mottled mucosa were observed endoscopically. Morphology showed diffuse infiltration of gastric mucosa by a monotonous population of small lymphoid cells, expressing CD3, CD5, Bcl-2 and CD8, without expression of CD10 and CD20, and low proliferation index. No intraepithelial lesion, glandular disruption, inflammatory activity or intestinal metaplasia were seen. Immunohistochemistry for H. pylori was negative. Morphology and phenotype were consistent with indolent T-LPD of the gastrointestinal tract. Clonal TCR rearrangement analysis is under progress. Peripheral blood analysis showed mild lymphocytosis. Bone marrow biopsy was normal. Thoracic, abdominal and pelvic CT showed no evidence of lymphadenopathy or extranodal disease.
Conclusion: We herein present a case of gastric involvement by T-LPD. Indolent T-LPD of the gastrointestinal tract poses a range of differential diagnosis between an inflammatory/non-neoplastic process and lymphoma, and its treatment and natural history are not yet fully established. Our case had exclusive gastric presentation, in contrast with most of previously reported cases, which were localized in the lower gastrointestinal tract.

E-PS-06-015
Somatostatin-producing NET of the ampulla of Vater: a case report
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Background & objectives: Somatostatinomas are functioning well differentiated neuroendocrine neoplasms, with uncontrolled somatostatin secretion causing somatostatinoma syndrome, whereas somatostatin-producing NETs are tumours composed of somatostatin-immunopositive cells but lacking the symptoms of somatostatinoma syndrome.
We report a case of somatostatin-producing NET of the ampulla.
Methods: Our patient, a 64-year-old man, presented with weight loss and mild indigestible disorders.
Endoscopic ultrasound and CT scan revealed a 2 cm ampullary tumour with dilatation of both the distal common bile duct and the main pancreatic duct.
A pancreaticoduodenectomy was performed.
Results: Macroscopically, an intramural mass was found in the ampullary region, measuring 1.8 cm in maximum diameter.
Histologically, the tumour was predominantly composed of tuboglandular structures, with numerous psammoma bodies.
Immunohistochemically, the tumour cells were positive for ker8/18, synaptophysin, chromogranin and somatostatin. The Ki-67 proliferative index was 1%.
Histological and immunohistochemical features were consistent with a somatostatin-producing well-differentiated neuroendocrine tumour, grade 1. Our patient received no further treatment and remain alive, 1 year after initial diagnosis.
Conclusion: Somatostatin-producing NETs of the ampulla and periampullary region typically manifest with symptoms related to bile duct obstruction, abdominal pain and cholelithiasis, whereas somatostatinoma syndrome is rarely observed. They have also been associated with von Recklinghausen disease.
Histologically, the glandular pattern and psammoma bodies may cause confusion with well-differentiated adenocarcinoma.
The treatment of choice is surgical resection. Tumours that are <2 cm or limited to the ampulla have a better prognosis.

E-PS-06-016
Neuroendocrine cell hyperplasia in colonic mucosa of patients with inflammatory bowel disease
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Background & objectives: Neuroendocrine cells (NEC) of the intestinal mucosa seem to play an important role in the pathophysiology of inflammatory bowel disease. The aim of this study is to evaluate the density of NEC in the colorectal mucosa of patients with IBD.
Methods: 52 patients with IBD (27 UC, 25 CD) and 49 patients screened for colorectal cancer underwent lower GI endoscopy. Two biopsies from every segment of the large intestine were taken. Immunohistochemical staining for synaptophysin (Syn), chromogranin A (CrA) and serotonin (5-HT) was performed. The number of neuroendocrine cells was counted manually for all crypts and expressed as a mean density/crypt/patient.
Results: In IBD patients, IHC reveals a patchy and superficial distribution of the NEC, forming nests of 3-5 cells and small nodules. The mean densities of CrA, Syn and 5-HT were significantly higher (1.84, 1.22, 0.91 NEC/Crypt) compared to the control group (1.01, 0.62, 0.37 NEC/Crypt), $p<0.05$. Each large intestine segment showed a significantly higher mean density of NEC, for all neuroendocrine markers ($p<0.01$).
We analysed the distribution of NEC according to their neuroendocrine expression: the highest density of CrA and serotonin was expressed in the rectum.
There was a significantly higher density of NEC positive for 5-HT in rectal mucosa of patients with UC than in patients with CD.
Conclusion: This study proves that in patients suffering from IBD there is a hyperplasia of NEC, evaluated on a significant, large number of crypts. Moreover, NEC positive for 5-HT might be a novel therapeutic target and could explain the symptoms associated with IBD. There is limited data regarding the density distribution of NEC in IBD patients and further studies are necessary.

E-PS-06-017
Common variable immunodeficiency and gastric cancer: a study of morphology, virus infection and immunological microenvironment
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Background & objectives: Patients with Common Variable Immunodeficiency (CVID) have a 6/10-fold risk of developing gastric carcinoma (GC), which represents the most common cause of death in this population. Objective: analysing histopathology, Helicobacter pylori,

Epstein-Barr-virus(EBV), Cytomegalovirus(CMV) infection and immunological microenvironment in CVID-associated GC.
Methods: Non-neoplastic mucosa (Non-NM) and GC from six CVID patients, four females, median age: 41.5y (range 27-62y), with previous diagnosis of infection by H. pylori (4/6), CMV (3/6) and EBV (2/6) and pernicious anaemia (2/6), were analysed by RNA in situ hybridisation (ISH) for EBV and immunohistochemistry (IHC) for CMV, CD20, CD4, CD8, FOXP3 (Treg-cells), GATA3 and PD-L1.
Results: Non-NM showed lymphocytic gastritis(6/6), atrophic gastritis (6/6) with active inflammation (2/6), lymphoid aggregates (3/6) and/or intestinal metaplasia (5/6). Most patients were diagnosed at early-stage: pT1a (n=3); pT1b (n=2); pT2 (n=1). Histopathology showed tubular (n=3), mucinous (n=2) and poorly cohesive (n=1) histotypes, with intestinal-type adenoma in two cases. EBV-ISH and CMV-IHC were negative in all cases. Digital automated counting of immune cells (nº positive cells/20x power-field) showed abundance of CD4+, GATA3+ and CD8+ T-cells in non-NM(stroma:245/152/181; intraepithelial:8/23/46) and CD4+, CD8+ and FOXP3 T-cells in GC (stroma:133/48/46; intraepithelial:27/33/26). Non-NM and GC immune infiltrate showed paucity of CD20+ B-cells (stroma:32/5; intraepithelial:0/0). PD-L1 was expressed exclusively in GC stromal cells: <1%(n=2); 1-10%(n=3); 10-50% (n=1).
Conclusion: We found that CVID-associated GC featured marked T cell infiltration in the absence of EBV/CMV, with heterogeneous expression of PD-L1 and high frequency of GATA3+ and FOXP3+ cells.

E-PS-06-018
An unusual case of osseous metaplasia in a metastatic colorectal carcinoma with endochondral ossification
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Background & objectives: Osseous metaplasia in colorectal carcinoma is a rare occurrence with incidences ranging from 0.15% to 0.4%. Although several articles report cases of such instances, very few cases with heterotopic ossification in metastatic colorectal carcinoma have been reported.
Methods: We present the case of a 60-year-old male patient with advanced metastatic colorectal carcinoma presenting with a hypogastric eventration adjacent to a terminal surgical stoma with suspected secondary lesions.
Results: The patient underwent right hepatectomy and liver lobectomy two years ago for metastasis and was currently being treated with chemotherapy. Prior to surgery, positron emission tomography-computed tomography showed an additional liver lesion as well as calcifications on the midline of the anterior abdominal wall, consistent with the suspected peristomal secondary lesions. Histopathological examination of the aforementioned lesions showed multiple metastases of colorectal carcinoma with extensive osseous metaplasia and focal cartilaginous endochondral ossification.
Conclusion: Heterotopic ossification or osseous metaplasia is defined by the extra-skeletal formation of bone tissue. This phenomenon is widely found in a variety of neoplasias, benign or malignant in nature. Studies suggest that a stromal pluripotent cell transformation into osteoblasts is involved rather than tumour cell differentiation. This case report underlines the possibility of bone formation in colorectal cancer metastases with diagnostic relevance to radiologists, oncologists, and gastroenterologists.

E-PS-06-019
Endothelial NOVA2 expression in gastric cancer as a prognostic factor
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Background & objectives: NOVA2, a splicing regulator with a role in angiogenesis and vascular development, is up-regulated in ovarian and colorectal carcinomas. The aim of the study is to assess its expression in gastric carcinomas and its correlation with clinico-pathological features.
Methods: Twenty-seven consecutive AGCs, treated only with surgery, in 1986 were immunohistochemically investigated for NOVA2 expression as well as ERG (endothelial specific marker) and mismatch repair proteins. Positive NOVA2 nuclei were counted along tumour invasive margin in five consecutive HPFs and the mean value was calculated. NOVA2 values were correlated with clinico-pathological features and statistical analysis was performed with SPSS.
Results: NOVA2 expression was observed in ECs inside the tumour and in the surrounding tissue, but not in tumour cells. A direct correlation between NOVA2 and ERG was found (R^2 = 0.5845, p<0 .001).
High levels of NOVA2 (>33 cells/HPF) are most frequently found in association with lymph-node metastases (p=0.07), intestinal-type GCs (p=0.024), stage III disease (61%) and mismatch repair (MMR) proficient system (57%). After a 20 years follow-up high levels of NOVA2 had a significant association to cancer-related death (p=0.007). Both diffuse histotype and high expression were unfavourable independent prognostic factors, at multivariate Cox regression analysis.
Conclusion: Advanced Gastric Cancer (AGC) has a limited number of therapeutic weapons, but from surgery. Thus, it is fundamental to identify new specific targets for therapy. As it was seen for ovarian and colorectal carcinomas, our data demonstrates that high levels of NOVA2 are related to poor prognosis and may affect AGCs progression. NOVA2 and its products, from alternative splicing, could represent a novel target for new therapeutic strategies.

E-PS-06-021
Malignancies that metastasise to the stomach
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Background & objectives: Metastasis to the stomach from other solid organs is extremely rare and this rate ranges from 0.2%-1.7% in clinical and autopsy studies. In the few studies found in the literature, lung and breast are the leading organs that metastasize to the stomach.
Methods: Clinical and histopathological findings of secondary gastric malignancies diagnosed with endoscopic biopsy and / or gastrectomy at the U.H.S Istanbul Training and Research Hospital pathology clinic were analysed.
Results: 39280 endoscopic biopsy materials from the six year period between 2013-2019 were scanned. A total of 10 metastatic lesions were detected. 4 of the cases were female and 6 were male and the average age was 60. Most of the lesions were localized in corpus and two showed multifocal involvement. Histopathologically, 4 cases were malignant melanoma, 3 cases were squamous cell carcinoma, 3 cases were adenocarcinoma,4

of them has skin origin, 4 had lung origin, and 2 were tumours with breast origin.
Conclusion: Since metastatic lesions in the stomach are frequently seen in patients with widespread disease, it is very critical to make an accurate diagnosis in treatment management because their prognosis is often poor.

E-PS-06-022
The role of cancer stem cells in gastrooesophageal junction adenocarcinoma
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Background & objectives: Gastroesophageal junction adenocarcinomas (GEJA) have increased in incidence in recent years and are associated with adverse clinical outcomes. We sought to determine the role of epithelial mesenchymal transition (EMT) and cancer stem cells (CSC) within aggressive areas of these tumours.
Methods: Paired samples were taken from 'indolent' and 'aggressive' areas of tumour from each patient, as defined histologically. Each sample was analysed using RT-PCR and immunohistochemistry to determine the mRNA, miRNA and protein expression patterns associated with EMT and CSC. Differences in expression patterns between paired samples were analysed. Additionally, these expression patterns were correlated with clinical outcomes for each patient.
Results: Our molecular studies identified a range biomarkers expressed in GEJA which were significantly associated with adverse clinical outcomes, including tumour regression grade, disease recurrence, overall survival and disease free survival. These biomarkers showed potential for use as prognostic biomarkers individually, or as part of a combined predictive model. Additionally, interrogation of mRNA and miRNA expression data revealed a number of signalling pathways involved in regulation of CSCs in GEJA.
Conclusion: Biomarkers of EMT and CSCs hold great promise in GEJA as prognostic aids and in development of drug therapies. Presently, GEJA are often treated with therapies designed for gastric and/or oesophageal adenocarcinomas, yet it is believed that GEJAs represent a biologically distinct subset of tumours. In light of the aggressive characteristics associated with CSC and EMT, accurate delineation and a greater understanding of these processes in GEJA is important to improve our treatment of patients with this disease.
Funding: BDIAP Trinity Translational Medicine Institute Trinity College Dublin

E-PS-06-023
Concomitant bifocal Kaposi sarcoma with tubular adenoma and hyperplastic polyp in a background of ulcerative colitis
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Background & objectives: Kaposi sarcoma is a Human Herpes Virus-8 associated vascular neoplasm characterized by spindle cell growth with formation of erythrocyte containing clefts. Incidence rate approaches 50% in immunocompromised individuals. Occurrence as primary colonic neoplasm is very rare with concomitant polyps.
Methods: We present the case of a 36 year male who was a known case of ulcerative colitis with long term immunosuppressive therapy and developed complications of steroid use. Grossly total proctocolectomy specimen received comprising of terminal ileum to rectum. One pseudopolyp is identified in transverse colon. One polyp is identified in descending colon. 04 polyps are identified in rectum
Results: Microscopy of descending colon polyp and smaller rectal polyp revealed a fascicular spindle cell lesion in submucosa with extravasated red blood cells and frequent mitoses. Cells demonstrated positive expression of CD31, ERG and focal HHV-8 positivity. Section from larger rectal polyp shows features of tubular adenoma and sections from transverse colon polyp shows hyperplastic polyp. Rest of the bowel shows features of ulcerative colitis.
Conclusion: Kaposi sarcoma with coexistent polyps of different types in ulcerative colitis is extremely rare. Immunosuppression with inflammatory bowel disease predisposes to the development of KS.

E-PS-06-024
Pouch associated cancer: an usual cancer in a rare location
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Background & objectives: An 60 y.o. woman with history of ulcerative colitis that was subject to total colectomy 30 years ago. Subsequent biopsies from the pouch showed marked inflammation without dysplastic change. During follow-up a polypoid mass was identified and biopsies were taken.
Methods: Multiple whitish biopsy segments from the pouch were received on maximum diameter 0,1 to 0,3cm.
Microscopical examination of the tissue was performed.
Results: Microscopic examination was consistent with a high grade adenoma -like dysplasia associated lesion or mass (DALM) with concurrent transformation to an invasive low grade adenocarcinoma
Conclusion: A meta analysis from thirty-four articles reported a cumulative incidence of pouch-related adenocarcinomas at 0.33% 50 years after the diagnosis and 0.35% 20 years after IPAA. In our case the previous biopsies showed no dysplastic-changes. In tandem with the presumed evolution of these adenocarcinomas from dysplastic precursor lesions maybe there is a need for general rather than specific surveillance as it might offer a time window for cancer prevention.

E-PS-06-025
A rare case of immunoglobulin G4-related oesophagitis mimicking dysplasia
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Background & objectives: IgG4-related disease is an autoimmune systemic condition characterized by tumour-like lesions with intense lymphoplasmacytic infiltrate and abundant IgG4-positive plasma cells. Oesophageal involvement is exceptional and only a few cases were reported so far.
Methods: We report a case of an 81-year-old man, operated 5 years prior for a squamous cell carcinoma of the lower third of the oesophagus (pT1), whose surveillance endoscopy showed a circumferential erosive lesion, above the gastro-oesophageal anastomosis. The first biopsies revealed severe ulcerative oesophagitis and areas described as suspicious for high-grade epithelial dysplasia. Subsequent biopsies were assessed in our department.

Results: Histologically, a wide area of the epithelium showed ulceration. In its lower third, adjoining the ulcerative lesion, the oesophagus lining was thinner, depicting features of cytonuclear atypia. However, in the context of acute inflammation, these alterations were rather in keeping with the diagnosis of indefinite for dysplasia, probably regenerative. Accompanying these findings, an unusual inflammatory infiltrate, rich in plasma cells, was observed in the sub-epithelial connective tissue. Immunohistochemistry showed >150 IgG4-positive plasma cells/HPF and the ratio of IgG4+/IgG+ plasma cells >80%. This allowed to make the diagnosis of IgG4-related oesophagitis.
Conclusion: Considering the lack of specific findings and its rarity, IgG4-related oesophagitis can be overlooked or misinterpreted as dysplasia, as shown herein in this patient with cancer history. Immunohistochemistry is mandatory to confirm the diagnosis and to provide adequate treatment.

E-PS-06-027
Cyclooxygenase-2 expression in colorectal carcinoma and corresponding normal colorectal tissues
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Background & objectives: Most available data suggest a prognostic role for cyclooxygenase-2 (COX-2) in colorectal carcinoma (CRC) in populations where this has been studied. Similar studies among the black population are scarce, thus necessitating this study.
Methods: Sectioned formalin-fixed paraffin-embedded colectomy tissues from CRCs and their corresponding non-tumour margin-of-resection were stained with COX-2 antibody and scored for percentage of stained cells (<5%=0; 6%-25%=1; 26%-50%=2; 51%-75%=3; 76%-100%=4) and intensity (no staining=0; yellow=2; yellowish-brown=3, brown=4). Total immunoscore (percentage + intensity score) ≥4 was classified positive (COX-2 overexpression). Clinicopathological data were statistically evaluated to determine COX-2 expression-associated and predictor variables.
Results: Ninety-five (95) CRC cases and 27 corresponding non-tumour tissues were included in this study. The overall patient mean age was 56.1 ±12.6years with a male-to-female ratio of 1.1:1.
COX-2 was differentially overexpressed in CRCs 69/95 (72.6%) whilst in non-tumour tissues 5/27 (18.5%) showed COX-2 overexpression. this difference was statistically significant ($p < 0.0005$). The histologic tumour grade, advanced pT-stage, tumour-infiltrating lymphocytes, and dirty necrosis were significantly associated with COX-2 expression ($p < 0.035$; 0.043, 0.035 and 0.004, respectively). Multivariate analysis showed that dirty necrosis (OR, 0.006; CI: 0.000-0.21) and crohn-like lymphocytic aggregates (OR, 11.312; CI: 1.652-77.45) were predictors of COX-2 expression ($p < 0.05$).
Conclusion: Our finding suggests that COX-2 is significantly overexpressed in CRCs compared to non-tumour colorectal tissues. Its significant association and relationship with tumour-associated lymphocytes, and, also, higher tumour grade and pT-stage, suggests a modulation of tumour immunity favouring tumour progression.

E-PS-06-028
Lymphoid cells containing Russell bodies as a prognostic factor in the survival of patients with gastric cancer
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Background & objectives: Lymphoid cells containing aggregated immunoglobulins in the form of Russel bodies (RB) are found in a variety of diseases. The aim is to evaluate the possibility of using RB-cells as a prognostic criterion for the immune response in gastric cancer.
Methods: The authors of the study collected 40 cases of gastric cancer with various morphological forms, divided into groups with short (1-2 years) and long (up to 10 years) postoperative survival. The material was stained with the three-color Masson method in combination with alcian blue at ph = 1.0. Electron-microscopic and immunohistochemical studies were performed selectively.
Results: In a retrospective study of a group of patients with long postoperative survival, regardless of the histological form of cancer, a significantly larger ($p < 0.01$) number of cells with Russel bodies in their mucous layer was recorded compared with a group of patients with short postoperative survival.
Conclusion: The data obtained expand the idea of the participation of cells with Russell's bodies in the antitumor reaction of local gastric immunity as a prognostic factor in the survival of patients with gastric cancer.

E-PS-06-029
Immunohistochemistry and molecular analysis of colorectal cancer in young patients
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Background & objectives: Microsatellite instability (MSI) is a recognized pathway in the development of colorectal cancer. Its diagnosis can be made through immunohistochemistry or PCR. We conducted a comparative study to find out the difference between these two methods regarding MSI detection.
Methods: In total, 59 colorectal cancer cases were studied for meeting at least one of the revised Bethesda criteria. In all cases, the expression of DNA repair proteins (MLH-1, MSH2, MSH-6 and PMS-2) was evaluated by immunohistochemistry. Real-time PCR of DNA repair proteins was conducted in all of them using the IdyllaTM Biocartis system.
Results: cases studied, the average age was 39.7 years, the most frequent side of tumour presentation was the left (54.23%) and the most frequent variety found was intestinal (50.84%). According to the results, 24 (40.67%) presented alterations in at least one of the DNA repair proteins through immunohistochemistry. The remaining 35 cases (59.32%) did not present any alteration. In the molecular analysis through PCR for all cases, 17 (28.81%) presented MSI-high phenotype and 42 cases (71.18%) were stable. Sen = 70.83%, Spe = 83.33%, PPV = 70.83%, NPV = 83.33%.
Conclusion: Immunohistochemistry has a good specificity to be used as a screening method. In case of an altered or inconclusive result, it is necessary to perform a molecular test to confirm the diagnosis. It is advisable to perform any diagnostic test available to all patients with colorectal cancer that are under 50 years of age, since MSI findings modifies patient management.

E-PS-06-030
A case of small bowel intussusception in an adult caused by heterotopic gastric mucosa in the jejunum: a case report
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Background & objectives: Intussusception is a common gastrointestinal emergency in paediatric patients. In adult it is rare and mostly caused by malignancy. we report an extremely rare case of intussusception in 20- year old boy caused by heterotopic gastric mucosa in the jujenum.
Methods: A 20 year old boy presented to the emergency department with one day history of abdominal pain, localized to right iliac fossa. . Computed tomography of the abdomen and pelvis showed a small bowel intussusception, likely involving distal ileal loops with severe dilatation. Subsequent emergency surgery revealed jejuno-jejunal intussusception with grossly dilated proximal small bowels with fecalization.
Results: The resected jejunum was opened to reveal a large protruding polypoidal mass seen in mucosal surface measures 3.5x2x2 cm. Cut section shows an invaginated thickened wall. Microscopic examination showed heterotopic gastric mucosa and heterotopic submucosal mucous glands composed of oxyntic-type gastric mucosa. The overlying foveolar epithelium exhibited a hyperplastic change. No dysplasia, malignancy, or Meckel diverticulum was present. The background small intestinal mucosa showed extensive mucosal ischemic change secondary to intussusception.
Conclusion: Approximately 90% of adult intussusceptions have an organic cause, malignant neoplasm being the most common. Jejunal heterotopic gastric mucosa is a very rare cause of intussusception among adults. A definitive diagnosis of heterotopic gastric mucosa is established by histopathological examination. Heterotopic gastric mucosa is usually clinically silent and surgical intervention can be considered in patients with complications such as gastrointestinal haemorrhage and intestinal obstruction

E-PS-06-032
Intramucosal adenocarcinoma on foveolar-type adenoma in proximal oesophagus: a rare case report
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Background & objectives: Foveolar-type adenomas are rare neoplasm in the stomach. Extragastric sites of foveolar-type adenoma include the gallbladder, duodenum, bile duct, and oesophagus. We present a case of foveolar-type adenoma in proximal oesophagus with evolution 4 months later an intramucosal adenocarcinoma.
Methods: A 64-year-old female with medical history of acromegaly and benign thyroid follicular nodule in follow up. Cervical ultrasound examination revealed a lesion suggestive of diverticulum at the level of cervical oesophagus. In a gastroscopic study, it was found to correspond to a polyp with maximal diameter 20 mm near to an area suggestive of columnar heterotopia of gastric origin.
Results: Histologically, a polypoid lesion consisting of gastric pyloric glands was initially detected, with an intramucous adenocarcinoma focus and heterotopic gastric mucosa (Inlet patch) in the oesophagus is an embryological lesion that has been described less than 10% of gastroscopies. The most common diagnostic challenge with foveolar-type adenomas have a well-formed apical mucin cap, label immunohistochemically with MUC5AC, and are negative for MUC6, in contrast to pyloryc glands adenomas. Immunohistochemical profile revealed positive MUCA5 and focal MUC6.Althought most of them are asymptomatic, as our patient, they can cause dysphagia or hearburn; even a rare association with adenocarcinomas has been described.
Conclusion: We think the patient has a inlet patch which proliferated and degenerated into an adenoma and adenocarcinoma, a extremely infrequent sequence for this frequent disorders.

E-PS-06-033
Gallbladder metastasis from clear cell renal cell carcinoma
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Background & objectives: Gallbladder metastasis from renal cell carcinoma (RCC) represents a rare site, as to our knowledge, only 59 cases have been reported in the literature. We report a case of intraluminal polypoid metastasis of clear cell RCC (ccRCC) in the gallbladder.
Methods: We present a case of a 71 year old woman who had undergone a radical nephrectomy for ccRCC, ten years ago. A polypoid intracystic gallbladder mass was incidentally discovered on U/S and MRI examination. The radiological findings were suggestive of primary gallbladder carcinoma. Therefore, the patient undergone a laparoscopic cholecystectomy.
Results: Grossly, the gallbladder cyst revealed a tan brown exophytic polypoid mass, arising from the posterior wall of the cyst, 2,5cm in maximum diameter. Microscopically, the polypoid mass corresponded to neoplastic tissue with extensive ulceration and necrosis on the surface. The neoplastic cells were large, with abundant clear cytoplasm and small, hyperchromatic nuclei. They were arranged in nests and islets, with no evidence of cyst wall invasion. A panel of immunohistochemical markers was performed in order to determine the origin of the tumour. The neoplastic cells were positive for Vimentin, CAM 5.2, CD10, CAIX and PAX8 and negative for CK7, Inhibin, HMB45 and napsin.
Conclusion: The above morphological and immunohistochemical features are compatible with a clear cell renal cell carcinoma (RCC). Taking into consideration the known patient's medical history of such a tumour, 10 years ago, it is concluded that the neoplasm is a metastasis from the RCC. Although the radiological features were suggestive of a primary tumour, it is clear that the final diagnosis is made on pathological examination and immunohistochemistry.

E-PS-06-034
Interobserver variability and value of histological examination in the diagnosis of inflammatory bowel disease (IBD) (experience of Hassan II University Hospital Fez)
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Background & objectives: Diagnosis of IBD include a histological examination by a statistically discriminants between ulcerative colitis and Crohn's disease (CD)
The purpose of this study is to evaluate the interobserver variability and the value of histological examination in the diagnosis of IBD.
Methods: 100 cases of IBD collected in the Department of Pathology of Hassan II university hospital of Fez were reviewed independently and without endoscopic or clinical information (ECI) by three pathologists. Their diagnoses were compared to the initial diagnosis retained by knowing the ECI. Interobserver

agreement in the diagnosis of various histological evidence was evaluated.
Results: The interobserver agreement examination in the diagnosis of various histological evidence was low to medium. The diagnosis of ulcerative colitis (UC) was concordant in 63% of Crohn disease in 38% of IBD and indeterminate in 33%. The architectural changes were more marked in UC (81% of cases) than in Crohn's disease. In the latter dominate the inflammatory infiltrate and especially the basal plasmacytosis in 96% of cases.
Conclusion: This work shows poor reproducibility of the histological criteria used in the diagnosis of IBD. Apart from a consensus definition of histological criteria, the diagnosis of IBD is contingent on histological, clinical and endoscopic confrontation.

E-PS-06-035
Metastatic lobular carcinoma presenting as a sigmoid colon stricture
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Background & objectives: Metastatic breast carcinoma to the gastrointestinal tract is rare, with an estimated incidence of 0.5%. The stomach is preferentially affected; reports of colorectal involvement are limited to small case series. In the overwhelming majority of patients there is a known history of breast carcinoma and the latency period is often years to decades. We describe a highly unusual case of metastatic lobular carcinoma mimicking a primary colonic tumour in a patient with no history of breast malignancy.
Methods: -
Results: A 55-year old woman presented to her general practitioner with fatigue. She was noted to be anaemic and referred for colonoscopy, which revealed stricturing of the sigmoid colon. Biopsy showed focal infiltration of the lamina propria by discohesive malignant cells, which were positive for CK7, GATA-3 and oestrogen receptor. CK20, CDX2, E-cadherin and HER-2 were negative, in keeping with lobular carcinoma of breast origin. She was subsequently seen in the breast clinic and underwent imaging, which revealed a unilateral breast mass. Upon biopsy, this was proven to be invasive lobular carcinoma and she was referred for systemic therapy.
Conclusion: This is a rare case of metastatic lobular carcinoma presenting in the colon of a patient with no known diagnosis of breast malignancy. Metastatic lobular carcinoma is associated with a range of clinical presentations and is diagnostically challenging as it can mimic primary carcinoma of the colon. Pathologists must have a high index of suspicion to ensure distinction between primary and metastatic disease, allowing prompt treatment and preventing unnecessary surgical intervention.

E-PS-06-036
Inflammatory fibroid polyp of gastrointestinal tract: report of two cases and review of the literature
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Background & objectives: Inflammatory fibroid polyps (IFP) are rare, benign neoplasms encountered in the gastrointestinal tract (GI) with distinct pathologic features and molecular profile. Two interesting cases are reported herein, while the second is associated with an adenoma.
Methods: First case: A 73year old woman presented with symptoms of intestinal obstruction. Intussusception was diagnosed and segmental resection of the affected part of the ileum was performed.
Second case: A 59year old man presented with anaemia. A protruding mass was revealed in the antrum, treated with partial gastrectomy. In direct continuity with it, a second polypoid mass was noted.
Results: On macroscopy, the masses had a white-greyish and gelatinous cutting surface. Histopathology in both cases revealed a submucosal neoplasm with medium cellularity consisting of spindle cells in a collagenous background. Abundant inflammatory cells were scattered throughout the neoplasm, while eosinophils clustered around the blood vessels. Mitotic rate was low. Immunohistochemistry demonstrated positivity for CD34 and CD99 and no reaction for ckit, DOG1, ALK, aSMA, Ck8/18 and S100. Both cases were diagnosed as IFP. A PDGFRa mutation (exone 12) was identified via PCR. The polypoid mass above the IFP was diagnosed as a tubular adenoma with focal high-grade dysplasia. The patients are disease-free 24 months after the initial diagnosis.
Conclusion: IFP should be considered in the differential diagnosis of ckit and DOG1 negative mesenchymal neoplasms of the GI. Surprisingly, It shares the same mutations with Gastrointestinal Stromal Tumours even they do not have metastatic potential or recurrences. To sum up, IFP may have a worrisome clinical appearance but has a benign behaviour.

E-PS-06-037
Analysis of the microsatellite instability in Tunisian colorectal cancer
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Background & objectives: Colorectal Cancer (CRC) represents a health problem whose frequency is increasing. Microsatellite Instability (MSI) status in CRC has prognostic and therapeutic implications.
Our aim is to study the frequency of the MSI in CRC and to analyse the clinicopathological particularities.
Methods: It is a retrospective study including 30 cases of CRC identified in the Department of Pathology of Farhat Hached University Hospital of Sousse (Tunisia). MSI analysis was done by PCR targeting five markers of Microsatellite: BAT-25, BAT-26, D5S346, D2S123 et D17S250.
Results: This study included 17 men and 13 women. Instability of D5S346 microsatellite was uncommon (10%).
MSI analysis showed 3 statuses: MSS in 15 cases (50%), MSI-H in 11 cases (37%) and MSI-L in 4 cases (13%). MSI-H CRC were significantly more common in patients under the age of 50 ($p = 0.002$). This phenotype was more frequent among men, in the left colon, in well differentiated forms and in advanced stages of parietal infiltration but without a significant association.
Conclusion: MSI is an important genetic marker in CRC that can be useful in diagnosis, prognosis, and even treatment. Further efforts should be made to improve molecular techniques developed for detection of MSI and to develop drug strategies based on specific tumour molecular characteristics.

E-PS-06-038

New immunohistochemical and molecular biomarkers in gastric carcinoma

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Background & objectives: The Lauren classification divides gastric carcinomas into 3 major types: diffuse, intestinal and mixed with a recent clustering in prognostic groups based on new protein expressions
Methods: The purpose of this study was to present a series of 17 cases of gastric carcinomas diagnosed in Fundeni Clinical Institute and their classification in prognostic groups. The immunohistochemical profile included a series of diagnostic biomarkers (EBV, the microsatellite instability profile - MLH1, PMS2, MSH2, MSH6, p53, E-cadherin, Muc2, Muc5AC, Muc6, CDX2, CD10, Her2neu)
Results: 12 were male patients with a mean age of 54.33 years and 5 female patients with an average age of 46.8 years. We studied the histopathological parameters, tumour budding, lymphovascular and perineural invasion in all cases. Seventeen cases showed an EBV negative, stable microsatellite phenotype with diffuse nuclear positivity for MLH1, PMS2, MSH2, MSH6 and diffuse positivity for E-cadherin. The difference in staining was observed with p53, placing them in the fourth and fifth prognostic groups, with subtyping based on aberrant Muc2, Muc5AC, Muc6 and CDX2 expression. Her2neu immunopositivity revealed 4 cases identified as 3+ (positive) and 8 cases established as 2+ (equivocal).
Conclusion: The classification of gastric carcinomas based on molecular and immunohistochemical biomarkers is applicable for diagnostic purposes in order to establish de novo gastric cancer prognostic groups and the novo targeted therapies, aside from Trastuzumab eligible patients with Her2neu positivity . The future aim of these studies is to increase the survival rate in gastric cancer (the current 5 year survival rate in gastric carcinomas is 20%)

E-PS-06-039

Collagenous gastritis in a teenager - a case report

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Background & objectives: Collagenous gastritis is a rare condition of unknown aetiology histopathologically diagnosed by the presence of a subepithelial collagen band accompanied by inflammation. We report a rare case of collagenous gastritis in a teenage Romanian girl.
Methods: A 17-year-old woman was admitted to the Fundeni Clinical Institute, Gastroenterology Department, in January 2020. The patient is known to have iron deficiency anaemia for several years for which she received iron supplements without constant improvement of the haemoglobin levels. Her laboratory profile revealed hypochromic Microcytic Anaemia (Hb 10.60 g/dl) and iron levels of 12μg/dl.
Results: Esophagogastroduodenoscopy was performed and showed oedema and hyperaemia accompanied by nodularity in the gastric body; duodenal mucosa looked normal. The gastric biopsy performed showed mild chronic gastritis and subepithelial collagen deposits highlighted by tenascin and trichrom stains on both antral and gastric body mucosa. Colonoscopy was also performed and showed a normal mucosal appearance.
Conclusion: Considering the rarity of this entity, especially in the paediatric population, the lack of etiological factors and the fact that it has not yet been proven the transition from paediatric-type to adult-type disease, endoscopic and histological follow-up of these patients is mandatory. No current treatments seem to be constantly effective or improve the evolution.

E-PS-06-041

Correlation of programmed death ligand 1 with the two antibody immunohistochemistry profile (PMS-2 and MSH-6) for microsatellite instability in colorectal carcinoma

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Background & objectives: Colorectal carcinoma is the third most common cancer in men and second in women worldwide. PD-L1, an immune checkpoint inhibitor is of interest currently. In our study, we correlated immunohistochemical expression of PD-L1 with PMS-2 and MSH-6 in colorectal carcinoma
Methods: Seventy nine colorectal carcinoma cases, 48.1% above the age of 60 years and male to female ratio was 1.2:1 were retrieved from Department of Pathology, Kasturba Medical College, Mangalore archives from January 2017 to December 2018. Preoperative treated cases were excluded. PD-L1 (CAL 10 clone), PMS-2 and MSH-6 immunostaining for microsatellite instability was done on paraffin embedded formalin fixed blocks.
Results: Of the 79 cases, most common histological type was adenocarcinoma (88.6%) with grade 2 seen in 57% patients. Most were T- stage 3 (51.9%) and 4 (20.3%) with 51.9% patients having nodal positive status. PD-L1 staining was quantified by intensity of staining and percentage of tumour positive cells. PD-L1 tumour cell intensity and percentage was highly significant with each other along with PD-L1 immune cell intensity and percentage, MSH-6, peritumoral lymphocytic response and significant with PMS-2+ MSH-6 loss of nuclear expression and tumour infiltrating lymphocytes. PD-L1 immune cell percentage had highly significant association with MSH-6, peritumoral lymphocytic response and significant with age, tumour infiltrating lymphocytes, lymphovascular invasion and tumour deposits.
Conclusion: PD-L1 tumour cell positivity (>5%) was seen in nearly third (41.1%) of the colorectal carcinomas cases studied. It was significantly associated with loss of MSH-6. The study suggests the possible scope for immunotherapy to be considered in our subset of Indian patients.

E-PS-06-042

A rare malignancy of perianal region: case report and review of the literature

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Background & objectives: Leiomyosarcoma(LMS) of non visceral soft tissues are rare tumours and there are limited numbers of tumour that arise from ischiorectal fossa. The diagnosis should be discussed with a multidisciplinary approach as it has uncommon clinical, radiologic and histopathological findings.

Methods: This case report describes the case of a 67 years old woman presented with a perianal mass with no medical history. During perianal examination no rectal mucosal lesion was found, the abscess was the preliminary diagnosis. After the pathologic examination of supericial biopsy, the mass located at ischiorectal fossa was excised. Superficial and excisional biopsy shared similar morphologic, immunohistochemical properties.
Results: Although the spindle and storiform areas with "cigar" shaped nuclei appropriate for the leiomyosarcoma was not included in the first superficial biopsy, immunohistochemistry was supportive for the diagnosis. Gross total excision was performed and macroscopic, microscopic examination revealed a malignant tumour with epithelioid morphology. Carcinomas and malignant tumours with epithelioid morphology were ruled out. Immunohistochemistry revealed that neoplastic cells expressed h-caldesmon, smooth muscle actin, muscle specific actin and smooth muscle myosin. Lenfovascular invasion and focal microscopic invasion of surgical margins were found.
Conclusion: Both epithelioid morphology of LMS and ischiorectal fossa location are quite rare. We review the morphologic characteristics, diagnostic pitfalls of LMS and add another case to the literature. Awareness of this "ignored" anatomic location and this rare malignant tumour is important.

E-PS-06-043
Amyloidosis of the duodenum: report of a case
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Background & objectives: We present a case of duodenal amyloidosis.
Methods: A 78 years-old man was presented in our hospital suffering from severe diarrhoea, melaena and abdominal pain. Gastroscopy was performed showing bile reflux in stomach and duodenum. Gastric mucosa of the body had micronodular appearance and antral mucosa was erythematous with erosions. The second-third and third-fourth portions of the duodenum were erythematous, with oedema, brittle and local dented.
Results: Histologically the duodenal mucosa revealed glassy pink material in the lamina propria and chronic inflammatory infiltrate predominantly composed of lymphocytes. Congo-Red staining demonstrated amyloid deposits in the duodenal specimens. These observations confirmed the diagnosis of duodenal amyloidosis. Gastric and colon biopsies showed no amyloid deposition.
Conclusion: The term amyloidosis includes a heterogenous group of disorders characterized by acellular hyaline deposits of proteinaceous substance referred as amyloidosis, The disease may be localized or systemic, affecting any organ or tissue, although all types of amyloidosis may affect the gastrointestinal tract. The stomach and the rectum are more likely to be involved than is the small intestine.

E-PS-06-044
Adenosquamous carcinoma of the oesophagus: a case report
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Background & objectives: Adenosquamous carcinoma (ASC) of the oesophagus is uncommon. It contains both squamous cell carcinoma (SCC) and adenocarcinoma (AC) components. We report a case of oesophageal adenosquamous carcinoma to show its epidemiologic, clinical, pathological and prognostic features.
Methods: We report a case of 29-year-old men presented with dysphagia and weight loss for 2 months. An oesophagogastroduodenoscopy with endoscopic biopsy showed an adenocarcinoma. Oesogastrectomy was performed
Results: Macroscopic aspect of the chirurgical sample showed an ulcerous and infiltrative tumour. Histopathologically, the tumour was composed of separate malignant squamous and glandular components. The SCC element contained keratin pearl formation and intercellular bridges, while the AC element had tubular and glandular structures. Perineural invasion and tumoral embols were detected. Five metastatic lymph nodes were detected among 19. An adenosquamous carcinoma was finally retained. The main differential diagnosis was Mucoepidermoid Carcinoma that is composed of an admixture of malignant epidermoid, intermediate and mucous cells. Two years later, the patient presented cerebral metastasis.
Conclusion: ASC is a rare tumour subtype among oesophageal carcinomas with aggressive clinical behaviour and a prognosis worse than either AC or SCC.

E-PS-06-045
Granular cell tumour of the rectum: a rare entity in an uncommon location – a case report
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Background & objectives: Granular cell tumours are mostly benign neoplasms arising from Schwann cells, more commonly occurring in skin, subcutaneous tissue, oral cavity, and gastrointestinal tract, with oesophagus being the most frequent location and with only a few cases described in the rectum.
Methods: We report the case of a 68-year-old male who is homozygous for a MUTYH-associated polyposis mutation, with previous history of colon adenocarcinoma, jejunal adenocarcinoma, multiple GI tract polyps and a gastrointestinal stromal tumour (GIST) of the colon, who has been under continuous surveillance in our institution, presenting with a novel polypoid rectal lesion.
Results: We received a 6mm polyp whose histological analysis showed colic-type mucosa with preserved glandular architecture and a subepithelial proliferation of spindle to epithelioid cells, occasionally forming intertwined cell bundles. A polymorphic inflammatory infiltrate was observed in the lesion periphery, which was centred on the submucosa and involved the lamina propria. There were no mitosis, necrosis, capsule formation nor vascular hyalinization. The neoplastic cells showed strong and diffuse expression using antibodies against S100 protein and were not immunoreactive for CD34, DOG1, SMA, CD117, Desmin and GFAP. The histochemical study using PAS and PAS after diastasis revealed the presence of intracytoplasmic eosinophilic granules. Endoscopic resection margins were free of neoplastic cells.
Conclusion: This case illustrates the main features of this extremely rare benign rectal lesion, which can have malignant variants. The potential association between the MUTYH-associated polyposis mutations and the development of granular cell tumours remains to be established.

E-PS-06-046

Calcifying fibrous tumour of small intestine – a case report of a rare entity and review of the literature

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Background & objectives: The calcifying fibrous tumour (CFT), initially described in 1993, is an extremely rare benign tumour with a predilection for children and young adults, usually arising in the subcutaneous and deep soft tissues, among other locations.
Methods: We report the case of a 46-year-old female with a two-day history of epigastric colicky pain, diarrhoea, nausea and vomits. C-reactive protein levels and leucocyte counts were increased. The CT scan showed a 13cm distal ileal segment invagination conditioning small intestine occlusion, with a non-specific calcium-like density in the invaginated lumen. The patient underwent surgery to resolve the intestinal occlusion.
Results: We received a 16cm long small intestine segment with a lobulated area 1,2cm from the nearest surgical margin. Upon section, we could observe a 2,7x2,5x2cm well-circumscribed neoplasia centred in the submucosa and muscular layers, firm, whitish and vitreous. The histological analysis showed an ileal segment containing a hypocellular neoplasia with well-defined borders and mainly composed by bland spindle cells imbued in abundant and dense stroma, with hyalinized areas and containing lamellar collagen. There were dystrophic calcifications and small aggregates of chronic inflammatory cell infiltrates. No mitotic figures or necrosis were observed. The immunohistochemistry study using antibodies anti-CD34, Desmin, CD117, DOG1 and Her2 showed only focal positivity for CD34.
Conclusion: This case illustrates the main features of this extremely uncommon benign small intestine lesion, which has been previously associated with a few cases of intestinal intussusception.

E-PS-06-047

Nuclear JAK-2 with serine 727 phosphorylated STAT-3 in colorectal cancer

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Background & objectives: An unclear Jak-2 nuclear downstream has not been explained and moreover the meaning of that is also unsolved to the present day.
The objective of the present study was to analyse the nuclear Jak-2 downstream
Methods: Ninety-eight cases of colorectal cancer were included to study. A tissue microarray was performed and micro-samples to DNA isolation were taken from FFPE blocks. We examined a Jak-2 V-617f, BRAF, KRAS, NRAS mutation and also Jak-2, serine 727 phosphorylated Stat3, anti-thymidyne phosphorylase, INI-1, NKX3, EZH-2, FOX-P1 by classical immunohistochemistry.
The study has been approved by the Ethical Commission.
Results: We observed low ratio Jak-2 V61fF mutation, comparable to other results disturbances of BRAF, KRAS, and NRAS, very common Jak-2 nuclear transfer positively correlating with INI-1 and NKX-3. All data are still under statistical analysis and will be presented during the poster session.
Conclusion: The study suggests nuclear Jak2 would be Stat3 independent.
The study was supported by financial resources of The Collegium Medicum Jan Kochanowski University in Kielce, Poland.

E-PS-06-049

Well differentiated liposarcoma presenting as a duodenal polyp: a rare case presentation

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Background & objectives: Despite being one of the most common soft tissue sarcoma in the retro-peritoneum and extremities, liposarcoma are extremely rare in the gastrointestinal tract. Only three cases have been reported in the duodenum in the literature.
Methods: A PubMed search was carried out for previous cases, using the reference terms; "small bowel", "duodenal" and "liposarcoma". A 77 year old patient presented with intermittent malena and endoscopy showed a 45 mm polypoid lesion in D2.
Results: Histology revealed a partially circumscribed adipocytic lesion containing variable fibrous septa with spindle cells including cells with enlarged hyperchromatic or multiple nuclei. The spindle cells were CD34 positive and negative for CD117 and DOG1. Interphase FISH studies performed revealed amplification of MDM2 gene, confirming the lesion as an atypical lipomatous tumour/ well differentiated liposarcoma.
Conclusion: The diagnosis of well differentiated lipomatous tumours apart from lipoma at unusual site such as gastrointestinal tract is extremely difficult on routine H&E examination. The use of FISH studies for MDM2 amplification would help in the confirming the diagnosis. Accurate diagnosis is important as surgical resection with negative margin is the mainstay of treatment for patients with well-differentiated liposarcoma.

E-PS-06-050

Epithelioid gastrointestinal stromal tumour (GISTs) simultaneous and rare coexistence with gastric schwannoma

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Background & objectives: Gastric GISTs represent 2% of all malignant tumours in the gastrointestinal tract, while the Schwannoma only 0.2%, the simultaneous occurrence is very rare. We report of a case in a patient with simultaneous coexistence of Schwannoma and GIST.
Methods: A gastric submucosal lesion was found on a follow up endoscopy of a 63-year-old male with a history of duodenal ulcer. CT revealed a 6.5 cm mass in the lesser curvature of the stomach. During the surgical resection, a second lesion of 0.8 cm was identified in the fundus. A laparoscopic gastric resection of the two lesions was performed.
Results: Microscopic examination revealed in the larger tumour spindle tumour cells proliferation surrounded by a peripheral lymphoid cuff, without atypia, mitosis and necrosis. The immunohistochemistry (IHC) showed positivity for S-100 and GFAP, and it was negative for CD34, CD117, DOG-1 and muscular markers. The smaller tumour was composed of epithelioid tumour cells without mitosis and Immunohistochemistry study was positive for CD117 and DOG-1 and negative for S-100. The larger tumour was classified as a schwannoma and the smaller as an epithelioid GIST.
Conclusion: GISTs and Schwannomas are mesenchymal tumours of the gastrointestinal tract and the synchronic occurrence of the two diseases is very unusual, with a few cases referred in the literature. Diagnosis of these entities is difficult with only endoscopy and diagnostic images, and requires a complete histopathological and immunohistochemical approach for a correct diagnosis and treatment of these lesions.

E-PS-06-051

Primary small bowel leiomyosarcoma as a subsequent malignancy in a retinoblastoma survivor: case report

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Background & objectives: Small bowel tumours are <5% of gastrointestinal(GI) malignancies. Small bowel leiomyosarcoma is rare and aggressive, 40-80% local recurrence, 55-70% metastasis rate. Secondary malignancies in patients with retinoblastoma-history may be side effects of radiation/chemotherapy, higher in hereditary-retinoblastoma13.7% rather than in sporadic1.5%.
Methods: A 54-year-old man with abdominal pain, weight loss and history of retinoblastoma treated at 2.5 years old with radiotherapy and enucleation. Resection of a small bowel segment with a 10.5 x 7 x 6 cm mesenteric mass was performed. 4 months later, liver metastases were detected. The patient refused further treatment.
Results: Microscopic examination revealed: spindle cells neoplasm with interlocking bundles and fascicles, with moderate nuclear pleomorphism, numerous atypical mitosis and necrosis. Immunohistochemistry, positive for muscular markers (caldesmon-calponin-demin), and EMA. Negative: CD10, DOG1, CD34 and S100. KI67: 60%. The diagnosis of a high-grade pleomorphic leiomyosarcoma was made, with intestinal submucosa involvement. Genomic study was performed (Foundation one): Microsatellite Instability: Intact, TMB-Tumour Mutational Burden: low, other genomic alterations: ATRX, E1288, RB1 V65fs14, tp53.
Conclusion: Primary Leiomyosarcoma in the small bowel is rare, treatment relies on accurate diagnosis and a surgical approach. Have a distinctive clinicopathological and immunohistochemical features and aggressive behaviour. Sarcomas need to be considered when facing patients with history of retinoblastoma, alterations of RB1 seem to be involved in the pathogenesis of the secondary malignancy and after treatment of retinoblastoma. Knowledge of this rare pitfall is important.

E-PS-06-052

A rare duodenal tumour with uncommon histopathological features and aggressive clinico-biological behaviour

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Background & objectives: Mixed neuroendocrine non-neuroendocrine neoplasms (MiNENs) are rare epithelial neoplasms of the gastro-entero-pancreatic tract with well-defined diagnostic criteria. We report a case of a duodenal MiNEN aiming to illustrate its site-specific clinical features focusing on its histopathological heterogeneity and treatment outcomes.
Methods: We describe a case of a duodenal MiNEN diagnosed in our pathology department and treated in surgical and medical oncology departments of Sfax and Gabes hospitals.
Results: A 56-year-old-woman presented with chronic painless jaundice, clay-coloured stools and darkened urines with biological cholestasis. Ultrasound, computed-tomography and magnetic resonance cholangiopancreatography showed extrahepatic cholestasis without evident obstruction. Upper-endoscopy revealed a 3cm-exophytic-duodenal-mass extending to the Vater's ampulla. Endoscopic-biopsy concluded to a grade 3-neuroendocrine-tumor (G3NET). A Whipple duodenopancreatectomy was then performed. Grossly, the tumour involved both duodenal wall and ampulla. The diagnosis of MiNEN was made based on the presence of a three-component-neoplasm: G3NET, intestinal-type-adenocarcinoma and squamous-cell carcinoma, accounting for nearly 30% of the tumour each. The patient was subsequently found to have an advanced disease and showed progression within 5 months despite a palliative chemotherapy following an adenocarcinoma-like protocol.
Conclusion: Due to the rarity of this entity and inconsistency of terminologies, MiNENs' management and outcomes remain controversial, although their prognosis is often poor driven by the neuroendocrine component frequently of high-grade.

E-PS-06-053

Terminal ileum endometriosis causing acute small bowel obstruction-case report and literature review

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Background & objectives: Endometriosis is a benign condition with existence of dynamic functioning endometrial tissues consisting of glands external to the uterine cavity. Terminal ileum endometriosis is extremely rare. Objective-To describe clinical pathological findings in a case of terminal ileum endometriosis and literature review.
Methods: We report a case of small bowel endometriosis which presented with recurrent massive ascites and acute intestinal obstruction. The case was retrospectively obtained from histopathology laboratory at Muhimbili National Hospital. Demography and other clinical information were recorded from the files. Histopathological diagnosis was confirmed by a routine Hematoxylin and Eosin stains. Microscopic photos of the histology slides were taken.
Results: A 23years old female presented at Emergency Department, with signs and symptoms of acute intestinal obstruction. In previous 6 months, she had recurrent ascites and was kept on trial ant-TB medications, despite negative results for Tuberculosis. Laparotomy findings were fibrosis and obstruction in the terminal ileum which was re-sectioned. Histology showed nests of endometrial glands with stroma embedded in submucosa and muscularis. Final diagnosis was endometriosis of terminal ileum.
Conclusion: Endometriosis occurs in 3%-37% of women in child bearing age. Gastrointestinal endometriosis does occur mostly in the rectosigmoid, small bowel endometriosis is less frequent and mostly reported in the distal ileum while terminal ileum endometriosis is extremely rare endometriosis, with massive ascites should be considered as masquerade of diseases due to its varied and disguised ways of presentation. It requires high index of suspicion among medical practitioners and confirmation made by histology of the affected segment.

E-PS-06-055

Primary pleomorphic intestinal liposarcoma: a case report

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Background & objectives: Liposarcomas are the most common group of malignant mesenchymal neoplasms. They usually arise in the extremities and retroperitoneum, being very rare in the abdominal area.
Methods: A 75 year old man was admitted to the hospital because of severe anaemia, with no evidence of bleeding. A 5 cm sized thickening of a jejunal loop was found in the CT scan, with adenocarcinoma as the first possible diagnosis and then, lymphoma. A small bowel resection was performed.
Results: We received a 79 cm long small bowel specimen with a 12x6 cm mural tumour, protruding into the lumen, it was a well defined, non encapsulated soft mass with a whitish-yellow colour. The microscopy showed an ulcerated mural neoplasm, its surface having an abrupt transition with a normal surrounding mucosa. Two cellular components were found, a sarcomatous background with very frequent bizarre lipoblasts and intermingled malignant spindle cells. There was a 20% of necrosis and up to 52 mitosis/40HPF. IHC studies showed intense vimentin and p53 expression of tumour cell and, focally, with MDM2. There was no MDM2 amplification with FISH.

Conclusion: Due to the rarity of primary pleomorphic intestinal liposarcoma with a handful of reported cases, one primary pleomorphic jejunal liposarcoma is presented, with varied differential diagnosis by imaging, being very relevant to arrive to the correct diagnosis.

E-PS-06-056

Digital pathology in colorectal cancer: using virtual tissue microarrays to determine the minimum number of cores for biomarker analysis

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Background & objectives: Tissue microarrays (TMAs) are used in biomarker studies to increase experimental efficiency. We used virtual TMAs to determine the minimum number of tissue cores needed to quantify biomarkers with the same precision as when using WTS in colorectal cancer (CRC).
Methods: Sections from 50 CRCs were stained with H&E, and immunohistochemistry for CD3, CD20, fibroblast activation protein (FAP) and α-SMA, CD68 and CD163. Digitized H&E WTS were divided into tumour centre and invasive margin regions. Virtual TMAs were created by overlaying 8 1mm circles in each region of the H&E WTS. Minimal number of TMA cores was determined by Bland-Altman plots.
Results: For all the biomarkers, a minimum of 4 TMA cores per region was necessary for adequate quantification compared with WTS. However, 3 cores were sufficient for separate analysis of anti-CD3, anti-CD20 and anti-CD68 in the tumour centre. Anti-CD20 had the most heterogeneous expression, while anti-FAP with anti-α-SMA and anti-CD3 were most homogeneously expressed.
Conclusion: The virtual TMA technique is a useful method to establish the minimum number of cores to be included when constructing tumour TMAs for biomarker analysis.
Funding: Health Research Fund of Central Denmark Region.

E-PS-06-058

The expression of epithelial-cadherin (e-cadherin) and beta-catenin (β-catenin) in colorectal neoplasm

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Background & objectives: E-cadherin and β-catenin have been examined as a potential oncogenic marker in colorectal neoplasm. The aim of this study is to compare the score of E-cadherin expression (membrane and cytoplasm) and β-catenin (membrane, cytoplasm and nucleus) in the colorectal neoplasm.
Methods: One hundred paraffin-embedded colorectal tissue diagnosed as colorectal adenoma, well-differentiated, moderately differentiated and poorly differentiated adenocarcinoma were examined by immunohistochemistry. The expression was considered positive for E-cadherin and β-catenin when a brown colour was found in the membrane, cytoplasm or nucleus. It was assessed using a score system based on the intensity and extensity.
Results: The results of the study indicate that there was a significant difference between the expression of E-cadherin and histological grading of colorectal neoplasm. Expression of E-cadherin is higher in colorectal adenomas compared to well-differentiated, moderately differentiated and poorly differentiated adenocarcinomas. Meanwhile, β-catenin expression is higher in poorly differentiated adenocarcinoma compared to adenoma and moderately differentiated and well-differentiated adenocarcinomas.
Conclusion: The results suggest that down regulated of E-cadherin expression and up regulated β-catenin expression play a role in the development of colorectal neoplasm. It provides additional information in define prognosis and predicting patient's outcomes in colorectal neoplasm.
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E-PS-06-059

Prediction of cellular damages to anti-cancer drugs by speed-of-sound

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Background & objectives: Degenerative effects need histological observation after anti-cancer drugs therapy. Although light microscopy fails to quantitatively evaluate cellular damage, scanning acoustic microscopy can assess both histology and mechanical stiffness by speed-of-sound (SOS). This study aims to estimate the quantitative cellular alteration of cells after anti-cancer drug incubation by SOS values.
Methods: The samples are clinical cytology specimens and culture cells in ethanol fixation. SOS images of the cells were followed after incubation in anti-cancer drugs.
Results: Alteration of SOS values of nuclei after anti-cancer drugs varied with the kind of medicines and also cancer cells. As a whole, SOS values decreased after incubation in anti-cancer drugs. Alteration of SOS images corresponded well to LM images.
Conclusion: Following SOS values of the cells can objectively indicate cellular damages. This method can predict the effects of anti-cancer drugs.

E-PS-06-060

Evaluation of P53 immunohistochemistry pattern as a biomarker of dysplasia in Barrett's oesophagus

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Background & objectives: Loss of heterozygosity of p53 plays an important role in metaplasia-dysplasia-neoplasia sequence.
We designed a retrospective case-control study in order to explore p53 expression in Barrett's oesophagus, evaluated in dysplastic and non-dysplastic epithelium.
Methods: We included 9 patients with dysplasia - 6 with low-grade dysplasia (LGD - 5 men and 1 woman) and 3 with high-grade dysplasia (HGD - 2 men and 1 woman). For each patient with dysplasia, we included a non-dysplastic patient (matching sex and age). p53 expression was evaluated as percents of positive epithelial cells.
Results: Cases with dysplasia had a higher expression of p53, in both types of epithelium (squamous and columnar). However, cases without dysplasia had a surprising high expression of p53: 12.7% of squamous cells and 8.1% of columnar cells. HGD cases had the highest average of p53 (46.7% squamous and 68.3% columnar), while in the LGD group, the rates were 16% in squamous and only 4.2% in columnar epithelium.
Conclusion: As a consequence of the significant degree of intraobserver and interobserver variability in the microscopic diagnosis of dysplasia, p53 staining it's a precious tool that can be helpful in treatment decision.

E-PS-06-061

Stercoral perforation of the colon related to chronic obstipation induced by antipsychotic treatment

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Background & objectives: Stercoral perforation (SP) is a rare complication of chronic obstipation, caused by increased pressure of

intraluminal contents. It represents only 3 % of all intestinal perforations, with only around 100 cases documented in the literature so far.
Methods: 61-year old obese female patient with chronic obstipation and history of schizoaffective disorder of depressive type treated with combination of antipsychotic therapy, was hospitalized for 53 days for bronchopneumonia followed by urinary tract infection. A week after successful treatment patient died with elevated CRP (289 mg/l) without apparent clinical correlation. Autopsy and subsequent histopathological evaluation of necroptic samples was performed.
Results: Autopsy revealed free air within the peritoneal cavity and considerably dilated large intestine, from 7 cm in diameter in ascending colon to 12 cm in sigma and rectum, fully filled with hardened intestinal contents. Visceral and parietal peritoneum were diffusely thickened, covered with grey-brown sheets. Oval perforation was present 40 cm from anorectal line, on the antimesenteric side of the redundant loop of sigmoid colon. Histologically, the wall of the intestine neighbouring the perforation showed mixed inflammatory infiltrate and superficial ulcerations. Serosa was covered with purulent inflammatory infiltrate with evidence of swift granulation tissue ingrowth, pointing out older age of the lesion.
Conclusion: Only 11% of SPs are diagnosed prior to surgery or autopsy, with mortality rate reaching 35%. Patients predisposed to SP are mainly older immobile patients with chronic therapy leading to obstipation – including mainly opioids, anticholinergic drugs or NSAIDs. Particularly prone are psychiatric patients, treated with antipsychotics or tricyclic antidepressants, which markedly promote constipation and might lead to attenuation of clinical symptoms, as in our case.

E-PS-06-062
Expression of claudin-1 and claudin-4 in the oesophageal mucosa as additional criteria for evaluation of efficacy in GERD therapy
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Background & objectives: Pathogenesis of gastroesophageal reflux disease (GERD) has close association with intercellular contacts. The aim was to determine the potential of standard morphological changes and markers of tight junction components as evaluation criteria for the effectiveness of GERD treatment.
Methods: 23 patients with GERD-related symptoms and endoscopic signs and 15 patients as controls were included. Standard proton pump inhibitor (control group) and in combination with chondroitin sulfate and hyaluronic acid on a bioadhesive carrier (study group) were used. Mucosal biopsies from distal oesophagus were taken for analysis by histopathology and claudin-1, claudin-4 and Ki-67 expression assessment by immunohistochemistry.
Results: GERD-specific alterations in the oesophageal mucosa were confirmed. Regression of clinical, endoscopic and histopathological parameters was noted in both groups after 4 weeks from the onset of treatment ($p < 0,05$). In both groups expression levels of claudun-1 were statistically higher after therapy ($p < 0,05$) whereas claudin-4 levels weren't significantly affected ($p>0,001$). Migration of claudin-1 expression towards the upper layers of oesophageal mucosa was revealed also. The Ki-67 level was lower after treatment, especially at the margins of the erosions ($p < 0,05$) . The expression levels of both claudins did not correlate with clinical features and had a weak correlation with histopathological parameters including dilated intercellular spaces.
Conclusion: The absence of significant differences between treatment options concerning reverse development of morphological parameters were established.Taken together, the expression of tight junction-related component claudin-1 and Ki-67 can be used as additional criteria for evaluation of efficacy in GERD therapy.

E-PS-06-064
Immature teratoma of the greater omentum-case report and literature review
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Background & objectives: Immature omental teratoma are rare. To best of my knowledge only three immature omental teratomas have been reported in literature. We hereby describe the clinical pathological findings of a primary immature teratoma of the omentum and the review of literature.
Methods: We report a case of a primary immature teratoma of the omentum which clinically was thought to be tuberculosis. Case was attended at Lugala Lutheran hospital in Singida, Tanzania and histology was reported at Mutokiti diagnostic laboratory. Demography and clinical information were recorded. Gross and microscopic photos were taken. Histological diagnosis was confirmed by the routine Hematoxylin and eosin (H/E stain).
Results: A 20 years old female underwent laparotomy due to a swelling originating from the greater omentum. Tumour was removed and tissue sent for histology. Histology showed partly cystic lesion with variable differentiation including immature endodermal glands, Gut and respiratory tract epithelium. Mesodermal were adipose tissue, cartilage and bone fragments. Ectodermal derivatives characterized by squamous epithelium with its adnexal. Focally glial tissue was found. Final diagnosis was Immature teratoma of greater omentum.
Conclusion: Omental teratomas may be difficult to diagnose clinically as it may present in protean ways due to its malignancy potential as it was in our case which was suspected to be omental tuberculosis. It is necessary for pathologist to have high index of suspicion, sample careful and examine histologically for the evidence of immature elements that are consistent with immature teratomas. Due to malignant potential of omental teratoma chemotherapy and/or radiotherapy might be needed on additional to surgery.

E-PS-06-065
Schwannoma in gastrointestinal system, a rare entity: report of two cases
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Background & objectives: Gastrointestinal mesenchymal tumours are a group of tumours originated from mesenchymal stem cells of gastrointestinal tract, consisting of gastrointestinal stromal tumours(GIST), leiomyomas, or schwannomas. Schwannomas are seldomly seen gastrointestinal mesenchymal tumours, mostly in stomach, rare in lower oesophagus and colon.
Methods: S-100, SOX-10, CD117, SMA(smooth muscle actin), DOG1, CD34 stains were used.
Results: Our first case, a 59-year-old male submitted to hospital with upper gastrointestinal bleeding. Endoscopic examination was performed which showed a round submucosal tumour with a central ulceration and bleeding over the upper body of the stomach. Microscopic examination revealed a mass with spindle cells, positive for both S-100 and SOX10, but nonreactive for CD117. Our second case, 43-year-old male patient had upper gastrointestinal tract bleeding. A nodular mass lesion 2 cm proximal to Z line was described by endoscopic examination. Thus, endoscopic US was additionally performed which revealed subepithelial mass lesion in distal oesophagus. Microscopically spindle cells were seen which stained positive for S-100, negative for CD117,SMA, DOG1, CD34.
Conclusion: Two of the cases' immunohistochemistry results supported diagnosis of schwannoma with spindle cell phenotype in both H&E ex-

aminations. Schwannomas are rarely seen, generally benign mesenchymal tumours, which need to be differentiated from GIST as schwannomas carry a good prognosis compared to GIST, which has malignant potential. In addition, differential diagnosis should be made with benign tumours such as leiomyoma.

E-PS-06-067

An unusual case of inflammatory myofibroblastic tumour located in appendix

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Background & objectives: Inflammatory myofibroblastic tumour is a low grade mesenchymal neoplasia which is composed of myofibroblastic spindle cells accompanied by plasma cell-rich inflammation. The most common localisations are lung, omentum and mesentery. Inflammatory myofibroblastic tumour has been reported very rarely in appendix.
Methods: 19-year-old female patient admitted to the emergency room with right upper quadrant pain. Upon detecting leukocytosis in laboratory tests, appendectomy was performed with a preliminary diagnosis of acute appendicitis. The macroscopic examination revealed a round, well-circumscribed, elastic-hard mass that completely obliterating the lumen with a diameter of 1.8x1.5x1.3cm in the middle part of the appendix.
Results: The macroscopic examination revealed a round, well-circumscribed, elastic-hard mass that completely obliterating the lumen with a diameter of 1.8x1.5x1.3cm in the middle part of appendix. The tumour composed of spindle cells with vesicular nucleus forming fascicules. Intensive inflammatory infiltration rich in plasma cells was accompanied by tumour. Thirteen, not atypical mitoses were seen in 10 HPF. Leiomyoma, GIST, schwannoma, follicular dendritic cell sarcoma, inflammatory myofibroblastic tumour, Ig G4-related appendicitis were included in the differential diagnosis.
Immunohistochemical studies showed only SMA positivity. Desmin, Caldesmon, CD34, CD117, DOG-1, S-100, CD21, CD23, ALK, IgG4 were negative.
The case was evaluated as "Inflammatory Myofibroblastic Tumour" with morphological and immunohistochemical findings.
Conclusion: Although inflammatory myofibroblastic tumour is very rare in the appendix, it should be recognized because of the risk of recurrence and metastasis and the need for follow-up. The possibility of inflammatory myofibroblastic tumour should be kept in mind in the presence of spindle cell lesions in the appendix.

E-PS-06-068

Two case reports of extragastrointestinal stromal tumours with an uncommon origin: gastro-colic omentum and great omentum

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Background & objectives: Gastrointestinal stromal tumours (GISTs) originate from the interstitial cells of Cajal and are the most usual mesenchymal neoplasia arising in the gastrointestinal tract. They may arise outside of the gastrointestinal tract, in which case they become extragastrointestinal stromal tumours (EGISTs).
Methods: Two cases of EGISTs are described, one originating from the gastro-colic omentum and one from the great omentum: a 65 years old man with an abdominal mass of 16cm on MRI, and a 62 years old patient, who presented to the emergency department for abdominal pain and vomiting, which the abdominal CT revealed to be an 18cm abdominal tumour.
Results: In the first case, the histological examination revealed a high mitotic rate, epithelioid EGIST (positive for CD117 and DOG1), IIIB stage group (AJCC, 2017). In the second case, the histological examination revealed also a high mitotic rate, mixed-cell EGIST (positive for CD117 and DOG1), IIIB stage group. Patients were treated with Imatinib but suffered multiple local relapses in the last two years.
Conclusion: EGISTs seem to have a more aggressive behaviour compared to the same tumours with a conventional origin. Due to high recurrence rates, the role of treatment with Imatinib is not clear, so a strict follow-up is necessary. Our case reports highlight the importance of considering EGIST in the differential diagnosis of solid tumours of the omentum.

E-PS-06-069

Occurrence of KRAS , NRAS and BRAF mutations in colorectal carcinoma among the Filipino population

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Background & objectives: Mutations in the EGFR signalling pathway, including KRAS, NRAS and BRAF, lie at the centre of colorectal cancer (CRC). CRC patients may benefit from EGFR targeted therapies. However, cases of chemotherapeutic resistance have been reported, thus, determining the EGFR mutational status of patients is necessary. This study aims to determine the occurrence of KRAS, NRAS and BRAF mutations and to correlate it with certain clinicopathologic parameters in confirmed CRC among Filipino patients of a tertiary hospital in the Philippines.
Methods: KRAS (exons 2, 3 and 4), NRAS (exons 2, 3, and 4) and BRAF (V600) genes were tested using reverse transcription-polymerase chain reaction (Amoy Diagnostics Co., Ltd., Xiamen, China) in 27 confirmed CRC cases among Filipino patients who underwent surgical resection.
Results: Five (18.5%) have KRAS mutations, two (7.4%) have NRAS mutations and one (3.7%) has BRAF mutation. Tumour size is significantly correlated to the mutations indicating that a larger tumour has a higher probability of having mutations. KRAS and NRAS positive cases showed well-to- moderately differentiated adenocarcinoma and are at the left side of the colon. BRAF positive case has mucinous adenocarcinoma and is on the right colon near the cecum.
Conclusion: Our results showed a low positivity rate for KRAS, NRAS and BRAF mutations among the Filipino population, a finding shared among patients from other Asian and Western countries.

E-PS-06-070

Histopathological prognostic stratication of gastrointestinal stromal tumours in a cohort of black Africans: a single-centre experience

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Background & objectives: Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal tumours of the gastrointestinal tract. The aim of this study was to show the histopathological features and prognostic stratification of cases of GISTs using the AFIP/Miettinen & Lasota's criteria.
Methods: All cases of gastrointestinal tract mesenchymal tumours (GMTs) diagnosed within the study period (January 2005 - December 2016) were retrieved from the records of the Department of Pathology in the hospital. Immunohistochemistry was done on the paraffin tissue blocks using DOG1, Desmin and S100 antibodies. The cases of GIST identified were stratified into histopathological prognostic groups using the AFIP criteria.
Results: There were fifty-four cases of GMTs, out of which twenty-four GISTs (44%) were identified with the aid of immunohistochemistry. The mean age of occurrence was 56 years and more than 80% of cases occurred after 40 years of age. The modal age group of occurrence was 60-69 years. The male-to-female ratio was 1.7:1. The tumours were most commonly located in the stomach (33%). The tumours were relatively

large with an average size of 15cm. 75% of cases were spindle-type GISTs and approximately 17% and 8% of the tumours were mixed and epithelioid histologic subtypes respectively. The largest number of cases (54%) were in the AFIP high-risk prognostic group.
Conclusion: Immunohistochemistry and prognostic risk stratification are important in the definitive diagnosis and management of GISTs. Histopathological prognostic risk stratification in this study showed that majority of cases had a high risk of disease progression, tumour recurrence and metastasis.

E-PS-06-071
Signet ring cell carcinocythaemia in an advanced gastric carcinoma
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Background & objectives: A 32-year-old male with severe gastrointestinal symptoms. A gastroscopy showed a tumour of the stomach, histologically diagnosed as poorly cohesive (diffuse) carcinoma with presence of signet-ring cells. A CT scan revealed an osteolytic/osteoblastic bone lesions highly suggestive of metastatic cancer.
Methods: Peripheral blood cell morphology was analysed with May Grünwald-Giemsa staining, then thin-layer preparation method (ThinPrep) plus Papanicolau stain cytology was performed.
Results: Peripheral blood smear showed ig atypical epithelial-like cells with prominent nucleoli and occasional signet-ring cells. Immunocytochemical stains for Cytokeratins (CKAE1/AE3) and Ber-EP4 antibody confirmed the presence of malignant epithelial cells, and thus, of carcinocythaemia. Germline analysis revealed the presence of a CDH1 mutation. There is evidence supporting that patients with gastric cancer and germline CDH1 mutations have worst prognosis.
Conclusion: To the best of our knowledge, carcinocythaemia in signet ring cell gastric carcinoma has not been previously reported. This diagnosis, together with the presence of CDH1germline mutation probably confers a dismal prognosis of this case.
This is the third case of carcinocythaemia in our institution. Peripheral blood cytology can be used as a minimally invasive diagnostic tool for metastatic epithelial malignancies.

E-PS-06-072
Incidental discovery of an extensive duodenal amyloidosis
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Background & objectives: Gastrointestinal involvement by amyloidosis is common. While the disease can be associated with inflammatory conditions, its association with cancer is unusual. We report a case of a duodenal amyloidosis revealed by an adenocarcinoma of the common bile duct (CBD).
Methods: A case of an incidental discovery of duodenal amyloidosis occurring in a patient with adenocarcinoma of the CBD is reported with a review of the related literature.
Results: A 70-year-old man was operated upon for an adenomatosis of the CBD. Frozen sections were made and revealed an adenocarcinoma in the lower part of the CBD. A cephalic duodenopancreatectomy was performed with resection of the CBD. On macroscopic examination, the duodenal segment had a thickened wall with friable mucosa and polypoid protrusions. Paraffin sections confirmed the diagnosis of adenocarcinoma of the CBD and showed extensive deposits of an amorphous material in the mucosa, submucosa and blood-vessel-walls of the duodenum. Polarized light microscopy using Congo red staining indicated the presence of amyloid deposits that exhibited apple-green birefringence. Immunohistochemistry showed negativity for anti-AA and was inconclusive for lambda-light or kappa-light chain.
Conclusion: Involvement of the small bowel is frequent in systemic amyloidosis. Clinical presentation is often not specific (pain, vomiting…). As far as we know this is the first case of a duodenal amyloidosis discovered while treating a cancer of the CBD.

E-PS-06-073
Hepatoid adenocarcinoma: rare tumour with diagnostic dilemma
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Background & objectives: Hepatoid adenocarcinoma (HAC) is a tumour with aberrant hepatocellular differentiation that occurs in extra hepatic organs. The objective is to study three cases of Hepatoid adenocarcinoma from three different sites and ascertain there characteristic features and immunoprofile.
Methods: Three cases of Hepatoid adenocarcinoma from Gall bladder, Lung and stomach were analysed. There clinical, pathological, immunological and serological correlations were seen.
Results: Histopathology features common to hepatoid adenocarcinoma at these three sites along with immunoprofile were ascertained. A panel of immunohistochemistry which helps in diagnosis was concluded.
Conclusion: It was concluded that all the tumours had a characteristic histomorphology of hepatoid cells which may or may not secrete Alfa-feto protein(AFP). A characteristic immunoprofile useful in diagnosis comprised a panel of CK7, CK20, Heppar1, TTF-1, P53, Synaptophysin, Chromogranin and Calretinin. In conjunction with histomorphology, serology and immunoprofile a confident diagnosis can be made.

E-PS-06-074
Gastric GIST tumour in a young female patient with a history of multiple paragangliomas - a pure coincidence?
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Background & objectives: GIST may be sporadic or syndromic, some of which are caused by germline mutation of the SDH subunit-encoding genes. SDH-deficient GISTs are frequently associated with paragangliomas (Carney-Stratakis syndrome or in association with pulmonary chondroma, as part of the Carney triad).
Methods: A 40-year-old woman with a personal history of recurrent paragangliomas (gastric, retroperitoneal, vertebral localization) since she was 26, for which she underwent numerous surgical resections, chemotherapy and radiotherapy is diagnosed with a lesser curvature gastric tumour during follow up. Elevated normetanephrine and chromogranin levels were observed, thus the suspicion of another recurrence. The patient underwent gastrectomy.
Results: Grossly, a nodular, ulcerated, 4 cm in diameter tumour was found. The histological examination revealed a tumoral proliferation composed of small-sized epithelioid cells, few fusiforme, with solid architecture, low nuclear and cellular pleomorphism. The mucosa was spared. Tumour cells were positive for DOG1, CD117; NSE and S100 were focally positive; Synaptophysin and Chromogranin were negative. Ki 67 index was 3% and the mitotic rate was 7/20HPF. SDHB staining is not available in our service. Following these findings we could disprove the initial clinical suspicion of a recurrent paraganglioma of the stomach and the diagnosis was Gastric GIST, category 5.
Conclusion: Based on the clinical history and exclusion of a pulmonary lesion, we suggested that a Carney-Stratakis syndrome is very likely. The patient was proposed for genetic counselling, followed by mutational analysis of the SDH genes, important for the treatment and patient follow up.

E-PS-06-075

Pathologic challenges of a right-sided colon tumour and a gastric tumour, with emphasis on immunohistochemical particularities and diagnostic significance: a case series report

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Background & objectives: Goblet cell adenocarcinoma is a rare appendiceal amphicrine neoplasm, composed of goblet-like mucinous cells, a variable number of endocrine and Paneth-like cells arranged as tubules resembling intestinal crypts. Rarely, this tumour was described in the stomach, small bowel and colon.
Methods: First case is a 55 year-old woman admitted for fatigue, abdominal pain and abdominal masses. Colonoscopy with biopsies revealed a right colon tumour and hemicolectomy was performed.
Second case is a 77 year-old woman with weight loss and intestinal occlusion. Imaging studies showed a stenosing tumour in the antrum and duodenum with peritoneal carcinomatosis. Palliative surgery and biopsies were performed.
Results: The hemicolectomy specimen revealed signed-ring cells invading the entire colonic wall, vascular emboli, perineural invasion, lymph node metastasis in 22/23. No appendiceal tumour was found. Tumour cells were positive for CK20, CDX2, MUC2, Synaptophysin, Chromogranin, NSE and MMR-proficient.
The second patients' round ligament biopsy showed tumour cells that were histologically similar to the first case, positive for AE1/AE3, CK7, CDX2, CEA, Synaptophysin and negative for CK20, MUC5, WT1.
Based on the pattern of invasion, with the colonic mucosa being mostly spared and the absence of desmoplastic reaction, associated with the immunohistochemical results, our diagnosis was Goblet Cell Adenocarcinoma; the differential diagnosis included a mixed neoplasm (MiNEN).
Conclusion: We highlight the importance of histologic, immunohistochemistry and clinical correlation in tumours that at the microscope might look familiar, but when looked at closely, have overlapping tumoral elements. The first patient died 6 weeks following the diagnosis, with metastatic complications. The second patient is living 3 months after the surgery, under palliative care.

E-PS-06-076

The background and precancerous processes in the gastric mucosa outside of the tumour node

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Background & objectives: A significant feature of gastric cancer is the presence of background and precancerous processes associated with carcinogenesis. Helicobacter pylori infection, chronic gastritis and intestinal metaplasia play important role in the formation of intraepithelial neoplasia and early gastric cancer.
Methods: Analysis of the background and precancerous processes in the mucous membrane of 49 patients with gastric carcinoma at a distance of 1 and 2 cm from the tumour node. Morphological features investigation using a semi-quantitative assessment in scores from 0 to 3 for histological and cytological structure evaluation carried out. Statistical analysis was performed using the IBM SPSS Statistics 23.
Results: A group of 49 patients with gastric cancer (m/f-26/23), age 64-69.5 years, was studied. Carcinoma localization: 1)body-42.86%; 2)cardia-14.29%; 3)antrum-28.57%; 4) pyloric department-10.20%.Studying the mucous membrane at a distance of 1 cm from the tumour node revealed the following background and precancerous processes:1)chronic gastritis (49),activity grade from I to III (I-14,II-19,III -16); 2) gastric glands atrophy (42); 3)intestinal metaplasia(33); 4) epithelial hyperplasia(37); 5) mild dysplasia(12)and severe grade(20),total 32. In the mucosa at a distance of 2 cm from the tumour: 1)chronic gastritis(49), activity grade from I to III (I - 23,II-19,III - 7); 2)atrophy of the glands(40); 3) colonic metaplasia(17); 4) epithelial hyperplasia(33); 5)dysplasia of mild(9) and severe grade(5), in total-14.
Conclusion: The research showed that at a distance from the gastric cancer node are detected background and precancerous processes such as chronic gastritis, gland atrophy, intestinal metaplasia, epithelial hyperplasia, and mild dysplasia. The severity of these changes decreases with distancing from the primary tumour node.

E-PS-06-077

Histo-and cytoarchitectonic of the central and peripheral compartments of gastric cancer

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Background & objectives: Oncological diseases are one of the main problems of humanity. Malignant neoplasms are one of the most common causes of morbidity and mortality. More than 10 million new cases are registered annually in the world, this number is growing every year.
Methods: The main goal of this research work was the analysis of the histo- and cytoarchitectonics of the central and peripheral parts of gastric carcinomas to study the heterogeneity of their structure using a semi-quantitative evaluation score from 0-3 of individual parameters of their structure. The data analysis was performed using the IBM SPSS Statistics 23.
Results: A group of 49 patients with gastric cancer (m/f-26/23), age 64-69.5 years, was studied. The most common localization of malignancies: 1) body-42.86%; 2) cardia-14.29%; 3) antrum-28.57%; 4) pyloric department -10.20%. Major part of cases were adenocarcinomas - 42 cases (G3 - 20, G2-17, G1–5). Undifferentiated cancer - 6; signet ring cell carcinoma - 1 cases. Studying of histoarchitectonics parameters in the central (c) and peripheral compartments (p) of adenocarcinomas, did not show statistically significant differences, however cytoarchitectonics studying revealed significant results ($P < 0.05$) according to the following parameters (C/P; H&Ex400): 1) mitoses -1.73 ± 0.23 / 1.33 ± 0.17; 2) nucleoli -1.43 ± 0.07/1.1±0.1; 3) hyperchromasia -1.27±0.23 /1.04 ± 0.04.
Conclusion: Studying had demonstrated central and peripheral heterogeneity of cytoarchitectonics of gastric adenocarcinomas. Research results suggest that the evaluation of such parameters as mitosis, the number of nucleoli and nuclei hyperchromasia in various parts of carcinomas should be necessarily made for accurate grade differentiation.

E-PS-06-078

An unusual finding in colon biopsy: metastatic lobular breast carcinoma

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Background & objectives: We report the case of a lobular breast carcinoma with metastases to the colon fourteen years after the initial diagnosis and mastectomy. We describe the microscopic image and the use of immunostains.
Methods: An 85 years old lady was under investigation for diarrhoea episodes and loss of weight. An ileocolonoscopy performed and several biopsies were taken from terminal ileum and colon. The endoscopist reported a normal colon and ileum mucosa and the clinical question was if signs of microscopical colitis were present in the material.
Results: Microscopically the ileum and colon epithelium had a preserved architecture, with normal villi and crypts without any intraepithelial lymphocytosis or any signs of activity such as microabscesses or cryptitis.

The lamina propria in many colon fragments showed a normal population of inflammatory cells but in few of them an abnormal cell population was identified. This cell population showed minimal pleomorphism, the cells were relatively small, the nuclei showed evenly dispersed chromatin and no nucleoli.
A search in the patient's medical history revealed that she had a lobular breast cancer 14 years ago.
The aforementioned cell population was positive with GATA3 and Oestrogen receptors and negative for progesterone receptors.
Conclusion: Pathologists and endoscopists must be aware of the possibility of the metastases of lobular breast carcinoma to the colon even many years after the initial diagnosis.

E-PS-06-079
Sclerosing epithelioid gastrointestinal stromal tumour of stomach mimicking solitary fibrous tumour
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Background & objectives: Gastrointestinal stromal tumours (GIST) characterize by a wide clinicopathologic spectrum in most sites. Microscopical features are site-dependent. The majority of cases present like spindle cell tumours and epithelioid, mixed or pleomorphic histology are found infrequently.
Methods: Sclerosing epithelioid variant contains polygonal tumours cells usually arranged in a syncytial pattern in a variably sclerosing stroma. Usually, that morphological subtype has a low mitotic rate, only with focal atypia.
A 65-year-old male after excision of the stomach tumour was admitted. The initial computed tomography revealed a greater stomach curvature tumour (diameter 11cm) and hypodense areas of necrosis.
Results: Histologically the tumour consisted of numerous epithelioid syncytial and partially dyscohesive cells, with mild cytological atypia and mitotic activity 2/50 HPF, with focal necrosis (<5%). In the stroma, massive sclerosis with numerous staghorn-like vessels was seen. Immunohistochemically, the tumour cells were: DOG1(+), CD117(-/+), CD34(+), CD31(-), ERG(-), STAT6(-), CKAE1/AE3(-), SMA(-),Desmin(-),S100(-), Ki67(+) in 1% of nuclei. Molecularly, a mutation in exon 18 of the *PDGFRA* gene: C.2525 A>T, p.(Asp842Val) was detected. The diagnosis of epithelioid sclerosing GIST, pT4, prognostic group 3b (intermediate risk), stage II was established. The patient was disqualified from adjuvant targeted therapy using a small molecule tyrosine kinase inhibitor while the *PDGFRA* D842V mutation is resistant to imatinib.
Conclusion: This is a case of FIST with some features overlapping the SFT morphology. Immunohistochemical DOG1 positivity together with STAT6 negative results supported with molecular PDGFRA testing were useful in achieving the final diagnosis.
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E-PS-06-082
Analysis of clinical and histopathological findings in lymphocytic gastritis
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Background & objectives: Lymphocytic gastritis (LG) is characterized by large numbers of lymphocytes infiltrating the surface and foveolar epithelium. It is a rare entity, comprises 1-5% of all chronic gastritis. According to the definition 25 lymphocytes/100 epithelial cells is required for the diagnosis.
Methods: Clinical data and histopathological findings including parameters of Sydney system such as Helicobacter pylori (HBP), intensity of neutrophilic, eosinophilic and mononuclear inflammation, activity, intestinal metaplasia, atrophy, dysplasia and associated disease of small and large bowel were evaluated in 16 LG cases diagnosed between 2012 and 2019. Histochemically Warthin Starry, PAS-AB and immunohistochemically CD3 were used in case of necessity.
Results: The mean age was 48(24-70) and M/F ratio 8/8. Eight of the cases were located in the antrum (8/16), seven in the corpus (7/16) and one in antrum and corpus (1/16). HBP was detected in four cases (4/16) located in the corpus. One of these HBP positive case was accompanied by Celiac disease (CD). Four of HBP negative cases had also associated with CD and all located in the antrum. Two cases showed intestinal metaplasia and three gastric mucosal atrophy. One of the atrophic oxintic mucosa also consisted neuroendocrine cell hyperplasia. One of the cases had tubular adenoma and one had hyperplastic adenoma in simultaneously sampled ascending colon biopsy.
Conclusion: The most common accompanying disease in LG is CD and second is HBP infection. CD associated cases are mostly located in antrum and HBP in corpus. LG has clinical/pathological significance since its recognition should prompt further evaluation for other disorders.

E-PS-06-083
Gastric leiomyosarcoma: a rare case report
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Background & objectives: Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal (non-epithelial) malignancies of the gastrointestinal (GI) tract. Gastric leiomyosarcoma is a variant of GISTs and it is an exceptionally rare tumour, representing 1-3% of gastric malignancies.
Methods: A 41-year-old male patient presented to the Surgery Department of our hospital with anaemia and black tarry stool. CT scan revealed a tumour of gastric wall measuring 5,5cm. Peripheral gastrectomy was performed.
Results: Histologically, the mass was composed of epithelioid cells with clear and eosinophilic cytoplasm, moderate atypia, some of them were multinucleated, with diffuse and nodular architectural pattern and fibrous septae. The stroma was myxoid, with very few areas of necrosis and 9 mitoses per 10 h.p.f were observed. Immunohistochemically, the neoplastic cells were positive to Vimentin, h-caldesmon, Calponin, SMA, CD34, BCL-2, CD99 and negative to C-KIT, DOG-1, Desmin, Calretinin, EMA, Melan A, Synaptophysin, MDM-2 and STAT6. Molecular studies for KIT and PDGFRA mutations were negative.
Conclusion: Due to positive smooth muscle stains and despite the epithelioid and clear cell morphology, the diagnosis of leiomyosarcoma grade 2 and score 5 according to FNCLCC, was defined. As the facilities for differentiating leiomyosarcomas are not easily available, gastrointestinal stromal tumours may remain underdiagnosed and undertreated in resource-limited areas.

E-PS-06-084
A rare case of a young patient with serrated colonic polyposis with traditional serrated adenomas
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Background & objectives: Serrated colonic polyposis may have any subtype of serrated polyp, traditional serrated adenoma being the least

common subtype. The condition is detected mostly in the sixth decade and is associated with a high risk of developing colorectal cancer.
Methods: A 28 years old male was hospitalized with a known history of colonic polyposis, diagnosed in the past 3 years with low and high-grade dysplastic adenomas. A multidisciplinary team agreed the patient should undergo total proctocolectomy. On gross examination, we found 57 pedunculated and sessile polyps, located throughout the colon, ranging from 3 cm to 7 cm in diameter.
Results: The large rectal polyps showed microscopically a villous pattern, areas of hypereosinophilia, slit-like serration and ectopic crypts. Areas of low-grade conventional dysplasia were common. High-grade dysplasia was seen focally. Isolated foci of serrated dysplasia were also present. The smaller polyps showed either a similar pattern or unclassifiable serrated features. Lymph nodes were negative for malignancy. Immunohistochemically, the tumour showed microsatellite stability. Genetic tests are pending.
Conclusion: This particular case highlights the importance of timely total colectomy to avoid colorectal malignancy in patients with serrated colonic polyposis.

E-PS-06-087
A rare case of small bowel obstruction due to melanoma
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Background & objectives: The worldwide incidence of melanoma has increased. Primary melanoma involving the digestive tract accounts for <1% of gastrointestinal malignancies. Metastatic melanoma to the small bowel is rare, with a reported incidence of 2-5% and is commonly diagnosed late or post-mortem.
Methods: We report a case of a 71 year old male patient, with unremarkable history and without any suspicious cutaneous lesion, presenting with nonspecific symptoms suggestive of small bowel obstruction. Routine laboratory tests revealed a mild ferropenic anaemia. A CT scan was performed showing an occlusive tumour in the ileum and a large left inguinal lymphadenopathy. The patient underwent segmentary enterectomy.
Results: The excised specimen revealed an ulcerated exophytic 17cm tumour. The histopathology report showed a multinodular proliferation of epithelioid cells, some with intracytoplasmic melanin pigments, extending to the subserosa. The cells were positive for S100, T311 and HMB45. The inguinal lymph node and other seven mesenteric were also invaded by the same tumour. Criteria favouring primary melanoma include absence of other primary site or negative lymph nodes but cases should be evaluated carefully even in the absence of melanoma history based on the fact that some of the cutaneous melanomas can regress spontaneously. The case was signed out as small bowel melanoma favouring metastasis due to presence of inguinal lymphadenopathy involvement.
Conclusion: Small bowel obstruction due to melanoma is unusual. Both primary melanoma and metastatic melanoma of the small bowel are rare entities. Metastatic melanoma of small bowel has a higher prevalence than primary tumours. Surgical treatment increases overall survival rate.

E-PS-06-088
Two faces of oesophageal spindle cell carcinoma
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Background & objectives: Spindle cell carcinoma is a malignant tumour of oesophagus that is composed of both carcinomatous and sarcomatous elements. Epithelioid component is usually squamous carcinoma. Sarcomatoid part usually resembles undifferentiated pleomorphic sarcoma, less frequently it can have low grade features.
Methods: First case, a 50-years-old woman was suffering from dysphagia. During endoscopy, at the 23rd cm from the incisors, a pedunculated polyp with 3.5 cm diameter was found and removed. In second case, a 37-years old woman had an oesophageal resection. Grossly, the grey-white coloured polypoid mass, measuring 2x1.5x0.8 cm, was located at 5 centimetres from the gastroesophageal junction.
Results: The first case had in situ squamous cell carcinoma on surface and moderately cellular spindled cells with collagenized stroma in subepithelial area. The epithelial part showed positive results for P40, P63, AE1-3, there was no expression of desmin, vimentin; in stromal component immunohistochemistry demonstrated expression of vimentin, AE1-3, p63 in focal isolated cells. These findings led us to oesophageal carcinosarcoma composed of in situ squamous cell carcinoma and low grade sarcomatoid component.
Second case, showed undifferentiated tumour which both showed epithelial and sarcomatoid differentiation. Tumour yielded positive results for AE1-3, p40, vimentin but desmin, S100, synaptophysin, chromogranin staining were negative. The tumour was defined as spindle cell squamous cell carcinoma.
Conclusion: Spindle cell carcinoma/carcinosarcoma is a rare type of malignant tumour that represents 2% of all oesophageal carcinomas. Histologically these tumours have biphasic growth pattern. Both of the components can be low grade / in situ or high grade pleomorphic which can only be distinguished by immunohistochemistry.

E-PS-06-089
Ectopic enterobius vermicularis infestation: an extremely rare cause of mesenteric lymphadenopathy
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Background & objectives: Enterobiasis a common helminthic infection in young children worldwide, presents with pruritis in perianal region. The worms typically reside in the caecum, appendix and distal ileum. Involvement of the mesenteric lymph nodes by enterobiasis is an extremely rare phenomenon.
Methods: Histopathological examination was performed of an appendectomy specimen along with multiple mesenteric lymph nodes.
Results: The appendiceal lumen showed cross section of gravid female worm along with acute inflammation in the muscle layer. One of the mesenteric lymph nodes showed necrotizing chronic granulomatous inflammation around degenerated adult worm.
Conclusion: Ectopic enterobiasis in extremely rare cases can be a cause of mesenteric lymphadenopathy. Enterobius vermicularis should be included in the differential diagnosis of cases with mesenteric lymphadenopathy especially in this region of the world where Enterobius vermicularis infestation is common. Thus, careful histologic examination of mesenteric lymph nodes suggested.

E-PS-07 Digestive Diseases Pathology - Liver

E-PS-07-001
A very unusual metastisation site of hepatocellular carcinoma: a case report and review
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Background & objectives: Hepatocellular carcinoma is a common malignant primary liver tumour frequently associated with chronic liver

disease. Extrahepatic metastization is relatively rare, even in advanced cases with intrahepatic metastases. Extrahepatic spreading is most common to the abdominal lymph nodes, lung and bone.
Methods: We report a case of a 55-year-old male with a clinical history of chronic alcoholism (80g/day) and hepatic cirrhosis of infectious and alcoholic origin who was hospitalized because of an involuntary alkaline corrosive ingestion. An upper gastrointestinal endoscopy revealed multiple polyps near the gastroesophageal junction, measuring up to 12 mm, which were biopsied.
Results: Microscopically, a malignant neoplasm was found within the lamina propria, lined by a stratified squamous epithelium with focal areas of ulceration. The malignancy showed a trabecular and solid pattern of cells with pleomorphic nucleus, prominent nucleolus and an abundant vacuolated cytoplasm. No signs of atrophy or dysplasia were found in the epithelium. The immunohistochemistry study was positive for CAM5.2, arginase, glipican3 and CEA. No immunoreaction was found for CK7, CK20, AE1/AE3, vimentin, HMB45, S100, p63, EMA, CK19 and CDX2. The patient was diagnosed with an oesophageal metastasis of hepatocellular carcinoma. This and only 13 other cases have been reported in English-published literature during the last 20 years, which were reviewed.
Conclusion: Unusual metastization sites of hepatocellular carcinoma like the oesophagus, although very rare, must be taken into account, as they can occur and resemble the morphology of primary malignancies of those same sites.

E-PS-07-002
A rare case of epithelioid haemangioendothelioma of the liver with a stationary status

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Background & objectives: Epithelioid haemangioendothelioma of the liver (EHL) is a very rare malignant vascular tumour, with an incidence of 1-2 in 1 million and approximately 200 cases described in the literature. The liver is the most common localization (21%).
Methods: We present a rare case of EHL which was incidentally found by abdominal imaging in a female patient with ovarian Brenner tumour. A 57-year-old woman who underwent abdominal radiologic investigations for ovarian tumour, was also found to have 14 hepatic nodules, with maximum diameter of 3 mm, diffusely distributed in the right lobe.
Results: A biopsy was performed and the liver proliferation was initially misdiagnosed as a mesenchymal hamartoma.
The patient underwent several other radiologic investigations annually for 5 years, which revealed that the nodules were stationary in number and size. During this period of time, she denied any symptomatology and the routine haematological investigations were negative.
After 5 years, a new liver biopsy was performed and microscopic findings showed epithelioid and spindle tumour cells with vacuolated cytoplasm representing intracellular small vascular lumina. Immunohichemical markers were positive for CD31, CD 34, ERG and the diagnosis of EHL was made.
Conclusion: Although diagnosing EHL is very difficult to make because of its non specific radiologic and clinical findings and the high proportion of asymptomatic cases, the immunohistopathological findings are important and facilitates a correct diagnosis.

E-PS-07-003
Prognostic impact of hepatotoxicity in colorectal cancer metastatic to the liver

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Background & objectives: The use of systemic chemotherapy and targeted therapies has improved the therapeutic management of colorectal liver metastases. However, neoadjuvant chemotherapy is often responsible for toxic damage to the non-tumour liver. The presence of chemo-induced liver damage can have a negative impact on the functional reserve of the liver. Our study aimed to evaluate the hepatotoxicity induced by neoadjuvant chemotherapy in patients with colorectal liver metastases and to assess its prognostic impact.
Methods: We retrospectively reviewed 50 cases of colorectal liver metastases treated by different neoadjuvant chemotherapy protocols and targeted therapies. These cases were diagnosed at the pathology department of the university hospital Mongi Slim of La Marsa over a period of four years and six months (January 2014 - July 2018).
Results: The mean age of the patients was 56 years with a sex ratio (M/F) of 1.38. Histological examination of the non-tumour liver revealed 28 cases of steatosis, two cases of steatohepatitis, 33 cases of sinusoidal obstruction syndrome and three cases of regenerative nodular hyperplasia. Median overall survival was 24 months. The prognostic factors were the number of liver metastases, the neoadjuvant chemotherapy protocol type and the use of targeted therapies.
Conclusion: Hepatotoxicity of neoadjuvant chemotherapy can lead to a high risk of postoperative morbidity. However, its impact on postoperative mortality has not been entirely established

E-PS-07-004
An unexpected diagnosis of ectopic pancreas in the liver

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Background & objectives: The ectopic pancreas is defined by the presence of pancreatic tissue in an abnormal situation, with no anatomical relationship to the main gland. We herein report a new case of an incidentally discovered ectopic pancreas in the liver.
Methods: This is the case of a 54-year-old hypertensive patient operated on two years previously for a sigmoid adenocarcinoma classified as pT3N1b. The evolution was marked by the installation of multiple metastases, which were predominant in the right hepatic lobe, hence, the initiation of neoadjuvant chemotherapy (4 FOLFOX - ERBITUX cures). The patient underwent a right lobectomy.
Results: Histological examination confirmed the presence of colorectal liver metastasis. There was associated a focus of pancreatic heterotopia including acini and excretory ducts organized in lobule. There were no islets. According to the Heinrich classification system, the heterotopic pancreas was classified as type 2. The postoperative course was uneventful, however, during the follow-up period; the patient developed liver metastases in the left hepatic lobe.
Conclusion: The diagnosis of heterotopic pancreas prior to surgery is difficult due to its non-specific clinical signs and symptoms. Diagnosis can only be established based on histopathological examination.

E-PS-07-005
An unusual and rare metastasis of hepatocellular carcinoma: gingiva

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Background & objectives: Hepatocellular carcinoma mostly presents with multiple intrahepatic occurrence and metastasis. Approximately one third of the patients develop extrahepatic metastasis-mostly to lung. Oral cavity, especially gingival metastasis is very rare with less than 20 cases in English literature.
Methods: 60-year-old male patient is presented with diarrhoea, nausea and fatigue ongoing for 2 months. Patient had spider angiomas on his face and palmar erythema. Peripheral blood test showed anaemia, increased AST, ALT, ALP and GGT with HBV DNA 49000 IU/ml. There was no evidence of acute inflammation. USG revealed 20x19x15 cm heterogeneous liver mass on the right lobe.

Results: Patient also had an ulcerative oral mucosal nodule of 2 cm diameter which slightly bleeds and causes pain and discomfort. An initial oral mucosal biopsy was performed by otolaryngologist before the scheduled liver tru-cut biopsy. Biopsy showed a diffuse trabecular infiltration of polygonal cells which had abundant granular eosinophilic cytoplasm under the normal stratified squamous epithelium of the gingiva. There was also focal yellow/light brown pigmentation in the cytoplasm. Immunohistochemistrically, pancytokeratin was weakly positive while vimentin was negative. MelanA, HMB45 and S100 was negative and Ki67 index was high (%60). TTF1 was weakly cytoplasmic positive while Heppar was diffusely strong positive and pCEA showed canalicular staining pattern.
Conclusion: Final diagnosis was hepatocellular carcinoma metastasis to gingiva. Patient history has an essential role on differential diagnosis of malignant oral mucosal tumours.

E-PS-07-006
Elementary lesions and prognostic correlations in paediatric non-alcoholic steatohepatitis
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Background & objectives: NAFLD is characterized by hepatic fat accumulation not due to alcohol abuse. Initial simple steatosis could evolve to NASH and subsequently to end-stage cirrhosis. The aim of this study is to evaluate the correlation between histology and disease stage.
Methods: We examined 7 liver biopsies from patients, aged from 3 to 18 years, admitted to our Hospital between 2001 and 2013. Immunohistochemical assessment for Cytokeratin 7, Cytokeratin 19 and Alpha-SMA were performed.
Results: Patients were classified into two groups based on the histological score: the first group including 5 patients with mild steatohepatitis and 2 patients with moderate steatohepatitis; the second group showed severe inflammation and diffuse ballooning degeneration with progressive disease.
Conclusion: NAFLD represents one of the most important liver disease. The prevalence of NAFLD among obese children is rising up to 40-70%. Liver biopsy is the gold standard for the diagnosis of NAFLD/NASH and is fundamental for evaluating the degree of necro-inflammatory changes and fibrosis. Liver biopsy in children with risk factors could allow early diagnosis, increasing the chances of regression and reducing the progression of the liver damage in adolescence.

E-PS-07-007
Light chain deposition disease associated to multiple myeloma in liver: an unusual presentation
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Background & objectives: Light chain deposition disease (LCDD) is a monoclonal immunoglobulin deposition disease with similar clinical-pathological manifestation to amyloidosis. The most frequent chain is Kappa and it can be associated to neoplastic disorders such as Multiple Myeloma or lymphoproliferative diseases.
Methods: A 49 years old male with previous diagnosis of Multiple Myeloma, costal plastocytoma and renal failure facing dialysis since 4 years ago, consulted for a generalised itching and dyspepsia. They just found out a colestatic pattern with Alcaline Fosphatase and GGT increased levels, without alterations in imaging tests. Autoimmunity and viral study were negative so they took an hepatic biopsy.
Results: The sample showed preserved hepatic architecture with diffuse sinusoidal rigidity due to linear deposits of an unknown material in Disse spaces resembling amyloid deposits. Immunochemistry demonstrated Kappa deposits that were negative to Congo Red or green in polarised light. After diagnosis, the patient levels of bilirubin increased and an hepatic failure caused him death.
Conclusion: LCDD consists in the deposition of monoclonal light chains in multiple organs. At first glance it is a challenge for histopathological diagnosis due to its specific characteristics and amyloidosis resemblance. This case is difficult because it rarely affects liver when amyloidosis frequently does and clinical manifestations of hepatic failure and cholestasis seen are rare in this entity. To add, diffuse hepatic infiltration has been described essentially as an autopsy finding.

E-PS-07-008
Combined hepatocellular-cholangiocarcinoma diagnosis
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Background & objectives: Combined hepatocellular-cholangiocarcinoma (HCC-CC) displays both hepatocyte and biliary phenotypes, likely to derive from same progenitor cell. With poor prognosis, there is lack of standard criteria for diagnosis and treatment.
Methods: A series of 89 hepatocellular carcinomas (HCC) were studied concerning 54 consecutive patients undergoing resection or liver transplantation. According to 2019 World Health Organization (WHO) histopathological criteria and CK7/CK19, αSMA actin and vimentin immunoexpression in single or clusters of tumour cells, HCC-CCs were searched in this group of tumours.
Results: Formerly classified as HCC, 8 cases expressed CK7 and CK19 where 5 cases presented combined trabecular and pseudo-glandular growth pattern. Vimentin was expressed in 6 cases and one case was αSMA positive. Microvascular invasion or intrahepatic satellite nodules were not present. Within 6 years after curative surgery, 4 cases recurred. Alcoholic liver disease was the clinical background for all patients and all were male.
Conclusion: Combined hepatocellular-cholangiocarcinoma is rare and frequently under-recognized due to the lack of clearly applied diagnostic criteria. This small series highlights the utility of histopathological report based on 2019 WHO classification and routine defined immunohistochemical panel.

E-PS-07-010
Primary hepatic marginal zone B-cell lymphoma presenting as a carcinoma
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Background & objectives: Among primary hepatic lymphomas constitute about 0,016% of all cases of non-Hodgkin's lymphomas, a primary hepatic low-grade marginal zone B-cell lymphoma is extremely rare and often misdiagnosed.
Methods: A 69-year-old man presented to our hospital because of a solitary mass in the liver, which was identified incidentally by ultrasonography. Physical examination showed no palpable splenomegaly or superficial lymph node swellings. Laboratory results included ALP, LDH, CEA and AFP levels were within normal ranges. CT imaging showed a hypodense mass, suspected as an intrahepatic cholangiocarcinoma and FNB was performed.
Results: Microscopic examination showed diffuse and monotonous infiltration of typical monocytoid lymphoid cells and lymphoepithelial

lesions observed on some bile ducts infiltrated with these small- to medium- sized lymphocytes. Immunohistochemistry findings were positive for CD20, CD79a and PanB, whereas they were negative for CD3, CD5, CD10, bcl6, cyclinD1, CD23 and DBA44. Ki67 was estimated 1%. The patient was diagnosed with primary hepatic MALT lymphoma, specifically a low-grade malignant extranodal marginal zone B-cell lymphoma.
Conclusion: According to literature review, the preoperative diagnosis of this tumour remains a challenge, due to the scarcity of specific clinical and imaging signs and should be considered in any patient at any age who presents with a liver mass or infiltration.

E-PS-07-012
Hepatobiliary schistosomiasis, a case report
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Background & objectives: Schistosomiasis is the second commonest parasitic infestation prevalent in subtropical and tropical regions. Hepatobiliary schistosomiasis can present with multiple cystic lesions that may be clinically and radiologically simulate inflammatory pseudo tumour or malignant liver lesions in appropriate clinical settings.
Methods: 70 year old male with a history of right partial nephrectomy for clear cell renal cell carcinoma having an uneventful post operative follow up for 2 years, underwent a surveillance CT scan. Multiple hepatic cystic lesions were identified and subsequent MRI and PET scan were performed for further evaluation and revealed suspicious for metastasis. Partial hepatectomy was performed.
Results: Biochemical indices of the liver were within normal. Macroscopically, there were multiple discrete cystic lesions in the liver parenchyma. Solid tan nodules were not seen. Histological examination revealed multiple necrotic hyalinised nodules with granulomatous inflammation within liver and dense neutrophil infiltration with microabscess formation. Within the central necrotic area are seen non-viable parasites eggs and part of worm in keeping with parasitic infestation, in keeping with Schistosomiasis. The eggs, not the worms, initiate the pathophysiology, which give rise to hepatic granulomata formation which is mediated by MHC class 11-restricted CD4+ T cells.
Conclusion: Hepatobiliary schistosomiasis is clinically and radiologically simulate inflammatory pseudo tumour or malignant liver lesions, either primary or secondary. Hence, proper sampling of these lesions with multiple deep level examinations along with histochemical stains is recommended for the definitive diagnosis.

E-PS-07-013
Direct analysis of virtual slide scanner data for liver fibrosis is correlated with Ishak score
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Background & objectives: We performed direct analysis of Virtual Slide Scanner (VSS) data by computer-assisted image analysis (CAIA) for liver fibrosis. In this report, we report that correlation between Ishak score (IS) and CAIA data.
Methods: Twenty-seven cases of non-cancer area of primary liver cancer surgical specimens were examined and IS was determined with Picrosirius Red (PSR) stained specimens as average of 2 observers. Detected PSR positive areas in VSS data was divided into two groups; 5-50 μm^2 area (separated small area: SSA) and 50-10,000,000μm^2 areas (connected large area: CLA), and their % was evaluated.
Results: CLA was distributed mainly in Glisson/septal area. While, SSA was observed in interlobular area and small area not detected as CLA in CLA-distributed area. CLA and IS showed moderate correlation (R=0.58986), which was identical to the data in the literature. While, SSA and IS showed no correlation (R=0.12653). The average of CLA and SSA was 7.8 % and 2.7 % without no correlated between them (R=0.15931). Interestingly, SSA+CLA and IS showed moderate correlation (R=0.53112). These results indicated that direct analysis of VSS data for fibrosis would be useful to evaluate liver fibrosis. That is, this method gives us a chance to evaluate entire specimen area without selection bias.
Conclusion: Our data indicated that our direct analysis of VSS data enabled to evaluate not only Glisson/septal fibrosis but also intralobular fibrosis simultaneously, which would be missed for evaluating liver fibrosis in ordinal image analysis by photo-images.

E-PS-07-014
The impact of bacterial translocation on the morphological structure of extrantestinal organs in rats with strangulated intestinal obstruction
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Background & objectives: The aim is studying the effect of microbial translocation on different internal in rat model strangulated intestinal obstruction (SIO).
Methods: 52 rats were allocated into 3 groups:I(BT+)20 rats with SIO model,2(BT-)20rats with SIO-model ,3-12 sham-operated rats. SIO was made by clamping of small intestine and mesentery vessels for 60min and reperfusion period for 2hours.As a marker of BT fluorescent E.coli was used and microbiological analysis .Morphological study of organs examined by "Leica DM 1000"microscope.The significance results was determined by Fisher's test
Results: in BT(+) group 80.0%(n=16) in the spleen and kidneys the capillary stasis, pulp plethora were observed, in liver – the lypodistrophy changes were seen. In the group with absence of BT histological structure was saved in all of organ samples and single site of damage were represented in 3% of rats. Histologic signs were not found in the sham group.
Conclusion: In conclusion, the BT leads up to changes of organ samples.

E-PS-07-015
Survival of patients with hepatocellular carcinoma in correlation with tumour differentiation, microvascular invasion and Ki67 proliferative index
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Background & objectives: The survival in patients with hepatocellular carcinoma (HCC) is difficult to predict. It is considered that the histological grade (G) and microvascular tumour invasion (MVI) influence the survival of HCC patients. Ki67 immunorepression may be a prognostic marker in HCC.
Methods: We analysed the influence of G, MVI and Ki67 immunoexpression on the survival in 60 consecutive patients with histologically proven HCC diagnosed and treated at the University Clinic of Gastroenterohepatology in Skopje.
The biopsy and operative material were analysed at the Institute of Pathology in Skopje. All patients were followed up from the date of HCC diagnosis till 24 months.
Results: There were 19 (31.67%) female and 41 (68.33%) male, ranging in age from 31 to 85 years, median 61.88±10.51,
We found statistically significant difference in survival of patients with G3 in comparison to G1 ($p<0.05$) and in patients with and without MVI ($p<0.01$)

Ki 67 immunoexpression was significantly higher in G3 and G2 HCC in comparison to G1 tumours ($p < 0.01$; $p< 0.01$).
Patients with MVI had higher expression of Ki67 in comparison to patients without MVI, but not significantly.
Ki 67 immunoexpression did not influence the survival of the patients.
Conclusion: Tumour differentiation and microvascular invasion influenced survival in patients with HCC. Ki67 expression was significantly higher in HCC with G2 and G3 in comparison to G1 tumours. Ki67 did not influence survival of HCC patients but was an indicator for worse differentiation.

E-PS-07-016
Reactive lymphoid hyperplasia of the liver with granuloma formation: a case report
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Background & objectives: Reactive lymphoid hyperplasia (RLH), also known as hepatic pseudolymphoma or nodular lymphoid lesion, is extremely rare. To the best of our knowledge, this is the first case with granuloma formation.
Methods: We reported a case of RLH showing that granulomas as an additional microscopic finding and discussed it's imaging and clinical background.
Results: A 55 years old female was found to have elevated liver enzymes and anti-mitochondrial antibody (M2). Liver biopsy suggested primary biliary cholangitis. On follow-up the radiology revealed a mass lesion suspicious for hepatocellular carcinoma. The lesion of 1.5 cm diameter was excised Microscopically the lesion consisted of mature lymphocytes, non-necrotising granulomas and lymphoid follicles with reactive morphology. Nodular lymphoid infiltration, granulomatous diseases, Castleman disease and extranodal marginal zone lymphoma were ruled out based on morphological, immunohistochemical and clinical data.
Conclusion: Awareness is necessary for the diagnosis of RLH which can be coexist with infectious, autoimmune or malignant processes.

E-PS-07-017
A case report of multiple hepatocellular carcinomas in a 56-year-old bodybuilder – something is growing on
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Background & objectives: Hepatocellular carcinomas are the most common primary malignant liver tumours of the adults. Anabolic steroids consumption has been described in patients diagnosed with hepatocellular carcinomas, but no relation is established between the intake of these substances and the tumour development.
Methods: A 56-year-old male referred to our centre for pain in the right hypochondriac regions. He was a bodybuilder and declared consuming androgenic anabolic steroids. The enhanced-MRI showed two hepatocellular lesions, on the right lobe (16 cm in diameter) and in the left lobe (5 cm in diameter). Right hepatectomy combined with left lobe (2 and 3) subsegmentectomy was performed.
Results: The surgery specimens were consisting of two well-differentiated, non-encapsulated hepatocellular carcinomas, with a pseudoacinar pattern. Vascular emboli were present. Distant liver parenchyma showed a discrete macrovesicular steatosis without any cirrhosis. The beta-catenin immunohistochemistry showed diffuse membranous, cytoplasmic and focal nuclear positivity. Glypican-3 stained focally positive in the tumour cells. NGS analysis revealed a D32H hotspot mutation of the CTNNB1 gene. The surgical specimen was staged pT3N0 V1L0P0R0. Follow-up was decided.
Conclusion: De novo hepatocellular carcinomas have already been described in patients with androgenic anabolic steroid consumption. On the other hand, the presence of beta-catenin hotspot mutations in hepatocellular carcinomas can suggest a possible progression from a hepatocellular adenoma (via the Wnt/beta-catenin signalling pathway).

E-PS-07-018
Melanoma metastasis in gallbladder - case report and literature review
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Background & objectives: Metastasis in gallbladder are rare events, but melanoma metastasis are the most frequent with 70 cases reported in literature, mostly in autopsy examination or in symptomatic patients. Thus, its rarity and clinicopathological characteristics could justify its presentation.
Methods: We report a 48 years-old male patient with temple superficial spreading melanoma with vertical grow phase, 3 mm Breslow index and positive sentinel node in October 2017. After interferon-dexamethasone regimen without symptoms, a control CT (may 2019) revealed a 22 mm soft tissue density mass in gallbladder, suspicious of malignancy. Therefore, surgical treatment was planned and morphologic description was performed.
Results: Gross examination revealed two well-defined polypoid blackish lesions (5x2x1.5cm and 0.9x0.7 cm) with blackish cut surface and moderate consistency. Microscopically, it is formed by cells with wide eosinophilic cytoplasm with eccentric nuclei, sometimes with nucleolus and nuclear pseudoinclusions and frequent mitotic figures. Abundant blackish brown pigment. It showed nuclear positivity to HMB45. A final diagnosis of "Gallbladder with bifocal melanoma metastasis" was made.
Conclusion: Gallbladder metastasis of melanoma are exceptional and we report a case with clinical, radiological and pathological correlation.

E-PS-07-019
Progressive familial intrahepatic cholestasis: a report of two cases
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Background & objectives: Progressive familial intrahepatic cholestasis is an inherited disorder of childhood which presents in the neonatal period and leads to death from liver failure.
In this study, we correlate morphologic features of the liver with clinical and biological findings in patients.
Methods: We report two cases of progressive familial intrahepatic cholestasis which have been recently diagnosed in our laboratory . It's about two children with average age 3 months, which derived from a consanguineous marriage. They presented an icter associated with a hepatomegaly. The laboratory findings included an elevated serum gamma-glutamyltransferase values with non remitting conjugated hyperbilirubinemia and moderately elevated liver transaminases.
Results: A Liver biopsy was done for both infants. It showed an intracanalicular cholestasis with lymphocytic inflammatory elements. One of those infants presented alsoperiportal fibrosis, a giant cell hepatitis with proliferation of the bile ducts. The diagnosis of progressive familial intrahepatic cholestasis (PFIC) subtype 3 in this case, was retained. For the second infant, in addition to the intracanalicular cholestasis, a mild lobular and portal fibrosis with biliary thrombi have been noted concluding to a progressive familial intrahepatic cholestasis (PFIC) subtype 2.
Conclusion: Diagnosis of progressive familial intrahepatic cholestasis (PFIC) is a challenging matter that involves the summation of clinical, laboratory, radiological, and liver histological parameters; in addition to specific investigations to exclude other causes of neonatal cholestasis.

E-PS-07-020

Primary epithelioid angiomyolipoma of the liver with recurrence after 16-year follow-up: review of the diagnostic criteria of malignancy

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Background & objectives: Hepatic angiomyolipomas (AML) is a rare mesenchymal neoplasm occurring most commonly in kidneys, being the liver the second frequent location. Malignant hepatic presentation is anecdotal, with the existence of 24 cases described in the literature, sometimes misdiagnosed as hepatocellular carcinoma.
Methods: 65-year-old patient, with history of chronic hepatitis C cured in 2002. In 2003 a central hepatectomy was performed due to an 8 cm tumour with a result of AML. After a follow-up of 16 years, a new 5 cm lesion was detected by ultrasound. A core biopsy was made with the diagnosis of Pecoma. Right hepatectomy was performed.
Results: Microscopic examination showed varying amounts of epithelioid cells, smooth muscle cells, adipose tissue and vessels. The immunohistochemical study was positive for HMB45, cathepsin K, smooth muscle actin and negative for CD34, with a mitotic count of 2 mitosis/50 high power fields, with presence of multinucleated cells and cellular pleomorphism, confirming the diagnosis of non-epithelioid malignant AML according to Folpe criteria and tumour of uncertain malignant potential according to Schoolmeester criteria. The histological review of the first tumour revealed presence of giant cell or pleomorphism, reclassifying the tumour as malignant.
Conclusion: Primary malignant hepatic AML is an infrequent tumour. Extrahepatic metastases and recurrences are common, and exhaustive follow-up is vital. With reports of metastases after primary surgical resection, there is need to review angiomyolipomas and to decide whether to reclassify them as slow-growing malignant tumours or whether de novo or metastatic lesions.

E-PS-07-021

Typical and atypical presentation of hepatic sarcoidosis: a case series with histological confirmation

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Background & objectives: Sarcoidosis is a systemic disease that most commonly affects the lungs and lymphoid system. Hepatic involvement is found in up to 80% of patients. However, evidence of hepatic dysfunction are infrequent and histological evaluation is only required in atypical cases.
Methods: We reviewed four cases of sarcoidosis hepatic involvement with histological confirmation. Two patients presented dissociated cholestasis with concomitant cutaneous, lacrimal and lung involvement. The other two underwent a percutaneous hepatic biopsy because of a chronic transaminasemia of unknown aetiology in absence of pulmonary or lymphatic disease.
Results: The patients were middle-aged women and a 35-year-old man. Histological findings were a predominantly portal or periportal-based non-caseating granulomatous inflammation formed by sarcoid-type granulomas in different evolutive stages. These compact epithelioid granulomas showed multinucleated giant cells with occasional eosinophils and characteristically intragranulomatous fibrosis highlighted by reticulin and collagen fibres special stains. Fungal and acid-alcohol resistant bacilli infections were ruled out with additional studies. After clinical and serological correlation, a diagnosis of confirmation was made in two cases whereas a first diagnosis of suspicious was made in the other two. Although the clinical management of hepatic sarcoidosis is controversial, corticosteroid-based therapy was initiated and remission of the hepatic alterations was achieved.
Conclusion: Hepatic involvement is frequent in systemic sarcoidosis (50-80% of the cases), and its usually asymptomatic Histological confirmation is required only in cases with atypical clinical presentation, such as analytical dissociated cholestasis, mass forming lesions in imaging technics or portal hypertension of unknown origin. On the other hand, isolated liver sarcoidosis might be the first clinical manifestation of the disease.

E-PS-07-022

Small cell neuroendocrine carcinoma of gallbladder: a case report

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Background & objectives: Neuroendocrine carcinomas make approximately 4% of all malignant neoplasms of the gallbladder, showing a female predominance and they are most common in the early to mid-seventh decade of life (age range: 29 - 63 years), being frequently associated with gallstones.
Methods: We report the case of a 77-year old male with a gallbladder tumour, who was subjected to a hepatic wedge resection including the gallbladder. Also a lymph node from the hepatic hilum was resected. On gross examination a tumour at the fundus of the gallbladder was revealed, 6,5 cm in greater diameter, extending to the neighbouring hepatic parenchyma.
Results: Microscopy of the tumour and the lymph node (H-E stains) revealed a poorly differentiated carcinoma, consisting of round or fusiform cells with hyperchromatic nuclei and inconspicuous nucleoli, arranged in nests or sheets. Less than 7% of the tumour resembled to a typical Biliary-type adenocarcinoma. Immunohistochemically, tumour cells were positive for CK8/18 (dot-like), Synaptophysin, Chromogranin, CD56 and p53. Ki-67 was very high (~95%). There was no expression of Serotonin, Somatostatin, ACTH and SSTR5. SSTR2a expression score was 1+ according to Volante scoring system. Based on the morphological and immunohistochemical findings, a diagnosis of Small cell Neuroendocrine Carcinoma of the Gallbladder was set.
Conclusion: Gallbladder neuroendocrine carcinomas have a very poor prognosis. Most of the patients show disseminated disease at diagnosis, with the median survival time for these carcinomas being < 1 year, and the 5-year and 10-year survival rates 20% and 0% respectively.

E-PS-07-023

Lipid rich hepatocellular carcinoma: a provisional subtype that needs to be characterised - report of a new case with literature review

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Background & objectives: Lipid rich hepatocellular carcinoma has been described as a provisional subtype. It looks similar to clear cell HCC but with different prognosis. We report a case to add data in order to define prognosis and behaviour of this new subtype.
Methods: The patient is a 58-year-old man with previous diagnosis of chronic viral hepatitis B and long-time risk alcohol consumption. He came to our hospital from Romania for hypertransaminasemia and a hyperechoic liver mass 6 cm diameter. After transarterial chemoembolization it recurred, as surgical resection was not possible (located at hilum) . Liver transplant was performed.
Results: Explant liver showed a 7cm nodule with ill defined borders and extensive areas of necrosis and fibrosis. The surrounding liver showed micronodular cirrhosis with septa and very scarce steatosis. The tumour was a solid macrotrabecular mass extensively necrotic in central areas.

There was a peripheral surviving area composed principally of tumour cells with abundant clear cytoplasm. On high power examination, tumour cells showed numerous tiny droplets of fat. Similar to microvesicular stetatosis and stained with adipophilin antibody. Also there were some cells intermingled with clear cytoplasms and ill-defined hyaline lumps. Macrovesicular steatosis was absent. No pericellular fibrosis was found. Lymphovascular invasion was present although the viable tumour was small and moderately differentiated.
Conclusion: "Lipid rich HCC" can look similar to clear cell HCC , steatohepatitic HCC or even be confused with a steatotic nodule if well-differentiated. It has been classificated as "provisional subtye" because more data are needed. We describe a case, presented for first time in relation to virus B and alcohol, with lymphovascular invasion and poor prognosis, in order to add knowledge to this new entity with very few cases previously reported.

E-PS-07-024
Intraductal papillary neoplasm of the bile duct: a case report
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Background & objectives: Intraductal Papillary Neoplasm of the Bile duct (IPNB) is a rare premalignant neoplasm of bile duct. IPNB is rarely seen in clinical practice in Egypt. Therefore, it is important that pathologists become familiar with its histopathological features for accurate diagnosis.
Methods: Herein, we present a case of 59-year-old Egyptian female with an accidentally-discovered mass. Radiological examination revealed a partially cystic, partially solid focal lesion involving the whole right lobe. CA19-9 was elevated. The patient underwent extended right hepatectomy. Pathological evaluation and immunohistochemical staining of CK7, CK20, ER and PR were done.
Results: Grossly, multiple polypoid masses were projecting into the lumen of a cystically dilated large bile duct with intracystic haemorrhage. Microscopically, there were prominent papillary proliferations with delicate fibrovascular stalks that lacked an ovarian-like stroma as evidenced by negative ER and PR. Epithelium showed multistep progression from low grade to high grade intraepithelial neoplasia without an invasive component and CK7/CK20 positivity indicating its pancreatobiliary epithelial origin. Thus excluding mucinous cystic neoplasm and proving the diagnosis of intraductal papillary neoplasm of the bile duct.
Conclusion: IPNB is a rare premalignant variant of the bile duct neoplasms, considered as the biliary counterpart of intraductal papillary mucinous neoplasm (IPMN) of the pancreas. It should be differentiated from other cystic lesions of the liver and bile duct like mucinous cystic neoplasm that has no communication to the bile duct system and has an ovarian-like stroma, at least focally positive for ER and PR, essential for its diagnosis.

E-PS-07-025
Undifferentiated embryonal sarcoma of the liver: a case report
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Background & objectives: Undifferentiated embryonal sarcoma of the liver is a rare primary malignant mesenchymal hepatic neoplasm occurring predominantly in children. Diagnosis remains challenging because of overlapping clinical& radiological characteristics with other liver tumours. Pathological& immunohistochemical assessment are necessary for an accurate diagnosis.
Methods: Here we present a case of 7-year-old female presenting with abdominal distension and dyspnoea. Radiological examination revealed a cystic lesion near totally replacing the right hepatic lobe with clinical suspicion of mesenchymal hamartoma. The patient underwent extended right hepatectomy. Pathological evaluation, immunohistochemical study using CD68, heppar-1 and CD34 and PAS staining were done.
Results: Gross examination revealed a mass measuring 23cm on greatest dimension replacing most of right hepatic lobe. Cut sectioning showed alternating glistening greyish-white solid areas and cystic soft gelatinous areas with areas of haemorrhage and massive necrosis.
Histological examination revealed infiltration by undifferentiated oval to spindle cells and bizarre multinucleated giant cells in a myxoid background with massive necrosis. Malignant cells exhibited high degree of anaplasia, indistinct cell borders, cytoplasmic hyaline globules, frequent mitosis. Immunohistochemical staining was negative for heppar-1, CD34, CD68. The cytoplasmic hyaline globules were positive for PAS stain thus proving undifferentiated embryonal sarcoma of liver and excluding other liver tumours.
Conclusion: Undifferentiated embryonal sarcoma of liver is a rare malignant neoplasm of paediatric age group that could be unexpected clinically. Clinical and radiological findings are non-specific that's why pathological and immunohistochemical evaluation are vital for early diagnosis for a favourable outcome.

E-PS-07-026
Drug-induced autoimmune hepatitis secondary to Levofloxacin: report of a case
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Background & objectives: Drug-induced liver injury (DILI) is a broad term that encompasses any liver injury caused by medication. It can have a wide spectrum of manifestations and show different patterns of hepatic injury. DILI can present as a Drug-induced Autoimmune Hepatitis (DI-AIH).
Methods: We present the case of a 68-year-old female that consulted with epigastralgia, itching and choluria. The patient reported having recently taken Levofloxacyn. She had been treated with Levofloxacyn on a previous occasion with no associated symptomathology. Initial bloodwork revealed hyperbilirubinemia (5,2 mg/dl) and hypertransaminasemia (AST/ALT: 1320/2091 UI/L). Viral serologies were negative and no autoantibodies (ANA, AMA, anti-LKM, ASMA) were detected.
Results: Follow-up analysis showed an increase in the level of transaminases and subsequently a liver biopsy was performed. The biopsy showed a pattern of periportal and pericentral necroinflammatory hepatitis with abundant plasmatic cells and eosinophils. The findings were reported as compatible with Autoimmune Hepatitis (AIH).
DILI can present as a DI-AIH, especially in cases of repeated exposition to a drug. The differential diagnosis between true AIH and DI-AIH can be challenging as clinical, biochemical, serological and histological patterns are similar, though patients with DI-AIH respond to immunosuppressants and do not relapse after treatment. In our case, the patient was treated with corticosteroids and responded, though in a protracted manner.
Conclusion: We consider that in patients with DILI, especially in cases of repeated exposition to a drug, an AIH-like process must be considered as it has implication on both treatment and prognosis.

E-PS-07-027
Frequency of hepatocellular carcinoma in Karachi, Pakistan: eight years (2010-2018) data from the largest public sector diagnostic & reference laboratory of Sindh
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Background & objectives: In Pakistan, incidence and prevalence of Hepatocellular carcinoma is rising due to en-mass conversion of previously HCV seropositive patients. In order to document frequency of HCC

we report eight years data detailing frequency of HCC within Pakistan.
Methods: For liver cancer statistics data was retrospectively collected from 2010-2018 after ethical approval from Dow University of Health Sciences (Ref no. IRB-459/DUHS/-14). All data were manually coded using the international classification of diseases (ICD-10, 2016 version) and indexed in Canreg software provided as a freeware by the International Agency for Research on Cancer (IARC), MS Excel as well as SPSS.
Results: A total of 14,759 were diagnosed as cancers. Of these cancer cases, a total of 317 (2.15%) were diagnosed as primary HCC. Of these 317 HCC cases, 191 (60.25%) were diagnosed in males and 126 (39.8%) in females. Crude rate of HCC was 2.17. Crude rate was 2.4 in males and 1.8 in females.
Conclusion: We report frequency of liver cancer in Karachi with increasing trends.

E-PS-07-028
Differential immune landscape of hepatocellular carcinoma: potential role of macrophages in hepatocarcinogenesis
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Background & objectives: In Pakistan, incidence and prevalence of Hepatocellular carcinoma is rising due to en-mass conversion of previously HCV seropositive patients.
The objectives were to investigate myeloid and lymphoid immune cell densities in tumour microenvironment of hepatocellular carcinoma.
Methods: A total of 42 patients (cases) diagnosed as hepatocellular carcinoma and a total of 10 control tissues (liver donor) were taken. In order to investigate immune cells densities immunohistochemistry was performed using antibodies for immunecells. Quantification of immune cells/mm2 was performed as per the College of American Pathologists' guidelines. A p-value of 0.05 was considered significant at all times.
Results: We report significantly increased infiltration of macrophages (mean macrophages= 306.57/mm2, p-value<0.05), moderately significant infiltration of neutrophils (p-value=0.06) and B-cells (p-value=0.07) while no significant infiltration of CD4+ T-cells (p- value=0.31), and CD8+ T-cells (p-value=0.39) in tumour microenvironment of patients with hepatocellular carcinoma
Conclusion: Our data describe tumour densities of myeloid and innate lymphoid cells in well characterized human samples of hepatocellular carcinoma. We provide evidence for increased macrophage infiltration in liver cancer microenvironment suggesting a potential role of these cells in hepatocarcinogenesis.

E-PS-07-029
Expression of some stem cell markers in hepatocellular carcinomas in correlation with clinico-pathological parameters and prognosis
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Background & objectives: The heterogeneity of Hepatocellular carcinoma (HCC) can be explained by the presence of cancer stem cells (CSCs). CD133 and EpCAM are used to identify CSCs. The aim is to assess the relationship between their expression and clinicopathological parameters and prognosis.
Methods: This retrospective study was performed on 100 cases of HCC selected randomly from surgical pathology laboratory at Gastroenterology Center, Mansoura, Egypt from 2011 to 2014. Immunohistochemical staining of CD133 and EpCAM was carried out on tissue microarrays.
Results: The results showed high CD133 expression in low grade HCC than in high grade (P=0.031). The expression of EpCAM showed no significant relations with the studied clinicopathological findings. Patients with positive CD133 and EpCAM expressions had better overall survival (OS) (P=0.000 and P=0.004) respectively. Expression of CD133 expression showed no significant difference in disease survival rate (DSR) (P=0.350) while patients with positive EpCAM expression showed a better DSR (P=0.001).
Conclusion: The role of CSC markers expression in the prognosis of HCC is controversial and our results concluded that there is no unique liver CSC marker and the combined use of more than one marker is required for a better efficacy.

E-PS-07-030
Primary hepatic Castleman's disease related to chronic hepatitis C virus: a case report
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Background & objectives: Castleman's disease (CD) is a primary lymphoproliferative disorder of the lymph node of two clinical and three histopathological types with rare cases reported in extra-nodal sites. Here we present a rare case of primary hepatic CD related to HCV.
Methods: An immunohistochemical study was done for primary antibodies CD3, CD20, CD10, BCL2, CD138, CD30 and EGFR
Results: A 62 years old, HCV infected male presented by abdominal pain. Serum alpha fetoprotein was negative. Triphasic computed tomography showed cirrhotic liver with segment II/III hypodense, non-enhancing, exophytic mass. The mass was whitish, fleshy and measured 7 cm on greatest dimension. Histopathological examination showed angiolymphoid hyperplasia formed of lymphoid follicles exhibiting atrophic germinal centre (GC), variable hyalinization, concentric rings of small lymphocytes "onion skin" and peripheral vascularity. Immunohistochemical staining for CD20 and CD3 mimicked the normal nodal distribution of B and T lymphocytes, respectively. CD21 showed constant follicular dendritic cells distribution within the GC.
Conclusion: illustrating the aetiological association of HCV and hepatic CD could emphasis the use of anti-viral therapy in management of viral related CD.

E-PS-07-031
Correlation of pathological changes in the liver and spleen in patients with cirrhosis
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Background & objectives: The study objective is to compare changes in liver stiffness and spleen stiffness in patients with cirrhosis of the viral aetiology and changes in liver volume and linear dimensions of the spleen.
Methods: 15 patients with cirrhosis were examined. Ultrasound linear measurements of the liver and spleen and their stiffness were performed on the SuperSonic Imagine's Aixplorer. Liver volume was calculated by the formula J.T. Childs: 343.71 + 0.84 * (maximum craniocaudal size of the right lobe * anterior-posterior size of the right lobe * anterior-posterior size of the left lobe) / 1000).
Results: Study showed that on average the volume of the liver was 2026.47 ± 162.69 ml, while the stiffness of the liver was 34.76 ± 3.35 kPa. The correlation coefficient between the liver volume and its stiffness was 0.33. The linear dimensions of the spleen were: length 14.43 ± 0.95 cm, thickness 6.52 ± 0.48 cm, while the spleen stiffness was 43.17 ± 1.32 kPa. A correlation between the linear dimensions of the spleen and its stiffness was not found. The correlation coefficient between the length and thickness of the spleen was 0.85. No correlation was found between the stiffness's of the liver and the spleen.

Conclusion: The results of the study showed that the stiffness of the spleen is, on average, higher than that for the liver, which allows us to recommend paying attention to spleen stiffness when monitoring patients with cirrhosis. The length and thickness of the spleen increase in direct proportion in patients with cirrhosis.

E-PS-07-032

The influence of diffuse liver diseases on the size and spleen mass coefficient, prognostic value of indicators

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Background & objectives: Spleen is the largest secondary lymphoid organ. Spleen sizes vary widely with various pathologies. When Spleen Mass Coefficient (SMC) exceeds 4 then it is splenomegaly. Goal – find out the spleen sizes and SMC changes at viral hepatitis and cirrhosis.
Methods: Ultrasound spleen examination was performed on SuperSonic Imagine's Aixplorer to 34 healthy volunteers, 30 with chronic HCV and HBV, 15 with cirrhosis. The formula m = 0.34*l2*t was used to determine spleen mass (l = length; t = thickness). SMC was calculated by: spleen mass (g) x 1000 / body weight (g). The average values were calculated for all groups.
Results: The average spleen length for healthy volunteers, patients with hepatitis B and C and patients with cirrhosis was 10.76 ± 1.15 cm, 10.35 ± 0.38 cm, 14.43 ± 0.95 ($p \leq 0.05$) cm respectively, the spleen thickness was – 5.21 ± 0.46 cm, 4.76 ± 0.17 cm, 6.53 ± 0.48 cm ($p \leq 0.05$) respectively. It turned out that the average SMC in healthy volunteers was 3.93 ± 0.28, in patients with hepatitis – 2.38 ± 0.14 ($p \leq 0.05$), with cirrhosis – 7.25 ± 1.24 ($p \leq 0.05$).
Conclusion: We found out that there are statistically significant differences in the spleen linear sizes and SMC with cirrhosis. It is not advisable to focus on the spleen linear sizes and SMC when assessing the condition of a patient with chronic viral hepatitis.

E-PS-07-033

Diagnostic significance of liver stiffness and the sizes of the caudate and left lobes with viral hepatitis and cirrhosis

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Background & objectives: The caudate lobe thickness to the left lobe thickness ratio is normally not more than one third. The goal: find out how the liver stiffness and the sizes of the caudate and left lobes with cirrhosis and hepatitis change.
Methods: Liver ultrasound examination was performed on SuperSonic Imagine's Aixplorer in 45 healthy volunteers, 30 patients with chronic HCV and HBV, 15 patients with cirrhosis. Ultrasound measurements of the caudate lobe (CL) thickness, the left lobe (LL) thickness, liver stiffness were performed. The ratio of the thickness CL / LL was measured. The average values for all groups were calculated.
Results: It was detected that on average in healthy volunteers the thickness of the CL, the thickness of the LL and their ratio were 22.58 ± 0.55 mm, 69.71 ± 1.99 mm and 0.33 ± 0.01 respectively, in patients with chronic HCV and HBV 24.56 ± 1.23 and 82.53 ± 3.31 ($p \leq 0.05$) and 0.30 ± 0.01 ($p \leq 0.05$) and in patients with cirrhosis – 33.60 ± 2, 24 ($p \leq 0.05$), 101.40 ± 4.16 ($p \leq 0.05$), 0.33 ± 0.03, respectively. At the same time, liver stiffness in healthy volunteers was 4.71 ± 0.13 kPa, in patients with hepatitis - 6.75 ± 0.43 kPa ($p \leq 0.05$), with cirrhosis – 34.76 ± 3.35 kPa ($p \leq 0.05$).
Conclusion: When assessing changes in the sizes of the liver with diffuse liver diseases, one should focus on the thickness of CL and LL, and not on their ratio, which can be the same among healthy people and for patients with cirrhosis. The changes in liver stiffness weakly correlate with the thickness of the LL in patients with cirrhosis (r = 0.35).

E-PS-07-035

Is M30 staining a reliable prognostic marker of fibrosis in protocolar liver biopsies in post-liver transplant paediatric patients?

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Background & objectives: Liver transplantation is currently a treatment of choice in patients with end-stage liver disease. Besides acute cellular rejection (ACR) and antibody-mediated rejection (AMR), fibrosis is also a cause of organ's loose. Apoptosis has been recently proposed as one of the mechanisms contributing to liver fibrosis in liver grafts. The aim of this study was to assess the utility of immunohistochemical (IHC) staining M30 (cytokeratin 18), as a prognostic marker of fibrosis in protocolar liver biopsies in post-liver transplant paediatric patients.
Methods: The study enrolled 58 patients aged 1,77 to 18,9 years (mead 13,84) who underwent protocolar liver biopsies taken 1-17 years after liver transplantation (mead 6,1). Immunohistochemical staining M30 and histochemical staining azan were performed in all specimens. The following changes were re-evaluated in each specimen: features of ACR and/or AMR; severity of fibrosis (Ishak scale); presence of cholestasis and steatosis.
Results: Histopathological changes were assessed in 59 biopsies. At no biopsy, M30 expression was elevated regardless of the time after transplantation, the treatment used, or the coexistence of other histopathological changes. M30 expression also did not correlate with the severity of fibrosis.
Conclusion: M30 staining, marker of apoptosis, does not correlate with fibrosis in late protocolar liver biopsies in paediatric liver transplant recipients.

E-PS-07-036

Primary hepatic neuroendocrine carcinoma: a case report; pathological and immunohistochemical study

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Background & objectives: Primary hepatic neuroendocrine tumours are rare. Most cases of hepatic neuroendocrine tumours are actually metastases from occult primary sites in the gastrointestinal tract or other sites. Here we discuss a rare case of primary hepatic neuroendocrine carcinoma.
Methods: Male patient, 31 years old, presented with abdominal pain ,imaging study revealed large hepatic focal lesion measured 20x15 cm , CT suggest HCC, MRI suggest fibrolammellar HCC. Virology negative, AFP within normal range. Surgical resection of the tumour was done. Pathological H&E and immunohistochemical assessments (Hep-par1, chromogranin, synaptophysin, CD56, smooth muscle actin, LCA, CD34,TTF1& Ki67) were done.
Results: Gross examination revealed soft greyish mass measured 13x10x6cm, with haemorrhagic cut surface. Microscopic examination revealed small to intermediately sized uniform population of tumour cells demonstrating abundant cytoplasm with round smooth contour nuclei and vesicular nuclear chromatin arranged around vascular spaces. No desmoplastic reaction was seen. Immunohistochemical study revealed that the tumour cells were negative for heppar1, LCA, CD34, TTF1 & SMA and positive for CD56, synaptophysin & chromogranin, Ki67 index of 50%. Diagnosis of PHNEC was done after exclusion of all origins by PET-CT and other investigations to exclude other primary sites. Three months later the patient developed recurrence tumour in the liver with metastasis to omentum and the stomach.
Conclusion: Primary hepatic neuroendocrine tumour, despite being rare, already could be diagnosed after thorough investigations to exclude other primary sites.

E-PS-07-037

Combined hepatocellular carcinoma and cholangiocarcinoma mimicking focal nodular hyperplasia – a case report

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Background & objectives: Combined hepatocellular carcinoma and cholangiocarcinoma (cHCC-CC) is a rare and aggressive tumour, which accounts for <1-5% of primary liver malignancies, defined by two morphologically distinct neoplastic components. We present a case of cHCC-CC that clinically mimicked a benign tumoral proliferation.
Methods: A 58 years old female was hospitalized with an expansive process in segment IV of the liver. Intraoperative echography described a well-circumscribed tumour, showing a capsule and central hypoechoic area, which was considered as suggestive for focal nodular hyperplasia. However, the patient underwent surgery, followed by gross examination and microscopic analysis.
Results: Microscopy revealed a well-circumscribed malignant proliferation of hepatoid cells with a trabecular pattern (well-moderate hepatocellular carcinoma), areas of solid and cribriform pattern, with desmoplastic stroma (cholangiocarcinoma), as well as intricate areas showing intermediate features. Tumour necrosis was present. Lesions of portal hepatitis were seen on the background hepatic parenchyma. Immunochemistry showed positivity for OCH1E5, Glypican-3 in hepatoid areas and positivity for CK7, CA19.9, MNF116 in ductal areas, and overall negativity for CK20, CDX2, TTF1, Chromogranin A, Synaptophysin, NSE. There was a proliferation index of 10% with Ki-67. All these features were consistent with a diagnosis of cHCC-CC.
Conclusion: Combined hepatocellular carcinoma and cholangiocarcinoma is a rare entity and this particular case, mimicking focal nodular hyperplasia highlights the importance of the pathological examination and immunohistochemical confirmation, even though the clinical and imaging context suggests a benign tumour.

E-PS-08 Digestive Diseases Pathology - Pancreas

E-PS-08-001

Pancreatic insulinoma associated with pancreatic heterotopia: a clinicopathologic and immunohistochemical study

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Background & objectives: Insulinoma is a rare form of functional pancreatic neuroendocrine tumour (PanNET) that causes inappropriate release of insulin.
A 71-year-old woman admitted to our hospital complained of frequent episodes of asthenia, fatigue, visual impairment and spontaneous hypoglycemic episodes determined at home.
Methods: During hospitalization she developed multiple symptomatic episodes of hypoglycemia. Blood samples taken at that time revealed low glucose levels (51 mg/dl) with corresponding high insulin levels (27.6 microU/ml). Abdominal contrast-enhanced computed tomography scan demonstrated a single lesion involving the head of the pancreas, measuring 15x22 mm, with enhancement during the arterial phase of contrast bolus.
Results: The patient underwent surgical resection consisting of cephalic duodenopancreatectomy (Whipple procedure) with anterograde cholecystectomy. On gross examination a nodular, well-defined, tan lesion with greatest dimension of 15 mm involved the head of the pancreas. Histological features corresponded to a G1 PanNET with mitotic index less than 2/10 HPF and proliferation index Ki67 less than 3%. Immunohistochemically, tumour cells showed a positive and diffuse staining for synaptophysin and chromogranin A. Pancreatic heterotopia within duodenal wall was noticed. Shortly after surgical treatment symptoms remitted completely; the glucose and insulin levels returned to normal.
Conclusion: Insulinoma remains a diagnostic challenge to clinicians. An adequate clinical and imagistic context should raise a high-grade suspicion. It has a favourable prognostic, surgical resection being the preferred treatment option with immediately remission of symptoms.

E-PS-08-002

Pancreatic mixed neuroendocrine-non-neuroendocrine neoplasm: a case report

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Background & objectives: MiNEN's are composed of morphologically neuroendocrine and non-neuroendocrine tumour components each constituting ≥30% of the tumour volume. Mixed ductal-neuroendocrine carcinomas should be distinguished from ductal adenocarcinomas with entrapped neuroendocrine islets and pancreatic neuroendocrine tumours.
Methods: 59-year-old male patient presented with nausea and vomiting ongoing for 20 days. Patient developed jaundice after several weeks of the initial symptoms. On abdominal CT scan, a mass was found at the pancreatic head. Whipple procedure was performed.
Results: Macroscopically, a solid yellow mass sized 2,5x2x2 cm was found in the pancreas and mucosal irregularity was observed in the ductus choledochus. Morphologically the tumour was composed of glandular, tubular structures within desmoplastic stroma accompanied with round islets of small uniform cells. PAS-AB, Mucicarmine positive tubular structures revealed immunohistochemically B72.3 and CEA positivity whereas the other round cell population was synapthophysin, NSE, PDX1 positive with a low Ki67 proliferation index.
Conclusion: The final diagnosis was MiNEN composed of ductal and neuroendocrine carcinoma with well differentiation. Mixed ductal-neuroendocrine carcinomas account %0.5-2 of all ductal adenocarcinomas. The occurrence of well differentiated neuroendocrine component is relatively rare. In a pancreatic ductal adenocarcinoma, islets of morphologically uniform round cell component should be further examined as a component of possible MiNEN.

E-PS-08-004

Pancreatic hamartoma: morphological and immunohistochemical features

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Background & objectives: Hamartomas are benign tumour-like malformations formed from the disorganized growth of normal cells and tissues. Pancreatic hamartoma is extremely rare. Malignancy must be excluded, especially in the pre-operative diagnosis.
Methods: We present the morphological and immunohistochemical features of a pancreatic hamartoma in a 41-year-old male diagnosed in a distal pancreatectomy sample. Hematoxylin-eosin stain and immunohistochemical studies were performed, including synaptophysin, chromogranin, beta-catenin, actin, CD34 and S100. Previous fine needle aspiration samples were reviewed.

Results: Grossly, the lesion was a homogeneous, solid nodule measuring 1.8 x 1.8 cm. Histologically we observe a well-circumscribed lesion composed of disarranged ductal, acinar and neuroendocrine cells embedded in a hyalinized or fibrocellular stroma. The lesion showed pushing margins with no infiltration of the surrounding pancreatic parenchyma. Some areas were composed of fibroblastic elements with non-atypical large nuclei. Beta-catenin stain was expressed focally in the fibroblastic-like cells, whereas the remaining were negative. Two previous fine needle aspiration cytologies were reviewed and diagnosed as mucinous neoplasms, based on the presence of scant and non-displastic columnar epithelium and abundant mucin. Diagnosis of pancreatic hamartoma was made in the surgical specimen.
Conclusion: Pre-operative diagnosis of pancreatic hamartoma is a real challenge. Differential diagnosis should be made with malignant entities, mucinous neoplasms, neuroendocrine and desmoid tumours. Histopathological examination is essential for an accurate diagnosis.

E-PS-08-005
Pancreatic mucoepidermoide carcinoma: the eleventh case in the literature
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Background & objectives: Mocoepidermoid carcinomas(MEC) of the pancreas are rare entity. Only ten cases have been reported in literature. Because of their rarities, preoperative clinical and radiological diagnosis of these carcinomas continues to be a challenge to differentiate them from others pancreatic neoplasms.
Methods: The clinical and histo-pathologic features of pancreatic MEC are poorly defined which motivated us to present this case report and review the literature.
We describe the case of a male patient who consulted for a left upper abdominal pain and deterioration of general status, and the diagnoses was performed in the pathology department of Farhat Hached Hospital-Sousse
Results: Computed tomography showed a low density tumour in the head of the pancreas. The preoperative symptoms and imaging were unspecific and the patient underwent a duodeno-cephalic-pancreatectomy surgery.
Macroscopically, we found a whitish, indurated and ill-defined tumour measuring 3.5 cm infiltrating the duodenal wall, the common bile duct and obstructing the wirsung canal.
Histologically, the tumour consisted of two components, well differentiated adenocarcinoma associated to epidermoid cells and the tumour was classified pT2N1 according to WHO2019-TNM2017.
Conclusion: As an uncommon entity, preoperative diagnosis of pancreatic MEC seems to be difficult in consideration of the rarity of disease and unspecific manifestations. However, further analysis is still required so as to establish better regimens and subsequently guide the preoperative diagnosis and treatment options of pancreatic MEC.

E-PS-08-006
Paraduodenal pancreatitis mimicking cancer
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Background & objectives: A 36-year-old male patient complains about burning abdominal pain and weight loss (> 10 kg). A 5 cm mass is found near to the uncinate process with compression of the duodenum and common bile duct.
Methods: Atypical spindle cells are found in the needle aspiration cytology, leading to a diagnosis of sarcoma. Subsequently, a Whipple procedure is performed. A severe endoluminal bleeding leads to an urgent revision. Later a bilateral basal pneumonia prolongs the recovery.
Results: Histologically a dense fibroblastic proliferation with lymphoplamacellular inflammation is seen. Destructed and/or dilated ducts show retained dense pancreatic juice. Immunohistologically an autoimmune pancreatitis is ruled out.
We diagnose a paraduodenal pancreatitis (groove pancreatitis).
This rare type of pancreatitis mainly occurs in males with a peak incidence in the 4th and 5th decade. The hallmark of disease is the presence of tumour-forming fibrosis in the pancreaticoduodenal groove. The duodenum is always involved by a chronic inflammatory process with various levels of stenosis. Paraduodenal pancreatitis has been suggested to occur via increased viscosity of the pancreatic juice caused by alcohol, thus predisposing to stone formation.
Conclusion: The diagnosis of paraduodenal pancreatitis is challenging on a clinical, radiological and morphological level.

E-PS-08-007
Acinar cell carcinoma of the pancreas
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Background & objectives: Acinar cell carcinoma (ACC) of the pancreas is a rare tumour that constitutes 1% of all pancreatic neoplasms. This tumour remains known poorly. This work aimed to study the clinico-pathological characteristics, the treatment and the prognosis of the pancreatic ACC.
Methods: It is a retrospective study including four cases of pancreatic ACC identified over a period of 11 years (2006-2017) in The Pathology Department, Farhet Hached Hospital, Sousse (Tunisia).
Results: Two men and two women with a mean age of 60 years presented with abdominal pain, asthenia or a cholestatic syndrome. Imagery showed a well circumscribed, solidocystic tumour of the pancreas with a focus of necrosis. Macroscopic examination showed a large mass with a mean size of 10 cm. It was generally well-circumscribed, sometimes multinodular. Histological examination showed a carcinomatous proliferation, organized into small glands and cords, made of cubo-cylindrical cells, with a strongly nucleated monomorphic nucleus. Foci of necrosis were observed. Immunohistochemistry showed diffuse expression of trypsin in all cases, a positivity of Pan-CytoKeratin. Synaptophysin was focally positive in 2 cases. Treatment was double bypass, spleno-pancreatectomy, or chemotherapy.
Conclusion: Pancreatic ACC is a rare tumour. Data about prognosis are controversial. Researches about the molecular mechanisms involved in the onset and progression of ACC are required for a better management.

E-PS-08-008
Solid pseudopapillary neoplasm of pancreas – case series
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Background & objectives: Solid pseudopapillary neoplasm (SPN) of the pancreas is a low-grade malignant pancreatic tumour. It is a rare primary neoplasm that typically affects young women with mean age of 28 years. It has nonspecific clinical presentation such as abdominal pain and nausea, and has vague radiological features. Histological features of this neoplasm are usually specific and there is a good immunohistochemical (IHC) panel, that can prove the diagnosis.
Methods: We present 3 cases of SPN of pancreas with emphasis of morphology and additional IHC stains. Three young women, between 28 and 30 years old, with no prior medical history. One of them presented with

complaints of epigastric pain with sudden onset. The other two patients had no complaints and were diagnosed on a routine medical check.
Results: In one of the cases the tumour was located in the head of the pancreas, whereas in the other two - in the tail. The tumour has some specific histology presentation - solid nests of poorly cohesive cells, forming pseudopapillary structures, situated in hyalinized stroma with degeneration features. IHC panel of B-catenin, CD56, PR, Vimentin, CD10, alfa1-antitrypsin, NSE and Synaptophysin, was used for the final diagnosis.
Conclusion: It is important for the pathologist to think about this lesion and it should be highly suspected when young female presents with pancreatic mass. Surgical excision offers the best chance for cure and patients have an excellent prognosis after surgical excision.

E-PS-08-010
Multiple pancreatoblastoma, a case report in a 30-year-old man with familial adenomatous polyposis
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Background & objectives: Pancreatoblastoma is a rare tumour, which affects mainly the paediatric population. Only about seventy adult cases have been reported in the English literature.
Methods: We report a case of a 30-year-old man previously diagnosed with familial adenomatous polyposis in his adolescence, complaining of recent abdominal pain and significant weight loss.
Tomodensitometry examination revealed four pancreatic nodules (1.1-3.8 cm), involving the head and the tail of pancreas. Biopsies of two lesions diagnosed well-differentiated neuroendocrine tumours. Consequently, a pancreaticoduodenectomy and a spleen-preserving distal pancreatectomy were performed.
Results: Macroscopically, the lesions were well circumscribed, white-brownish, showing solid and cystic features.
Histopathological examination revealed the same aspect in all tumours, showing lobular pattern, with two different cellular components: one of solid and acinar architecture composed of midly atypical cells with scarce cytoplasm and round-ovoid nuclei with small nucleoli, intermixed with squamoid nests formed by large cells with abundant eosinophilic to clear cytoplasm and oval-shaped nuclei.
In the solid/acinar component, the cells expressed chromogranin A, synaptophysin, CD56, Bcl10, with a proliferation index (Ki67) up to 20%. The squamoid nests expressed EMA, chromogranin A, synaptophysin and beta-catenin (nuclear staining).
Conclusion: Pancreatoblastoma can mimic a neuroendocrine tumour or an acinar cell carcinoma on biopsies, especially in adults, where this diagnosis is unexpected. This case report raises concern about its association with familial adenomatous polyposis syndrome, advocating for a careful examination in these patients.

E-PS-08-011
Nuclear protein lamin A and emerin expression is down regulated in carcinoma originated from intraductal papillary mucinous neoplasm
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Background & objectives: Alteration of nuclear lamin and emerin is known to affect nuclear size and shape. In the present study, we investigated the expression levels of lamin-A and emerin in adenoma or carcinoma of intraductal mucinous cystic tumour (IPMN) cases.
Methods: Twenty cases of IPMN (13 cases of adenoma: IPMA and 7 cases of carcinoma: IPMC) were immunohistochemically stained. Then the expression of lamin-A and emerin were examined. The expression intensity of the protein was evaluated manually and classified into score 0-3. Then, the highest and lowest intensity in the specimens were compared. P value less than 0.05 was considered significant.
Results: The maximum value of lamin-A showed no significant difference between IPMA and IMMC (3.000 ± 0, and 2.857 ± 0.378, $p = 0.173$), respectively. On the other hand, the lowest value of lamin-A was significantly different between the two groups (3.000 ± 0 and 1.857 ± 1.345, $p = 0.003$). Similarly, the maximum value of emerin showed no significant difference between the two groups, (2.231 ± 0.599 and 2.000 ± 0.816, $p = 0.508$). On the other hand, the lowest value of emerin was significantly different in two groups, (1.385 ± 0.506 and 0.714 ± 0.756, $p = 0.042$).
Conclusion: Our results suggested expression of both proteins, especially lamin-A was maintained in IPMA, but both proteins were down regulated during progression to IPMC.

E-PS-09 Electron Microscopy

E-PS-09-001
Review and case presentation: the value of tubuloreticular inclusions (identified with electron microscopy) in the diagnosis and management of connective tissue autoimmune diseases
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Background & objectives: Renal involvement in connective tissue diseases (CTDs) is common.
Tubuloreticular inclusions (TRIs) are seen in connective tissue diseases at the ultrastructural level (electron-microscopy), however, there is no quantifying criteria to assess the significance of TRIs in the diagnosis of CTDs.
Methods: This case presentation is to highlight the importance of TRIs identification in a case that lead to diagnosis alteration based on electron microscopy identification of TRIs; that are different from the ones seen in other conditions.
We propose creating a method for performing a morphometric analysis of TRI's that could be used to more reliably discriminate between different renal conditions.
Results: We noticed from this case and other cases of CTDs related renal changes that ultra structuralstudies (electron microscopy) show significant numbers of large TRIs. These are different to the ones seen in other renal conditions.
Conclusion: TRIs are an important clue to the diagnosis of CTDs, particularly, when significant numbers of large RTIs are seen on electron microscopy.
We propose creating a method for performing a morphometric analysis of TRI's in order to be able to more accurately describe them, and then to test the hypothesis that this more accurate information could be used to more reliably discriminate between those renal conditions where they have been found

E-PS-10 Endocrine Pathology

E-PS-10-001
Primary thyroid lymphoma simulating anaplastic carcinoma
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Background & objectives: The thyroid gland is commonly the target of neoplastic diseases, such as primary thyroid lymphoma (PTL), a non-Hodgkin lymphoma subtype. PTL is a rare and aggressive neoplasm, the manifestation of which may resemble anaplastic carcinoma, requiring microscopic differentiation. The objective is to describe a case of a patient with PTL mimicking thyroid cancer that obtained an excellent response to treatment.
Methods: Female, 59 years, reports cervical mass growth associated with dysphonia a month ago. Cervical tomography revealed lymph node enlargement and enlarged thyroid, compressing and deflecting the trachea to the right. Histopathology confirmed high grade diffuse large B cell lymphoma. Started treatment with six chemotherapy sessions following the R-CHOP protocol and although the advanced disease, showed a complete response to treatment.
Results: The main differential diagnosis is anaplastic cancer because of the rapid evolution, and is the most lethal of thyroid malignancies, with an average survival of six months. Therefore, the histological differentiation of the two neoplasm is highly relevant, which is based on the presence of cellular inclusions and the absence of lymphoglandular bodies to characterize. Such findings do not correspond to the reported patient, allowing differentiation and characterization as LPT.
Conclusion: In patients with rapid mass growth in thyroid topography, the hypothesis of lymphoma should be listed, being paramount the rapid diagnosis and aggressive conduction.

E-PS-10-002
Medullary thyroid carcinoma: a 14-year retrospective study in a tertiary hospital
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Background & objectives: Medullary thyroid carcinoma (MTC) represents 3-10% of thyroid carcinomas. This study aims contribute to the knowledge of the correlation between citology and histology, clinicopathological features and prognosis, and between serum calcitonin (SCa) and tumour dimension.
Methods: Retrospective study, with clinical and pathological data collected and analysed from all patients diagnosed with MTC at our institution, over 14 years (January/2006 - December 2019). All cases were restaged according to the AJCC 8th edition.
We have found 26 cases of MTC diagnosed in this period.
Results: A median age of 46y (6-85) was observed, with predominance of females (10M:16F) and a median tumoral dimension of 21mm (2-98). Hereditary MTC represented 11.5% (3 cases), all associated with MEN2A syndrome.
Cytology have diagnosed 50% of MTC, and in 77% of all cases the result was suspicious for malignancy (category V of Bethesda reporting system) or malignant (category VI of Bethesda reporting system). Regarding staging, 54% of cases were in stage I.
Pre-surgery SCa was elevated in most available cases (77%), without proportional relationship with tumour size. Serum calcium was normal in all cases.
Five-year survival rate was 93%.
Conclusion: CMT is an aggressive neoplasm, usually with metastasis at the time of diagnosis. Elevation of SCa is considered a sensitive and specific tumour marker, and was elevated in most of our cases. Serum calcium do not seems to be a good tumour marker, because all cases remained within normal values.
Survival at five years (93%) was slightly higher than the referred in the literature (86%).

E-PS-10-003
Follicular thyroid carcinoma decreasing tendency among well-differentiated thyroid carcinomas in a 10-year cohort
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Background & objectives: Follicular Thyroid Carcinoma (FTC) is a relatively uncommon malignancy, as increases in thyroid cancer are attributed to Papillary Thyroid Carcinoma (PTC).
We summarize the pathological features of FTCs diagnosed through a 10-year-period, evaluating its percentage among Well-Differentiated Thyroid Carcinomas (WDTC).
Methods: Well-Differentiated Thyroid Carcinomas (WDTC) diagnosed from 2010 to 2019 were identified on laboratory databases, on a total of 544 cases. Tumours were classified according to WHO Classification of Tumours (4th edition). Data were analysed using IBM SPSS v24.
Results: The FTC´s percentage among WDTC decreased from 5,0% during 2010–2014 to 2,0% in the 2015–2019 period. Overall percentage of FTCs was 4,0%, which is significantly lower than 6% usually attributed to FTC (t(543)=-288, p=0,004).
Relative percentages on Follicular Variant of PTC (FVPTC), a differential diagnosis to FTC, was not statistically significative between both time periods (t(459,17)=-1,34, p=0,182).
FTC´s median age at diagnosis was 58 years-old (30–79 years-old); 75,0% were women. The mean size of the tumours was 20,50 mm. 55% were pT2 and most developed in a background of benign nodular disease. 75% were minimally invasive, 15% encapsulated angioinvasive and 10% widely invasive.
Conclusion: A progressive reduction of FTCs among WDTC is a global trending. Accordingly, we report a FTCs percentage of 4%, statistically lower than published data, with a decreasing tendency. Our remaining pathological data matched the published literature on FTCs.

E-PS-10-004
Deep into neuroendocrine tumours of the thyroid gland, a discussion based on a recent case report
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Background & objectives: Thyroid neuroendocrine tumours are rare and represent a diverse group. The most frequent neuroendocrine carcinoma of the thyroid gland is medullary carcinoma, representing <2-3% of all thyroid malignancies.
Methods: A 56-year-old male, prior heavy smoker, with no other relevant clinical history, presented with sporadic dysphonia. Clinical investigation revealed a solitary left side thyroid nodule, measuring 7,5 cm. There were no other associated symptoms.
A fine needle-aspiration cytology was performed. The diagnosis was a Follicular Lesion of Uncertain Significance.
He was submitted to a left-sided thyroid lobectomy.
Results: The surgical specimen consisted of a solid, non-capsulated, brownish, thyroid nodule.
The tumour had an insular pattern, with medium size cells, coarse nuclear chromatin and amphophilic cytoplasm.
There was no evidence of necrosis.
The cells were positive for CKs, Cromogranin A, Sinaptophysin, Somatostatin and CEA and negative for TTF-1, PAX-8, Thyroglobulin, Calcitonin, CGRP, CDX-2 and S100; Ki-67 3%.
Congo red stain was negative.
CEA/ Calcitonin serum levels were within the normal range.
Conclusion: The final diagnosis was a well-differentiated neuroendocrine tumour.
We cannot define with certainty if primary/metastatic.
After a 3-month follow-up, the patient had no complaints or evidence of a residual/recurrent disease.

We present a peculiar thyroid lesion that reminds us that not all thyroid neuroendocrine tumours are medullary carcinomas, how important is the correlation with clinical data and how all these considerations are crucial for patient management and therapeutic approaches.

E-PS-10-005

Mucinous well-differentiated follicular cell-derived carcinoma of the thyroid gland: an immunohistochemical and molecular study

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Background & objectives: Mucinous thyroid carcinoma (MucTC) is a rare malignant neoplasm characterised by neoplastic cells surrounded by extensive extracellular mucin deposition. MucTC should be distinguished from other primary or metastatic tumours. We describe a case of mucin-producing well-differentiated follicular cell-derived thyroid carcinoma.
Methods: A 83-year-old euthyroid man presented with a rubbery mass in the right thyroid lobe. There was a history as an ex-smoker, with high blood pressure and ischemic heart disease but with no radiation or family history of thyroid cancer. Fine-needle aspiration biopsy indicated follicular neoplasm (category IV-Bethesda) and a right thyroidectomy was performed latter followed by a left thyroidectomy.
Results: The tumour measured 52 mm. It was partially encapsulated showing microfollicular to macrofollicular architecture with extensive intrafollicular mucin production. Some nuclear characteristics of papillary carcinoma were occasionally detected. Capsular invasion and angioinvasion were also detected. Ki-67 index was 3%. Mucicarmine and Alcian blue stains, TTF1, PAX8, thyroglobulin and thyroperoxidase were positive; but calcitonin, CEA, CK19, MUC1/MUC2, HBME1 and galectin-3 were negative. BRAF, NRAS, KRAS and TERT mutations were not detected.
Conclusion: Our findings confirm the existence of cases of mucinous well-differentiated follicular cell-derived thyroid carcinomas that must be distinguished from true MucTC.
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E-PS-10-006

Giant cell medullary thyroid carcinoma - a challenging diagnosis in cytology

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Background & objectives: Cytological diagnosis of medullary thyroid carcinoma (MTC) can be difficult and even challenging when associated with unusual morphological features. We present a case of a rare variant of MTC which caused diagnosis difficulties on FNA cytology.
Methods: A 59-years-old female presented for bilateral thyroid mass. Neck ultrasound identified multiple nodules in both thyroid lobes. A high calcitonin serum level raised the suspicion of MTC. A FNA was performed in a ultrasound suspicious small nodule, situated in upper part of the right lobe.
Results: The smear was highly cellular with two cell-types: small plasmacytoid cells with single or double monomorphic nucleus, corresponding to conventional MTC, and clusters and isolated bizarre giant cells, with highly pleomorphic nuclei, associated with mitotic figures. These unusual cytological features prompted a differential diagnosis with anaplastic carcinoma. The gross examination of the surgical specimen revealed, apart multiple goitrous nodules, an 8mm white-tan nodule with central calcification. On microscopy, the same two cells-types as in cytology were found: those corresponding to conventional MTC but also giant, binucleated or multinucleated cells with highly pleomorphic nuclei and prominent nucleolus. In immunohistochemistry both cell-types expressed Calcitonin, CEA and Chromogranin and were negative for Thyroglobulin.
Conclusion: The microscopical features and the immunohistochemical panel confirmed the diagnosis of giant cell MTC. The presence of giant cells in MTC is a very unusual situation, and represents a challenge for the differential diagnosis not only in cytology, but also in histology.

E-PS-10-007

Mixed medullary and papillary carcinoma of the thyroid: a phaenotypic and molecular study

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Background & objectives: We describe a case of mixed medullary and papillary thyroid carcinoma, a rare primary malignant epithelial neoplasm of the thyroid gland showing morphological and immunophenotypical evidence of coexistence of papillary thyroid carcinoma (PTC) cells and medullary thyroid carcinoma (MTC) cells.
Methods: A 49-year-old euthyroid man presented with a mass in the left thyroid lobe and left lymphadenopathy that he had noted one month before. There was no history of radiation or family history of thyroid cancer. Serum calcitonin and CEA levels were elevated. Fine-needle aspiration biopsy indicated MTC; total thyroidectomy and lymphadenectomy were performed. No RET germline mutation was detected.
Results: Thyroid tumour showed polygonal cells (positive for calcitonin and CEA) intermingled with follicular cells (positive for thyroglobulin) with nuclear features of PTC. This dual cell differentiation was confirmed by ISH showing mRNA positive for calcitonin and thyroglobulin. Some metastatic lymph nodes (5/32) also showed MTC and PTC areas. Immunopositivity for BRAF was limited to the PTC areas. Somatic BRAF, NRAS, KRAS and TERT mutations were not detected in MTC component.
Conclusion: Our data confirmed that, at least in some mixed medullary and papillary thyroid carcinomas, the two tumour components display distinct molecular pathways.
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E-PS-10-008

Primary thyroid lymphoma: histological features in two unconventionally treated cases

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Background & objectives: Thyroid primary lymphomas are very rare neoplasms, representing about 5% of primary thyroid malignancies and 2% of extranodal lymphomas; they are more frequent in women and with an average diagnostic age of 65 years-old.
Methods: We present two cases. The first is a 72 year-old woman, being followed for a thyroid nodule.
The second is an 84 year-old woman with a diffuse goiter, with progressive growing that started to cause obstruction symptoms, and that in consequence needed urgent surgery.
Results: In the first case there was an initial cytological diagnosis of atypia of unknown significance, but suggestive of a lymphoproliferative disorder, that after staging is submitted to total thyroidectomy.
Histological examination of both cases revealed a background of lymphocytic thyroiditis, and in both a concomitant diffuse lymphoid proliferation, in the first with immunochemistry in favour of a MALT lymphoma and in the second with diffuse large B-cell lymphoma.

Both patients are free of disease (with a 3-year and 1-year follow-up, respectively).
Conclusion: Although in the second case the urgency for decompression rushed into a surgical approach, systemic drug therapy is usually preferred over total thyroidectomy, and it's important the roll of an accurate previous diagnosis for appropriate therapy. In the first case, despite having a previous cytology with the suspicion of a lymphoproliferative disease, it was not taken in account in the decision for performing a thyroidectomy.

E-PS-10-009
Thyroid disease: an exceptionally uncommon association of amyloid goiter and papillary carcinoma
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Background & objectives: Amyloid goiter is a rare condition characterized by diffuse thyroid enlargement due to amyloid deposition; may be asymptomatic and can be found in up to 80% of patients with primary or secondary amyloidosis; association with malignancy is very rare.
Methods: We present a case of a 52 year-old woman with background of chronic renal failure and multinodular goiter for several years, which presented to consultation for symptoms of dysphagia and dysphonia with increased vocal effort. CT scan revealed an enlarged multinodular thyroid gland, with a dominant nodule with 3 cm and a diffuse infiltration suggestive of adipose or amyloid material.
Results: A fine needle aspiration cytology of the nodule was performed, and the result was suspicious for a Hürthle cell tumour. Consequently, and together with progressive obstructive symptoms, patient was submitted to a total thyroidectomy.
Histological examination of the nodule revealed a well circumscribed neoplasm composed of follicular cells with nuclear enlargement, elongation and overlapping, ground glass nuclei, nuclear grooves and nuclear pseudoinclusions, compatible with a Papillary Carcinoma; within the adjacent stroma there was a diffuse deposition of an amorphous eosinophilic material, that had a bright "apple-green" birefringence with Congo Red stain, admixed with mature adipocytes, consistent with amyloid goiter.
Conclusion: Association of these entities is extremely rare, and to our knowledge and after literature review, only 4 cases are reported.
The awareness of this association facilitates the diagnostic accuracy, especially in cases with a background of multinodular goiter or malignancies, where the deposition of amyloid substance, especially if not as intense as in our case, can easily be overlooked.

E-PS-10-010
Intrathyroid paraganglioma with loss of SHDA
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Background & objectives: Intrathyroid paraganglioma is a rare tumour which can mimic other more common or metastatic tumours. Recognition is essential as-well-as immunohistochemical investigation of various proteins, to triage genetic testing as 30% of head and neck paragangliomas are associated with various syndromes.
Methods: A 41-year-old woman was subjected to total thyroidectomy due to an asymptomatic mass in the external surface of the right thyroid lobe, measuring 2.8cm in greatest diameter. Thyroid function tests and calcitonin levels were within normal range.
Results: Microscopy revealed an encapsulated tumour composed of round cells with moderate amount of granular cytoplasm and finely granular nuclear chromatin, arranged mainly in a nesting pattern (zellballen). The capsule was invaded but no lymphovascular invasion was present. Immunohistochemistry yielded positivity for chromogranin, synaptophysin, Gata-3 and Tyrosine Hydroxylase, with S100 and vimenting staining the sustentacular cells. CK8/18, EMA, pCEA, calcitonin, TTF-1, thyrogloblulin and PAX-8 were negative. The above findings were consistent with a diagnosis of a intrathyroidal paraganglioma. Immunohistochemically somatostatin receptor type 2a (SSTR2a) was positive (score 3/Volante). Further investigation revealed concurrent immunohistochemical loss of SDHB and SDHA. The mitotic count was low (0.8 mitosis/per 10 high-power-fields) and GAAP-score was 5.
Conclusion: Intrathyroid paragangliomas are rare neoplasms.
In this case immunohistochemical results point to an underlying mutation in the SDHx genes, particularly in the SDHA-gene.
Due to the immunohistochemical results the patient was referred for genetic testing and was placed under close follow-up.
Germ-line mutations in the SDHA gene are found in less than 5% of paragangliomas. These mutations are associated with a low-metastatic potential and as such their recognition is vital.

E-PS-10-012
Morphological and molecular heterogeneity in adrenocortical carcinoma: about a case
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Background & objectives: It has been proved that adrenocortical carcinoma can be a heterogeneous entity both histologically and for molecular studies. It has also been linked to Lynch syndrome. We expose a case of molecular heterogeneity with diagnostic and prognostic relevance.
Methods: We present the case of a 47-year-old man diagnosed by biopsy and surgical specimen with an adrenal cortical carcinoma with liver metastases. The existence of two intermingled areas in the surgical specimen both macroscopically and histologically was notory. We studied both areas by immunohistochemistry and molecular techniques (NGS).
Results: Macroscopic study of the tumour showed an heterogeneous appearance, distinguishing two intermingled areas of varying colour. Yellowish area corresponded to a proliferation of large oncocytic cells. Proliferation index (Ki67) was 3%. p53 was not overexpressed and no loss of repair proteins was observed. Whitish area corresponded to a high-grade proliferation of granular eosinophilic cytoplasm cells with hyperchromatic nuclei. Proliferation rate (Ki67) was 15%. P53 overexpression was objectified, in addition to loss of MSH2 and MSH6. Next Generation Sequencing (NGS) was performed in both tumour areas as well as in normal tissue. Somatic mutations were identified in p53 and MSH2 in the high-grade tumour area.
Conclusion: A remarkable percentage of adrenocortical carcinomas show morphological and molecular heterogeneity. This fact must be taken into account when making a correct sampling of the specimen. High-grade tumour area was related to somatic mutations in p53 and MSH2. Loss of repair proteins by immunohistochemistry study must be demonstrated by molecular studies in order to discard a Lynch syndrome.

E-PS-10-013
Papillary thyroid carcinoma with tall cells and features of aggressive behaviour
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Background & objectives: Papillary thyroid carcinoma (PTC) is the most common malignancy of the thyroid, usually exhibiting an indolent course, excellent overall prognosis and long-term survival rate. Some

variants, however, have an increased risk of recurrent disease and aggressive behaviour. Tall cells variant (TCV) of PTC, which is defined by the WHO-2017 classification as having ≥30% of tall cells, is recognized as an aggressive neoplasm. Here we describe the pathological findings of a peculiar thyroid nodule.
Methods: A 43-year-old female, euthyroid, with no relevant pathological history, presented with a 5-month-old palpable cervical mass. Thyroid ultrasound showed a 4 cm isoechogenic nodule in the right lobe, TI-RADS3. Ultrasound-guided FNAC was performed using a 23G needle, resulting in a diagnosis of malignancy (PTC). Total thyroidectomy was performed, and the entire gland was included for study.
Results: Specimen of 26g, consisting of right lobe (4×1.5x0.5cm) and left lobe (3.6×1.7×0.5cm). In the right lobe a 4.2×1.7cm tan tumour with a poorly-developed thin-capsule and finely granular appearance was found. Histologically, papillae and typical nuclear changes of conventional PTC could be seen, with 10-20% of the tumour showing areas of TCV. Twenty microcarcinomas (<1mm) were found, with bilateral affectation. Vascular and lymphatic invasion, as well as, lymph-node infiltration were identified.
Conclusion: We describe a PTC with tall cells showing unusually aggressive pathological features. These findings support the idea that the presence of tall cells regardless of their percentage, should be mentioned in the pathological report given their potential clinical risk.
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E-PS-10-014
Corticomedullary mixed tumour of the adrenal gland: a case report
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Background & objectives: Corticomedullary mixed tumour of the adrenal gland is a rare entity with at least 20 cases reported. The aim of this work is to present a case of this unusual tumour and describe its clinical, radiological and histological features.
Methods: The patient was a 50 year old woman with high levels of catecholamines and cortisol, as well as related symptoms. An adrenal mass was discovered on TC scan and it was surgically removed. We received an adrenalectomy specimen which showed a well defined, 4 cm, uniform tumour. Representative sections were included for microscopic study.
Results: On microscopic examination we found a well delimited tumour with nested architecture, composed by two cell populations. One population consisted on cells with round nuclei and abundant eosinophilic cytoplasm, and they were arranged on the periphery of the nests. The second population showed a scarcer and more basophilic cytoplasm, resembling cells of the adrenal medulla. On the immunohistochemical study, the cells on the periphery of the nests exhibited positivity for Melan A, inhibin and calretinin, whereas the cells in the centre, presented positivity for chromogranin and synaptophysin. Both populations were negative for CKAE1/AE3 and lack the S-100 sustentacular cells staining pattern.
Conclusion: There is little information on the literature about this entity, excepting for the case reports published until now. Therefore, it is difficult for the pathologist to achieve the diagnosis. Moreover, the pathogenesis and prognosis of it still remain unknown.

E-PS-10-015
Prognostic markers for neuroendocrine neoplasia
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Background & objectives: Neuroendocrine tumours (NETs) arise from various tissues and organs, and have diverse biological behaviour. The aim of this study was to correlate various morphological parameters of the NETs from different localisations to the serum Chromogranin A (CgA) levels.
Methods: We analysed immunohistochemical expression of CgA, Synaptophysin, NSE, CD56 and Ki67 in 72 operative materials from patients diagnosed with NET of various organs (gastrointestinal, respiratory, endometrium, breast and adrenal gland, as well as metastatic cases with unknown primary). All patients were analysed for CgA levels in the serum by ELISA before the surgery.
Results: The mean age of the patients was 55 (15-80). 38 were benign and 34 malignant, out of which 16 were with localized and 18 with advanced disease (lymphonodal and distant metastases). 11 of the malignant tumours were well differentiated and 23 were moderately to poorly differentiated. All tumours were positive for at least two neuroendocrine markers. The proliferative index (Ki67) ranged between 1 and 90%, and was strongly correlated ($p<0,05$) to the biological behaviour, grade, stage and to the expression of CgA and Synaptophysin in tumour cells. The serum levels of CgA were increased in 43 of the patients, and were strongly correlated only to the grade of the tumours.
Conclusion: We conclude that the proliferative index (Ki67) is an important independent prognostic factor for NETs, and that the serum level of CgA is prognostic marker of lower sensitivity.

E-PS-10-017
Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (nift-p) of the thyroid gland, a diagnosis challenge
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Background & objectives: The non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFT-P) is a thyroid tumour of uncertain malignancy potential, with excellent prognosis.
The motivation for this study is to refine diagnostic criteria for NIFT-P, and raise the main differential diagnoses.
Methods: We report a case of a NIFT-P in a 26-year-old woman who presented a neck mass. The patient had a family history of thyroid cancer. An initial ultrasound showed a nodular lesion in the right thyroid lobe. A right loboisthmectomy were performed.
Results: The macroscopic examination showed a solitary, well demarcated nodule, whitish colour with focal haemorrhage. An intraoperative pathology consultation was done, showing an oncocytic-like vesicular lesion. The final pathological examination showed a well demarcated tumour with follicular growth pattern without any vascular or capsular invasion images. The vesicular structures are lined by cells with nuclear features of papillary carcinoma. There was nor tumoral necrosis neither mitosis. However, an immunohistochemistry study was done. The tumour cells express intensely the CD56 and less intense for CK19. The galectin 3 was focally positive. The peripheral tumour cells were immunoreactive forHBME-1.
Conclusion: The introduction of NIFTP is a subset of low-risk thyroid neoplasms that are over treated. Multiple reports showed the excellent prognosis of this encapsulated/well-delimited tumours without vascular and capsular invasion after complete resection. The emerging literature indicates that the adoption of strict inclusion and exclusion criteria is essential to correctly diagnose NIFTP.

E-PS-10-018
Diffuse sclerosing variant of papillary thyroid carcinoma: a source of misdiagnosis in the frozen sections
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Background & objectives: Diffuse sclerosing papillary thyroid carcinoma is characterized by tumour islands, diffuse fibrosis, calcifications, and

abundant lymphocytic aggregation. An intraoperative diagnosis is challenging in the absence of nodules.
The aim of this review is to critically analyse the histological features of this entity.
Methods: We report one case of diffuse sclerosing variant of papillary thyroid carcinoma diagnosed in our laboratory of pathology. It was about a 55-year-old woman with a family history of thyroid cancer. She presented a neck mass with cervical lymph nodes. An initial ultrasound showed an enlarged thyroid lobes with a suspicious nodular lesion in the right thyroid lobe and lymph nodes.
Results: A right loboisthmectomy and ipsilateral neck lymph node dissection were performed, and an intraoperative pathology consultation was done. It showed thyroiditis lesions with lymph node metastasis of papillary carcinoma. An additional left lobectomy and left lymph node dissection were performed. The total thyroid gland and the bilateral neck lymph nodes were submitted for a pathological examination. Microscopically, all lobes of the thyroid and twenty among twenty seven lymph nodes showed tumour with follicular growth pattern. The vesicular structures were lined by cells with nuclear features of papillary carcinoma. It showed also diffuse stromal fibrosis, prominent lymphoid follicle, and numerous psammoma-type calcifications.
Conclusion: Diffuse sclerosing variant of papillary thyroid carcinoma is a distinct thyroid neoplasm presenting in female patients with signs and symptoms most suggestive of a thyroiditis, although the lymph node metastases are a clue to the underlying disease.

E-PS-10-020
The expression of claudin-1 in the thyroid neoplasm
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Background & objectives: The objective of this study is to evaluate the difference of Claudin-1 expression in follicular adenoma, follicular carcinoma, follicular variant papillary thyroid carcinoma, and papillary thyroid carcinoma.
Methods: Seventy five paraffin-embedded specimens divided into four groups: 20 samples of follicular adenoma, 20 samples of follicular carcinoma, 15 samples of follicular variant papillary thyroid carcinoma, and 20 samples of papillary thyroid carcinoma. The expression of claudin-1 in the cytoplasmic membrane was detected by using immunohistochemistry method with anti claudin-1 polyclonal antibody.
Results: The results of this study indicate that there were significant differences of claudin-1 expression between follicular adenoma and follicular variant papillary thyroid carcinoma ($p=0.0016$), between follicular adenoma and papillary thyroid carcinoma ($p=0.001$), and between follicular carcinoma and papillary thyroid carcinoma ($p=0.002$). There were no significant correlation between follicular adenoma and follicular carcinoma ($p>0.05$), between follicular variant papillary thyroid carcinoma and papillary thyroid carcinoma ($p>0.05$).
Conclusion: This result reveals that claudin-1 may play a role in the progression of thyroid neoplasm and it has a potential ability to become diagnostic marker for follicular adenoma, follicular carcinoma, follicular variant papillary thyroid carcinoma, and papillary thyroid carcinoma.

E-PS-10-021
Analysis of pituitary adenoma expression patterns suggests a potential role for the NEUROD1 transcription factor in neuroendocrine tumour-targeting therapies
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Background & objectives: NeuroD1's roles in the pathogenesis of pituitary adenomas and in the biology of the normal adult pituitary gland have been insufficiently researched. Much of the work investigating its expression patterns has yielded contradictory results.
Objective: morphological study of NeuroD1 transcription factor expression in different types of pituitary adenomas and in normal adult human pituitary glands.
Methods: This study analysed 9 normal pituitary glands and 48 pituitary adenomas: 7 plurihormonal adenomas, 8 corticotropinomas, 10 mammosomatotropinomas, 8 prolactinomas, 2 somatotropinomas, 5 gonadotropinomas, and 8 null-cell adenomas. We used immunohistochemical study with antibodies to NeuroD1, 6 adenohypophysis hormones, Ki-67, CK7, GH/NeuroD1 and PRL/NeuroD1 cocktails and confocal laser scanning microscopy and electron immunocytochemistry with NeuroD1 and double detection NeuroD1/GH.
Results: NeuroD1 expression was detected in all 57 cases. This transcription factor was expressed at significant levels on average in 96% of tumour cells. The average numbers of NeuroD1 expressing cells in normal adenohypophysis were significantly lower than in the adenomas overall ($p=0.006$). NeuroD1 expression was confirmed by double stain immunohistochemistry, confocal laser scanning microscopy, and electron immunocytochemistry.
Conclusion: Our study demonstrates a NeuroD1's key role in the pathogenesis of pituitary tumours, regardless of their hormonal state. These findings suggest that NeuroD1 should be investigated further as a potential molecular target in tumour-targeting therapies.

E-PS-10-022
A case report of primary hyperparathyroidism associated with chronic urticaria
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Background & objectives: This is a report of the 7th case of Primary hyperparathyroidism associated with chronic urticaria. A 43year old female developed unexplained episodes of severe refractory itching. Similar to the previous 6 reported cases the skin symptoms resolved completely after parathyroidectomy.
Methods: A 43year old Caucasian female presented with a history of urticaria. The itching started from the lips but extended over the eyelashes, the hands, the face and the upper legs. It was persistent and not responsive to topical treatments. Dermatological assessment suggested possible stress and prescribed both local and general antihistamine treatments.
Results: Patient had itchy and erythematous lesions. Blood tests revealed elevated adjusted calcium levels and PTH. Sestamibi(Tc-99m) showed uptake in right inferior parathyroid consistent with adenoma. Total parathyroidectomy performed with frozen and paraffin section diagnosis of parathyroid adenoma. There was complete resolution of symptoms. Histology revealed a well-circumscribed, capsulated nodule without infiltration. Tumour cells were mostly chief-type, in solid architecture and small cysts without necrosis or atypia, consistent with parathyroid adenoma.
Conclusion: Our case confirms the association between parathyroid adenoma & urticaria. Wherein, there was resolution of symptoms within few hours post surgery. Our aim is to increase awareness among dermatology & endocrine specialists to perform further investigation for parathyroid function in presence of refractory urticaria.

E-PS-10-023
BRAF V600E mutation negative cases tend to lose lamin A expression in papillary thyroid carcinoma
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Background & objectives: Here we describe relevance of BRAF mutation to nuclear proteins and nuclear shape in papillary thyroid carcinoma (PTC).
Methods: Forty PTCs were stained with anti-BRAFV600E antibody and classified into V600E mutation positive and negative groups. Then, those were stained with anti-Lamin-A antibody and anti-Emerin antibody. The staining intensity was evaluated and scored (0-3) by two independent observers. The average number of intranuclear cytoplasmic inclusions in a high-power field was also examined.
Results: A weak correlation (R = 0.3654) was observed between the staining intensities of Lamin-A and Emerin. On the other hand, Lamin-A staining intensity tended to be stronger in the BRAFV600E mutation positive group than the negative group (p = 0.0688). While, there was no difference in Emerin staining intensity between 2 groups (p = 0.1490). The number of intranuclear cytoplasmic inclusions was 2.48/HPF in the BRAF mutation positive group and 1.31/HPF in the negative group, although there was no statistically significant difference (p = 0.1829). Our data indicated that Lamin-A expression would be decreased and intranuclear cytoplasmic inclusions would be less frequently appeared in BRAF mutation negative PTC.
Conclusion: Lower expression of Lamin-A and Emerin results in swelling and elliptical changes of the nuclei. It is possible that lower expression of Lamin-A in BRAF mutation negative cases results in nuclear swelling leading to difficulty in changing nuclear shape.

E-PS-10-024
Neuroendocrine tumour of the female genital tract – a case report
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Background & objectives: Introduction: Neuroendocrine tumours (NET) arise from the diffuse neuroendocrine cell system and are typically located in gastroenteropancreatic system. Primary neuroendocrine tumours are rarely seen in the gynaecologic tract comprising 2 % of gynaecologic cancers creating a clinical and diagnostic challenges.
Methods: Methods: A 81- year-old-female was presented to the Gynaecology department with a steadily growing swelling in the abdomen accompanied by pelvic pain, fever, constipation and bladder disfunction. Computer tomography was performed showing well-circumscribed, solid mass (243x177x245mm) with cystic and necrotic zones with uncertain origin – ovary or uterus. As epithelial ovarian cancer was suspected, ROMA index and percutaneous biopsy were performed.
Results: Results: The histopathology revealed a dense population of small to medium ovoid cells arranged in solid nests and trabeculae separated by connective tissue septa. Tumours cells have abundant pale cytoplasm and hyperchomatic nucleus with "salt and pepper" chromatin. Immunohistochemical stains showed positive reaction for CK AE1/AE3 and neuroendocrine markers (CD56, Chromogranin and Synaptophysin). KI67 > 50%. The oncology committee decided to send the patient for chemotherapy after staging with OctreotideScan.
Conclusion: Conclusion: In summary, we presented a rare case of neuroendocrine tumour of the female reproductive system with probable origin from the ovary or uterus. Accurate diagnosis is essential for both therapeutic and prognostic purposes.

E-PS-10-026
Thyroid abscess developed within a Hashimoto thyroiditis: a challenging diagnosis
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Background & objectives: Thyroid abscesses are a potential-endocrine-emergency accounting for less than 0,7% of thyroid's gland surgical pathology. This report aims to describe clinico-radiological and histopathological features of this entity and emphasizes the pathologist's role in establishing the right diagnosis.
Methods: We report a case of thyroid abscess developed within a Hashimoto thyroiditis diagnosed in oto-rhino laryngology, radiology and pathology departments of Sfax hospital.
Results: A woman aged 54 years old with a history of type II diabetes and Hashimoto thyroiditis, presented with an acute-anterior-neck-swelling, fever, odynophagia and dyspnoea. CT-scan evidenced a well-defined non-enhanced hypodensity involving both isthmic and right lobe and extending into the prevertebral-space, suggesting the diagnosis of a complicated-thyroid-cancer. A total-thyroidectomy was then performed. Grossly, we objectified a 5cm-greyish-necrotic-area on the posterior part of the right lobe. Histological findings revealed a large ischemic and suppurated area within a background of a chronic lymphocytic thyroiditis consistent with a Hashimoto thyroiditis. Operating-site sampling isolated Klebsiella Pneumoniae. The diagnosis of a thyroid abscess developed within a Hashimoto thyroiditis was finally retained.
Conclusion: Thyroid abscess is an uncommon form of infectious acute thyroiditis. Establishing an appropriate diagnosis may be challenging. Correlating clinical, radiological, microbiological and pathological findings is crucial to avoid diagnostic pitfalls.

E-PS-10-027
Usage of galectin-3, HBME-1, Cytokeratin-19 and CD56 in the differential diagnosis of thyroid neoplasm
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Background & objectives: The thyroid neoplasm has increased significantly in Mongolia over the past few years. Nevertheless, with the help of ancillary tests, such as immunohistochemistry (IHC), differences between thyroid lesions can be distinguished.
Methods: Total 93 thyroid neoplasm's cases collected from September 2017 to December 2019 at National Cancer Center of Mongolia. In all cases, IHC staining was performed using tissue microarrays and CD56, HBME-1, Galectin-3 and CK19 primary antibodies on paraffin-embedded thyroid neoplasm sections.
Results: The thyroid neoplasm from 93 patients, 14% males and 86% females were researched. The mean age was 46.7±14years. The diagnosis of thyroid nodules was papillary thyroid carcinoma (PTC) in 66 (71%), follicular thyroid carcinoma in 3 (3.2%), follicular adenoma in 19 (20.4%), and medullary thyroid carcinoma in 2 (2.2%), respectively. The difference in expression of Galectin-3, HBME-1, CD56 and CK19 was significantly significant in malignant compared to benign tumours (p=.000). Out of 66 cases of papillary thyroid carcinoma, Galectin-3 and CK19 showed positive in 61 (92.4%) cases while expressions of HBME1 was seen in 46 (69.6%) PTC cases. Diffuse CD56 expression was present in 70.8% of follicular lesions, except PTC.
Conclusion: Galectin 3 is most sensitive (93.8%) and specific (76.1%) marker for papillary thyroid carcinoma.

E-PS-10-028
Metastasis of a neuroendocrine carcinoma in a non-invasive follicular thyroid neoplasm with papillary-like nuclear features: a case report
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Background & objectives: Metastases in a pre-existing primary thyroid tumour are exceedingly rare. We report a case of a patient with pulmonary cancer who was diagnosed with a thyroid metastasis in a non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).
Methods: A 61-year-old male diagnosed of symptomatic multinodular goiter, was referred to the Surgical Department. A total thyroidectomy was performed. The patient's medical history was significant for pulmonary cancer.
Results: On macroscopy the surgical specimen revealed in the left thyroid lobe a 24 mm thyroid nodule. The microscopical examination showed a well-defined lesion of microfollicular architecture with papillary-like nuclei. In the centre of the nodule an area with distinctly different histologic features was present: cells arranged in islands and cords with central necrosis. The tumour cells presented abundant eosinophilic cytoplasm, marked nuclear pleomorphism and numerous atypical mitoses. Immunohistochemically these cells expressed Chromogranin, Calcitonin, CEA and TTF1. Based on the morphological features and the immunohistochemical profile the diagnosis of a metastatic NEC in a NIFTP was set.
Conclusion: Metastatic NEC occurring in a NIFTP has never been reported before. This exceptional case was a diagnostic challenge due to the fact that the metastasis was identified concurrently to a pre-existing primary tumour.

E-PS-10-030
Prevalence and prognostic value of PD-L1 expression in medullary thyroid carcinoma: a systematic review and meta-analysis
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Background & objectives: Expression of programmed death-ligand 1 (PD-L1) has shown prognostic value in several tumours. The aim of this study was to review published evidence on PD-L1 expression in medullary thyroid carcinoma (MTC), for which little is known.
Methods: Pubmed, Embase and Scopus databases were systematically searched. Studies on PD-L1 expression in MTC and its correlation with clinicopathological variables and survival were included. A random-effect meta-analysis was performed for PD-L1 expression, odds ratios (ORs) for association with clinicopathological variables and hazard ratios (HRs) and risk ratios (RRs) for overall survival (OS) and disease-free survival (DFS).
Results: Of 670 records, 5 studies were included. Pooled prevalence of PD-L1 expression was 12.4% (CI 4.4-23.2%, I2 83%, τ2 0.02). No significant association of PD-L1 expression was found with sex, size, TNM stage, heredity, laterality, multifocality. Weak association was found with nodal metastasis (OR 1.98, CI 0.96-4.07, I2 0%, τ2 0.001). Pooled RR for OS for PD-L1 positive was 2.01 (CI 0.53-7.60, I2 22%, τ2 0.27).
Conclusion: Expression of PD-L1 in MTC appears to be low and not correlated with clinicopathological variables and OS. This is in line with findings in other neuroendocrine malignancies, but more data are needed to strengthen the evidence. Given the small number of studies and their small sample size, further studies will help to refine the estimates of PD-L1 expression and its prognostic value in MTC.

E-PS-10-031
Concomitant papillary thyroglossal duct carcinoma and papillary microcarcinoma of thyroid with lymph node metastasis - a case report and review of literature
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Background & objectives: Thyroglossal duct cyst is the most common cervical congenital anomaly. Malignancy arising in thyroglossal cyst is rare with <1% reported in literature. We hereby report one such case.
Methods: A 47 year old gentleman presented with neck swelling and an ultrasound examination identified a 3cm suprahyoid thyroglossal cyst and normal thyroid gland. A Fine needle aspiration was performed and cytological analysis raised the possibility of papillary carcinoma. The patient underwent a Sistrunk procedure that confirmed a 2cm papillary carcinoma arising in thyroglossal cyst. This was followed by total thyroidectomy.
Results: The denovo origin of papillary carcinoma in thyroglossal cyst was supported by suprahyoid location, squamous epithelial lining and presence of ectopic benign thyroid glands. The total thyroidectomy identified two incidental foci of papillary microcarcinoma (5mm, 2mm) with no extrathyroidal extension. Metastatic disease was observed in one level VI lymph node. Whether this is a skip metastasis from thyroglossal duct carcinoma or metastasis from papillary microcarcinoma of thyroid gland is unclear.
Conclusion: This case adds to the collection of rare reported numbers of thyroglossal duct carcinoma published in literature. Histological examination is necessary as clinical presentation and radiology of thyroglossal duct carcinoma and benign thyroglossal cyst do not vary greatly. Given the rarity of thyroglossal duct carcinoma, there are no clear guidance on the prognosis, especially considering the contemporary appearance of papillary thyroid carcinoma. Surgery however is the mainstay of treatment.

E-PS-11 Gynaecological Pathology

E-PS-11-001
Endometrial high-grade neuroendocrine carcinoma with serous endometrial carcinoma – a case-report
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Background & objectives: Endometrial neuroendocrine tumours are rare, representing <1% of endometrial cancers (1). Because of their rarity, endometrial neuroendocrine tumours can create a diagnostic challenge to the pathologist.
This case report represents the diagnostic difficulty we faced in identifying this tumour.
Methods: A 72-year-old female presented with vaginal bleeding and found to have uterine mass on radiological studies. Endometrial curettage biopsy showed endometrial serous carcinoma. The patient then underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and full staging.
Results: Microscopic examination of the uterine mass shows a malignant neoplasm with a component of serous carcinoma composed of glands and papillae along with a solid component. The solid component composed of monotonous , dis-cohesive cells having round to spindle shaped nuclei, exhibiting frequent mitosis and apoptosis. This component shows diffuse AE1/AE3 positivity and wild type P53 positivity. At this stage it was difficult to reach to a diagnosis. The case was sent abroad for expert opinion, where additional immunohistochemical stains were performed. The neoplasm showed retention of nuclear immunoreactivity with mismatch proteins, SMARC A4 and SMARC B (INI 1) and there was wide spread positivity for synaptophysin and CD 56.
Conclusion: This case represents a combined endometrial serous carcinoma and high-grade neuroendocrine carcinoma. Primary neuroendocrine carcinoma of the uterine corpus often arises out of another tumour type, as in this case.

E-PS-11-002

Synchronous endometrioid tumours of the ovary and endometrium: a case report

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Background & objectives: Synchronous primary tumours are rare and controversial entities in diagnostic and therapeutic point of view what makes it important to identify and differentiate from primary tumour with metastasis. The challenge presented makes laboratories holds to strict histopathological criteria for diagnosis.
Methods: A 46-yo female from Ceara state, in Northeast Brazil, complained of abnormal vaginal bleeding, weight loss and increased abdominal volume. A right ovary tumour mass and endometrial thickening (12,0mm) were found in ultrasound examination. Endometrioid adenocarcinoma (EA) grade 1 was diagnosed by an hysteroscopic biopsy. This case was approved by Federal University of Ceará's Ethical Committee.
Results: A hystero-salpingo-oophorectomy was performed that showed a concurrent EA grade 2 in the uterus, with deep myometrial invasion and no parametrial spread. The right ovary showed a low grade EA (30,0cm to the greatest extent) with ovarian surface and ipsilateral tubal involvement. Linfovascular tumour emboli was detected in the right fallopian tube. Lymph nodes were negative for tumour cells.
Conclusion: The major diagnostic criteria for synchronous neoplasia presented in this case was an unilateral high volume ovarian tumour with low hystologic grade, extensive uterine tumour and lymphovascular emboli seen only in right fallopian tube, otherwise none of this is conclusive. Primary synchronous tumour has a better global disease–free survival than metastatic tumours. Recognizing this entity has an impact on patient prognosis, especially for those in low stages. Despite her high stage disease the patient remains disease-free after chemotherapy.

E-PS-11-005

Perivascular epithelioid cell neoplasm (PEComa) of the uterus – a case report

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Background & objectives: Perivascular Epithelioid Cell tumours (PEComas) are rare mesenchymal tumours, composed of distinctive perivascular epithelioid cells that express both melanocytic and smooth muscle markers. In the female genital tract, uterine PEComas are commonest with around 78 reported cases to date.
Methods: We present a case of PEComa of the uterus in a 47-years-old Omani patient came with heavy vaginal bleeding. The ultrasound showed large uterine hypoechoic mass measuring 8.5 cm in maximum dimension. MRI pelvis revealed a big oval well delineated intramural solid mass with necrotic vs. cystic area and with very prominent vascular supply.
Results: In view of uncertain nature of the lesion, the patient underwent total abdominal hysterectomy with bilateral salpingectomy. Gross examination of the uterus reveals a large mass that is filling the endometrial cavity, measures 16.0 x 8.0 x 8.0 cm with solid and cystic areas. Microscopic examination shows sheets of epithelioid cells with clear to eosinophilic cytoplasm, vascular invasion is present. The tumour cells were smooth muscle actin, oestrogen and desmin positive (diffuse); HMB-45, Melan A, CD10 & H-caldeson positive (focal). During follow up period, the patient is free of recurrent disease after surgery, without receiving any adjuvant treatment.
Conclusion: PEComa of the female gynaecological tract is a rare entity presenting with variable symptoms and different prognosis for each individual case. Distinguishing among mesenchymal neoplasms, including PEComas, endometrial stromal sarcomas, and leiomyosarcomas, can be difficult. The diagnosis is based on histopathology and immunohistochemistry reports and the optimal treatment is the surgical resection of the tumour.

E-PS-11-006

Acute abdomen, an unusual presentation of hydatid cyst

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Background & objectives: A 20-year old female, presented with increasing abdominal pain over a period of 6 weeks. There was no associated vomiting, no previous history of sexual encounter, peptic ulcer disease or abdominal distension. She presented as a case of acute abdomen
Methods: Remarkable investigations carried out include abdominal ultrasound scan which showed a hypoechoic mass attached to the right adnexa. Full blood count showed raised eosinophilia and neutrophilia. Other investigations were within normal limit.
An emergency exploratory laparatomy was done and a 10cm by 10cm pelvic cystic mass was excised and sent to histopathology for evaluation. It was adherent to adjacent structures.
Results: Macroscopic histological examination showed a large cystic mass containing cloudy, serous fluid.
Microscopic examination showed hydatid cyst with helminthic elements.
Conclusion: The incidence of hydatid cyst is higher in endemic areas. However, the high rate of transcontinental migration increases the risk in low endemic areas. The aim of this presentation is to create a high level of suspicion in surgeons and physicians for better patient care.

E-PS-11-007

Bilateral ovarian gonadoblastoma overgrown by dysgerminoma in a patient with Swyer's syndrome

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Background & objectives: Swyer's syndrome"XY gonadal dysgenesis" is a type of hypogonadism in a person with 46,XY karyotyping. The patients have normal female external genitalia, with functionless fibrosed gonads having significant risk of developing malignancy, if left unremoved surgically.
Methods: A 17-year-old female with Swyer's syndrome showed, during radiological assessment, mildly enlarged gonads those were removed laparoscopically (maximum dimensions: Right = 4.5 cm, Left= 1.5 cm). All the biopsy material was submitted for routine histopathological examination.
Results: Microscopic evaluation revealed bilateral gonadoblastoma. The tumours were formed of germ cell and sex cord stroma elements. The germ cell component shows large cells with abundant cytoplasm, vesicular nuclei with prominent nucleoli with presence of fibrous septae infiltrated by lymphocytes. The sex cord component has smaller cells with darker nuclei. Hyalinization and calcification are present. By Immunohistochemistry, germ cell component are positive for CD117 and PLAP. The sex-cord stromal component is positive for inhibin, calretinin and WT1. The right sided ovary showed, in addition, overgrowth by dysgerminoma. The patient was treated with combination chemotherapy (bleomycin, etoposide and cisplatin), and is in complete remission for two years.
Conclusion: Patients with XY gonadal dysgenesis are at high risk of developing germ cell tumours. Their ovaries should be, prophylactically, surgically removed even without the presence of obvious lesions.

E-PS-11-008

Histopathological study of human papilloma virus (HPV) induced cervical epithelial lesions and their mimics: experience of Sultan Qaboos University Hospital

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Background & objectives: Carcinoma of the cervix is mainly caused by HPV. These cancers progress through a pre-noplastic stage characterized by the presence of well described precursor lesions. However, some of lesions might have diagnostic difficulties as they mimic other benign lesions.
Methods: This retrospective study was conducted at Sultan Qaboos University Hospital (SQUH) including randomly selected 109 women with pre-neoplastic and neoplastic cervical lesions between 2011 and 2017. Hospital information system (HIS) was used for obtaining the clinical parameters and pathological characteristics. Analysis of the data was obtained using SPSS software.
Results: The mean age of the women was 45.95 ± 11.564, S.D ranged between 25 and 88. Cervical lesions were prevalent more in 40 to 49 age group. The distribution of the various diagnostic entities was as follows; CIN I: 26 cases "23.9%", CIN II: 13 cases "11.9%", CIN III: 11 cases "10.1%", SCC: 17 cases "15.6%", Koilocytic changes: 11 cases "10.1%", adenocarcinoma: 3 cases "2.8%", cervicitis: 28 cases "25.7%". Immunohistochemical markers (p16, Ki67 and HPV) were found to be helpful in confirming the diagnosis and in the exclusion of the benign mimics.
Conclusion: The present study explored cases of pre-neoplastic, neoplastic and non-neoplastic cervical lesions and their relation to HPVamong women populationin the area served by SQUH.

E-PS-11-009
The cross talk between HPV types and cervical intraepithelial lesions: national centre-based analysis
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Background & objectives: To study the prevalence of HPV (human papillomavirus) types in patients with squamous intraepithelial lesions (SIL) and squamous cervical cancer.
Methods: We recruited 145 women investigated colposcopically, with multiplex PCR for typing of HPV 21 types, cytologically (liquid-based), histologically (biopsy). The patients were subdivided based on cytological diagnosis: 31 patients (21,3%) with NILM, 30 patients (20,6%) with chronic cervicitis (histologically confirmed), 37 patients (22,7%) with LSIL, 31 patients (21,3%) with (group IV) and 14 patients (9,6%) with cervical cancer.
Results: The most significant risk factors for cervical intraepithelial lesions are: early sexual initiation, great number of sexual partners (>4), sexual transmitted infections (STI) history. The most frequent HPV types were 16, 31, 33 and 51 types. We demonstrated that HPV type 16 was significantly more prevalent in the group with HSIL and squamous cervical cancer compared to group II (chronic cervicitis) and group III (LSIL). HPV31 and 33 types are more prevalent in the group with HSIL. According to our results, there is the prevalence of the group A9 HPV in women with LSIL, HSIL and cervical cancer compared to group II (chronic cervicitis).
Conclusion: We demonstrated the key role of A9 HPV group in the development of intraepithelial and squamous lesions. Moreover, there is a trend to increase the incidence of HPV groups A7, A10, A5 and A9 HPV group in LSIL patients.

E-PS-11-010
Endometrial stromal nodules may harbour novel genetic alterations
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Background & objectives: Endometrial stromal nodule (ESN) is a rare benign tumour composed of endometrial stroma-like cells, typically whorling around arterioles. Most ESNs harbour t(7;17)(p21;q15) which results in a fusion between JAZF1 and SUZ12. Here we describe an ESN with yet undescribed genetic alteration with a potential target for biological treatment.
Methods: The medical records, imaging tests, pathological findings and genetic studies of the patient have been studied and are presented.
Results: A 35 years old patient presented with uterine bleeding that lasted for 6 months following a labour. Ultrasound demonstrated a 1.6 cm uterine mass. Hysteroscopy revealed a 3.5 cm mass bulging into the uterine cavity. On histological evaluation the resected mass showed a cellular tumour of bland oval to spindle cells with multiple arterioles. The tumour cells stained positively for CD10, SMA, desmin, ER and PR (caldesmon, CD117 and WT1 were negative) and the tumour was diagnosed as an ESN. Next generation sequencing (NGS) was performed on RNA extracted from the tumour paraffin block using the Archer FusionPlex Sarcoma kit. This kit simultaneously detects fusion of 26 genes associated with soft tissue tumours and allows the identification of novel fusions. No typical JAZF1 fusion was detected but a yet undescribed LTBP1-ALK fusion was identified.
Conclusion: The newly detected LTBP1-ALK fusion in the described ESN carries a potential target for biological treatment. As genetic analysis becomes more accessible, additional novel alterations are expected to be found in ESN and may serve as targets for biological treatment.

E-PS-11-011
Ruptured left ovarian endometrioid adenocarcinoma associated with granulomatous peritonitis, a possible cause of acute surgical abdomen
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Background & objectives: 125,000 patients die annually due to ovarian cancer. Ovarian endometrioid adenocarcinoma is a histological variant that accounts about 10% of ovarian carcinomas, often encountered in association with endometriosis.
Methods: A 57-year-old patient, second parous, presents at the Emergency Department from the Maternity of Oradea, accusing severe diffuse abdominal pain and tachycardia that started a few hours ago. Paraclinic investigations revealed leukocytosis (19,540 / mm3), and the CT examination revealed a pelvic tumour, heterogeneous, 10.5x8.5cm, suspected of malignancy, with the origin most probable located in the ovary.
Results: An exploratory laparotomy was urgently performed, which revealed a giant left adnexal tumour that was ruptured, on the surface covered by a creamy, amorphous material. Abdominal hysterectomy with bilateral anexectomy and omentectomy was performed. Definitive histopathological diagnosis: Endometrioid adenocarcinoma with morular squamous metaplasia, FIGO grade II, with ruptured ovarian capsule and granulomatous peritonitis (pT1c).
Conclusion: In menopausal patients presenting with severe diffuse abdominal pain, one of the differential diagnoses should be the spontaneous rupture of an ovarian malignancy.

E-PS-11-012
Primary poorly differentiated neuroendocrine tumour of the breast: a case report
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Background & objectives: Primary Neuroendocrine tumour of the breast is rare. The diagnosis requires expressing neuroendocrine markers in more than 50% of the cell, synaptophysin and/or chromogranin.
Here in we describe clinico-pathological and immunohistochemical features of primary neuroendocrine tumour of the breast.

Methods: A case of a 50 year-old woman presented with a 7 cm inflammatory mass of the left breast with skin infiltration. There is no past medical history. Clinical examination didn't reveal axillary lymph nodes. The mass was classified ACR 4 on mammography. Biopsies were performed.
Results: The samples showed a trabecular infiltrative growth pattern. The tumour cells had pleomorphic nuclei with granular chromatin. They presented a high numbers of mitosis and large areas of necrosis. There was no in situ component.
The immunohistochemical study revealed a diffuse and strong staining with synaptophysin and TTF-1 and chromogranin were negative. The diagnosis of primary poorly differenced neuroendocrine tumour of the breast was retained. The patient has recently started radio-chemotherapy with a good response.
Conclusion: Primary Neuroendocrine tumour of the breast is rare. It accounts for 0.1% of breast cancers and occurs between 43 and 70 year old. The morphological and immunohistochemical patterns are similar to its pulmonary counterpart. That's why a metastatic origin should be firstly eliminated. The presence of a ductal carcinoma in situ or conventional-type mammary carcinoma component with negativity of TTF-1 confirms the primary nature. The prognosis is poor.

E-PS-11-013
Struma ovarii with follicular thyroid-type carcinoma
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Background & objectives: Struma ovarii is a monodermal variant of ovarian teratoma. Thyroid-type carcinoma arising in struma ovarii is rare. The most common type is papillary carcinoma, followed by typical follicular carcinoma, and the new entity of follicular carcinoma-highly differentiated follicular carcinoma of ovarian origin; other forms occur rarely.
Methods: A 75-year-old hypertensive patient consulted for the sensation of a painless pelvic mass that has been progressing for 6 months. The abdominopelvic ultrasound showed a right-lateralized abdominopelvic mass measuring 14x13x8 cm with a solid and cystic double component. The patient underwent a unilateral adnexectomy.
Results: On gross examination, the tumour was yellowish-white in colour and had cystic cavities with colloid content. On histological examination, it was an ovarian goiter formed of vesicular structures of variable size filled with a dense colloid and associated with a malignant tumour proliferation arranged in sheets, trabeculae and vesicular structures. The tumour cells were cubic or polyhedral moderately atypical. Tumour cells showed positive immunostaining with TTF1. Postoperative course was uneventful.
Conclusion: Thyroid-type carcinoma of struma ovarii is rare. The exact prognosis of thyroid-type carcinoma arising in struma ovarii is still unclear. However, limited case reports and a small-series review demonstrated a good prognosis.

E-PS-11-014
Disseminated peritoneal leiomyomatosis: an easy clinical misdiagnosis
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Background & objectives: Disseminated peritoneal leiomyomatosis is a rare, benign condition, with less than 150 cases reported in English literature; it is characterised by the presence of multiple smooth muscle, myofibroblastic and fibroblastic nodules disseminated throughout the peritoneum, omentum and pelvic structures.
Methods: A 45-year-old female with a history of right ovarian cyst, presented to the emergency room accusing intense pain in the right-lower quadrant; transvaginal ultrasonography showed a giant cystic tumour in the right ovary. The patient underwent total hysterectomy, bilateral salphingo-oophorectomy, as well as omentectomy. The case was referred to our department with the diagnosis of ovarian neoplasm with peritoneal carcinomatosis.
Results: In the hysterectomy specimen we identified conventional leiomyomas, with no other pathological findings. The right ovarian tumour was a multilocular cyst, with papillary projections on both the internal and the outer surface of the lesion, measuring 18/10/5 cm; histological sections revealed a serous cystadenoma with focal epithelial proliferation. We found small nodules, with diameters of 2-6 mm, disseminated throughout the omentum; histopathologic examination exhibited interlacing bundles of smooth muscle cells with myofibroblasts and fibroblasts; the immune profile (positivity for smooth muscle actin, desmin and progesterone receptors) was supportive for the diagnosis of disseminated peritoneal leiomyomatosis.
Conclusion: Disseminated peritoneal leiomyomatosis is a rare, benign entity, which clinically and macroscopically can easily mimic disseminated intra-abdominal malignancies, especially when associated with an ovarian tumour. Therefore, an accurate diagnosis of this lesion is essential, considering the completely different therapeutic management required for each of them.

E-PS-11-015
Case report: mesonephric adenocarcinoma of cervix
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Background & objectives: Mesonephric adenocarcinoma of the cervix is a rare tumour which originates from the mesonephric duct remnants, typically occurs in middle-aged women and presents as a cervical mass or vaginal bleeding. There is scarce evidence regarding its behaviour, prognosis, and management.
Methods: A 42-year old woman was referred from primary care for findings of atypical glandular cells in routine cervicovaginal cytology. A curettage was performed which turned insufficient for diagnosis so a cervical conization was done.
Results: Microscopic study showed an infiltrative lesion constituted by ductal structures lined by hobnail cells with moderate atypia. Some sites demonstrated more complex architecture and isolated mitosis. These cells showed positivity for vimentin, napsin, p16, PAX8 and cytokeratin AE1/AE3. GATA3, oestrogen, progesterone, WT-1, p53, calretinin were negative. CD10 reacted against the luminal surface. Ki67 index was <10%. A central mesonephric duct was found and remnants and hyperplasia in the periphery.
Conclusion: Mesonephric adenocarcinoma is a diagnostic challenge since it exhibits a mixture of morphological patterns and has nonspecific immunohistochemistry. This tumour must be found within a mesonephric hyperplasia background.

E-PS-11-018
Vulvar squamous cell carcinoma: characteristics, treatment and outcomes of 77 women
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Background & objectives: Vulvar cancer is rare gynaecologic malignancy accounts for0.6%of all cancer diagnoses and 5%of gynaecologic cancers. Vulvar squamous cell carcinoma(VSCC)represents more than 90%of the malignant tumours of the vulva. Our aim is to describe epidemiologic-clinico-pathologic features of VSCC in the centre of Tunisia.

Methods: Sousse registry Cancer centre Database was used to identify women diagnosed with vulvar SCC from 2010–2019.Patient's clinical presentation, operative and pathological details were included in a database. Follow up details regarding recurrence and management and future outcomes were also noted
Results: We identified a total of 77women with vulvar SCC. The median age at diagnosis was 66 years(43-90)and more than 85%were more than 60-years.The symptomatology was dominated by tumour sensation in 53%of patients followed by vulvar pruritus in 23%of cases. The most frequent stage was IV(40%) followed by stage I(34%),stage III(25%) and stage II(12%).Moderately differentiated SCC was the most frequent histological grade by 76%of cases. Initial management was surgical for 94%of patients;64% vulvectomy with bilateral inguinal-lymph-nodes associated to radiotherapy in 48%of cases,23% simple vulvectomy and 5%hemivulvectomy.The median follow up was 5 years.9 cases received after one-year and 5 patients died in 2-years.
Conclusion: Vulvar SCC is a rare disease, occurs mostly in elderly women, and is diagnosed at advanced stages. Our findings emphasize that a greater effort should be made to facilitate early diagnosis and improve the management of this cancer.

E-PS-11-019
Vulvar melanoma: a rare tumour about two cases
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Background & objectives: Vulvar melanoma is a rare malignant cancer,representing 7-10%of all malignant vulvar neoplasms and is extremely aggressive with an overall poor prognosis. Given their rarity, the treatment paradigm isn't clearly defined.
Methods: Standardized and systematic documentation of clinical and histologic findings is needed to advance knowledge, that's what motivated our study.
Sousse registry Cancer centre Database was used to identify women diagnosed with vulvar Melanoma from2005–2019.The main prognostic factors of vulvar melanoma are represented by American Joint Commission on Cancer(AJCC) tumour stage(8th edition),Breslow's thickness and lymph-nodal status and were used in our study.
Results: We identified two women, the first was a postmenopausal-63-year-old and the second was younger,36-year-old and pregnant at diagnosis. Both of them underwent Radical vulvectomy with bilateral lymphadenectomy. Histopathology of the specimen showed the diagnosis of nodular melanoma. For the older patient, the lesion measured 0.7cm,Clark's level III, Breslow's indice 5mm and no metastasis in 20 lymph-nodes, but the lower right limit was invaded by the tumour. The second patient had an ulcerated-lesion measured 1cm,Clark's level III, Breslow's indice 6mm,micro-metastasis in one-lymph-node from 17 and all the limits were tumour-free. Despite complete surgical resection, the first patient developed urethral metastasis after 6months, and the second patient was lost to follow up.
Conclusion: Radical vulvectomy with bilateral lymphadenectomy hasn't shown to improve overall survival and is becoming a questionable and obsolete treatment approach. Alternatively, initial management of vulvovaginal melanomas is complete surgical excision and sentinel-node lymphadenectomy, which offers the best opportunity for long-term survival.
So surgery has to reach a balance between quality of life and aggressiveness to avoid needless morbidity, which needs a strong collaboration between health makers.

E-PS-11-021
Uterine perivascular epithelioid cell tumour (PEComa): a case report and literature review
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Background & objectives: Uterine perivascular epithelioid cell tumours (PEComa) are rare, underrecognized, mesenchymal uterine tumours with about 100 cases reported in the English literature, so far.
We present a case-report of a uterine PEComa, to raise awareness to the importance of this entity.
Methods: A 48-year-old woman, without relevant previous medical history, presented with abdominal pain and distension with 10 days of evolution.
On physical examination, the patient had a large pelvic mass, with associated pain.
Computed Tomography scan showed a large pelvic mass with abdominal extension, most likely of adnexal origin.
She underwent a total hysterectomy and bilateral adnexectomy.
Results: The surgical specimen was sent to the pathology department for evaluation.
The macroscopic examination revealed, in the uterine corpus, a tumour that bulged into the intact serosa; on the cut surface, it measured 34cm, it was mainly solid, yellowish, with a cystic area with 4cm, elastic and well circumscribed.
The microscopic examination showed a tumour with fusocellular pattern, with a clear interface with the adjacent myometrium; necrosis and one mitosis per fifty high power fields were noted.
The immunohistochemical study was consistent with the diagnosis of PEComa.
Conclusion: PEComa tumours, though sharing overlapping morphological and immunohistochemical features with the much more frequent and well studied smooth muscle tumours, have unique features and different management.
We need to study and compile more cases of these rare tumours to try to define with more accuracy their behaviour and consequently how to best manage them.

E-PS-11-022
Mixed (endometroid and serous) endometrial carcinoma: histopathologic and immunohistochemical issues for a correct diagnosis - case report
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Background & objectives: Mixed endometrial carcinomas (MEC) account for less than 10% of all malignant epithelial tumours of the uterus, being the endometroid and serous carcinoma the most common combination. Most of tumours initially diagnosed as MEC have an ambiguous morphology.
Methods: We present a case from our hospital, which is a 62-years old woman with uterine bleeding who underwent radical histerectomy. Personal and familiar medical history was unremarkable.
Results: On cut section there was a 3 cm-mass in upper third of the uterus body, which presented histologically two well distinguished components. Morphologically, despite both component showing glandular pattern, serous one showed areas of papillary growth, greater cytologic atypia, and budding / exfoliation of tumours cells.
With immunohistochemical study (IHQ), serous subtype was negative for oestrogen receptor (ER) and positive for P16 with aberrant diffusely positive staining of P53.

Endometroid subtype was positive for ER, negative for P16, with wild-type P53 and loss of staining for MSH6 (MLH1 and MSH2 demonstrated normal expression). Microsatellite instability-high (MSI-H) was seen by PCR and germline mutation was later ruled out.
Conclusion: Despite MEC remaining as a common interobserver disagreement, we emphasize the suitability of using a basic panel of IHQ to help confirm the subtype of each component, also according to its molecular pathogenesis.
Our case presented a MSH6 loss of expression with MSI-H in the endometroid part, which is a rare finding in MEC, according to literature. Finally, we suggest the individual genetic origin of each component, as previously reported.

E-PS-11-023
Ovarian lymphangioma
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Background & objectives: Lymphangiomas are benign lesions of the lymphatic system that can arise in any part of the body. They can easily be confused with a malignant ovarian mass especially in menopausal patients.
Methods: A 55 year- old patient was submitted to the hospital due to lower abdominal pain. Trans vaginal ultrasound showed multiple cystic and of mixed consistency lesions on the right ovary and its hilum. Semi radical hysterectomy with bilateral salpingo-oophorectomy was performed.
Results: Macroscopically, in the myometrium multiple leiomyomas of 0,5-6 cm in diameter were present. In the hilum and the cortex of the right ovary a cystic, bloody- chylous lesion measuring 3x2x1,3 cm was observed. Microscopically, the ovarian lesion was consisted of multiple, anastomosing and of variable size lymph vessels that were filled with lymphocytes and eosinophylic material. The surrounding stroma was haemorrhagic and oedematous. Immunohistochemistry (CD31+, CD34+, FVIII +, SMA +) confirmed the vascular origin of the lesion.
Conclusion: It is uncertain whether ovarian- hilar lymphangiomas represent as true neoplasms, hamartomas, or lymphangiectasias. They should be included in the differential diagnosis of malignant ovarian cystic masses. Their benign histologic appearance may not indicate their clinical behaviour. A few cases of recurrence or peritoneal dissemination have been reported. Complete wide excision and follow- up are suggested.

E-PS-11-024
Ovarian haemangioma in a postmenopausal woman - a case report
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Background & objectives: Ovarian haemangiomas are very rare mesenchymal tumours frequently of the cavernous haemangioma-type usually found during imagistic studies. They affect women of any age, ranging from infancy to 81 year-old. We report a case of capillary ovarian haemangioma with anastomosing features.
Methods: We report the case of a 67year-old woman with a previously ultrasonographically described right ovarian cyst. The computed tomographic examination revealed an adnexal tumoral lesion measuring 46x46x42 mm in diameter, with solid and cystic areas, highly iodophilic, with a small blade of peritoneal free fluid.
Results: A total hysterectomy with bilateral adnexectomy and peritoneal washings were performed. The peritoneal lavage was negative for tumoral cells. Gross examination of the right adnexa revealed an enlarged ovary, 3,5x3,2x3 cm, with haemorrhagic appearance on cut surface. Frozen section examination yielded the following result: benign lesion, with two differential diagnoses: ovarian haemangioma and adenomatoid tumour. Histological and immunohistochemical examination established the diagnosis of ovarian haemangioma with anastomosing features.
Conclusion: Although an uncommon entity, ovarian haemangioma should be kept in mind whenever an ovarian tumour is incidentally or clinically discovered. Thorough examination is required because it can mimic endometriosis or other ovarian neoplasms. When the anastomosing aspect is prominent, attention should be given to exclude an angiosarcoma. Leydig cell hyperplasia can be encountered. Ancillary studies can help establish the correct diagnosis. Surgical removal is both diagnostic and therapeutic.

E-PS-11-026
Mural nodule in a seromucinous borderline tumour of the ovary
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Background & objectives: Although rare, mural nodules occur mostly in ovarian mucinous tumours, where an anaplastic carcinoma component is associated with poor prognosis. The only reported case of a seromucinous borderline tumour(SMBT) with a mural anaplastic carcinoma nodule was associated with good prognosis.
Methods: We report a second case of SMBT with a mural anaplastic carcinoma nodule with an aggressive clinical course.
Results: A 79-year-old patient presented with bilateral ovarian tumours. After surgery, a diagnosis of bilateral pT1c SMBT with microinvasive carcinoma(<5 mm) and one mural anaplastic carcinoma nodule was rendered. The anaplastic carcinoma was composed of large, clear and anaplastic cells positive for cytokeratins, PAX8, and p53 "wild-type". Peritoneal washing was positive for neoplastic cells. Hotspot KRAS mutations in the mural nodule and tumour were not found. She underwent adjuvant chemotherapy. Eighteen months later, disseminated lymphadenopathy was found. FNA of an axillary lymph node confirmed metastatic adenocarcinoma morphologically and immunohistochemically akin to the anaplastic carcinoma nodule. Shortly after, the patient died due to a pulmonary thromboembolism.
Conclusion: Although SMBT have excellent prognosis, the presence of an anaplastic carcinoma component in a mural nodule likely renders its prognosis unpredictable. Advanced age, positive peritoneal washing and involvement of the ovarian surface might also explain the unexpected aggressive course of this case.

E-PS-11-027
Association of HEY2 gene rs13328928 polymorphism with the risk of endometrial hyperplasia
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Background & objectives: The article presents the prevalence of polymorphism rs13328928 gene HEY2 and reveals its association with the risk of endometrial hyperplasia.
Methods: The study included 180 residents of the Republic of Tatarstan. The main group - 79 patients with endometrial hyperplasia without atypia, the control group - 101 women without endometrial pathology. Determination of rs13328928 gene HEY2 was carried out by the method of real time polymerase chain reaction. The study performed a $\chi 2$ test and evaluated the odds ratio.
Results: It has been established that the presence of the C allele and the C/C genotype of the HEY2 rs13328928 are factors that increase the risk of developing endometrial hyperplasia without atypia in 180 women living in the Republic of Tatarstan. The prevalence of alleles and genotypes of the HEY2 gene was comparable with the European one.

Conclusion: The study revealed a dependence of the risk of developing endometrial hyperplasia without atypia with the polymorphism rs13328928 HEY2 gene.

E-PS-11-028

Benign multicystic peritoneal mesothelioma as a rare cause of amenorrhea and abdominal pain in a young female: a case report of an unusual entity

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Background & objectives: Benign Multicystic Peritoneal Mesothelioma is an unusual neoplasm that arise from the peritoneum, typically found in young females, with a high incidence of local recurrence, and less than 200 cases reported. We present a case of this rare cystic lesion.
Methods: We report the case of a 17-year-old patient with history of long-standing secondary amenorrhea and abdominal pain. Imaging studies showed a pelvic multicystic mass, composed of fluid-filled translucent cysts, connected by varying amounts of fibrous tissue. Total resection was performed.
Results: On gross examination, large multilocular and unilocular cysts were both observed. On histological evaluation, showed multiple medium-sized thin-walled cystic lesions containing, with variable proportions of eosinophilic fluid, lined by mesothelial cells without atypia. Foci of mesothelial hyperplasia were also present. Mesothelial cells showed immunoreactivity for CK5/6 as well as podoplanin.
Conclusion: Benign multicystic peritoneal mesothelioma, that occurs most frequently in women of reproductive age, is a very uncommon tumour not associated with asbestos exposure. Although recurrence is high after resection, it does not present a tendency to transform into malignancy.

E-PS-11-029

Uterine carcinosarcomas, a 10-year retrospective study in a tertiary institution

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Background & objectives: WHO defines carcinosarcoma as a malignant biphasic tumour of Müllerian derivation composed of high-grade carcinomatous and sarcomatous components. This is a rare, aggressive neoplasia and often diagnosed at an advanced stage.
Methods: We conducted a 10-year-retrospective transversal study at Coimbra University Hospital, a tertiary hospital in Portugal (2009-2019) and reviewed all uterine sarcomas (n=45). Relevant clinical and pathological data was extracted from the hospital database.
Results: A total of 22 cases of carcinosarcomas were found, representing 48,9% of uterine and cervical sarcomas. The median age at diagnosis was 74 years (range:55-93 years) and the median survival was 36.2 months (range:1,2-133,6 months). Tumour size ranged from 1.8 to 28cm.
In our cohort, 2/22 of the cases were diagnosed in a biopsy and 20/22 in the surgical specimen. The most common location was the uterine corpus, all cases except one arose in the cervix.
Conclusion: Uterine carcinosarcoma is a rare entity, with high morbidity and mortality, due to a high rate of relapse and metastases affecting predominantly postmenopausal women.

E-PS-11-030

Bilateral ovarian haemangiomas: a case report and review of the literature

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Background & objectives: Less than 60 cases of ovarian haemangioma have been well documented. Its coexistence with non-ovarian neoplasm such as cervical carcinoma and endometrial carcinoma has also been reported, therefore careful examination of contralateral ovary and endometrium are essential.
Methods: A 47-year-old female with medical history of lung carcinoma treated with radical surgery in 2012. Six years later, the serum CA-125 level was 49 U/mL(normal <35 U/mL) and CEA was 33,6 ng/mL (normal <3 ng/mL). CT scan revealed a heterogeneous mass in left ovary that measured 52 x 40 mm. The patient underwent a radical hysterectomy, bilateral salpingo-oophorectomy and appendectomy.
Results: Sections of both ovaries revealed vascular lesions with dilated thin-walled vessels, containing red blood cells in their lumen, lined by a single layer of endothelial cells.. Inmunohistochemistry analysis reveals that vascular endothelial markers (CD31 and CD34) are strongly positive but the aetiology is unknown and controversial. WT-1 was also positive in bilateral lesion, which are in favour to a neoplastic roliferation, not an anatomic malformation. A diagnosis of bilateral ovarian haemangiomas of cavernous type was made. Diffuse abdominopelvic haemangiomatosis was ruled out in our patient.
Conclusion: Most of ovarian haemangiomas, are discovered as an incidental finding and tumour is usually unilateral o bilateral, as our case. Surgical removal of the involved areas is treatment of choice and appears to be curative.

E-PS-11-031

Implementation of MMR deficient endometrial cancer diagnosis with IHQ

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Background & objectives: Lynch syndrome is a predisposition to cancer due to an autosomal dominant germline heterozygous mutation, in MMR genes.
We aim to determine an optimal identification of patients with alterations in the MMR system proteins in endometrial cancer.
Methods: Our study includes all patients diagnosed with endometrial carcinoma who have undergone hysterectomy from January 2017 to May 2019.
IHQ study of the PMS2 and MSH6 proteins was performed as primary screening. If negative, studied MLH1 or MSH2 respectively.
The prediction of germline mutational status is compared for combinations of tumour morphological features, presence of lymphovascular invasion, location and age.
Results: The total amount of patients that took part in our study was 96. The average age at diagnosis was 63.4 years. 82 cases (84%) was endometrioid histotype and, of them, 75 cases (78.8%) were grade I. 28 of them (29%) were located in the isthmus-lower uterine segment. The presence of lymphovascular invasion was noticed in 17 cases (17.7%). The MMR protein deficit was detected in 10 patients (10.4%). All cases were due to protein deficit in MLH1.
Conclusion: Propose an universal study of repair proteins in our area. Identification in patients with endometrial cancer of MMR protein alteration by gradual IHQ tests.

Statistically significant relationship between the presence of dMMR and the location in isthmus, higher degree in endometrioid subtype and presence of lymphovascular invasion.
No statistically significant relationship between these two groups (MMR / dMMR) and the average age, endometrioid - non-endometrioid histotype and higher pT.

E-PS-11-033
Mature teratoma of the lower uterine segment: a case report of a rare entity
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Background & objectives: Teratomas arise from primordial germ cells and are usually found in the gonads with occasional occurrences in extragonadal locations along the migration route of the germ cells. There are 10 documented cases of teratomas in endometrium and cervix.
Methods: A 55-year-old female presented with complaints of irregular peri-menopausal bleeding. Endometrial curetting showed strips of mucinous epithelium. No significant dysplasia was noted but a low grade mucinous neoplasm could not be ruled out. A hysterectomy was hence performed and the specimen sent for histopathological analysis and review.
Results: Macroscopic examination demonstrated a well demarcated multiloculated, firm, cystic lesion in the lower uterine segment. Microscopy showed a cyst containing ectodermal, endodermal and mesodermal elements comprising mature cartilage, adipose tissue, glands lined by goblet cells with mucin extravasation along with lymphoid tissue, bowel wall epithelium and gastric mucosa. No malignancy was noted. The myometrium and endometrium was normal. Diagnosis of a mature teratoma (dermoid cyst) was made.
Conclusion: Mature cystic teratomas of the lower uterine segment are very rare and presence of only one element such as mucinous epithelium can lead to a misdiagnosis of a carcinoma on biopsy or curetting.
Although rare, uterine teratoma should be considered in the differential diagnosis in patients especially when encountering endometrial biopsies with glandular or squamous elements.

E-PS-11-034
A rare example of a vaginal transitional cell carcinoma occurring metachronously with a bladder transitional cell carcinoma
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Background & objectives: Vaginal transitional cell carcinoma (TCC) is extremely rare. Fewer than twenty cases have been reported, most occurring metachronous to a bladder TCC. We report a case of an exophytic, non-invasive vaginal TCC occurring 6 years after a non-invasive bladder TCC.
Methods: An anterior pelvic exenteration was required for excision of the vaginal tumour. The bladder mucosa was inflamed but otherwise unremarkable. The vaginal tumour comprised a large, exophytic, carpet-like growth consistent with a non-invasive TCC. When reviewed with the original non-invasive bladder TCC, the morphology was very similar with both displaying regions of squamous differentiation.
Results: The pathogenesis of a vaginal TCC can be difficult to determine but could include a primary lesion, metastatic spread from the bladder, direct invasion from the bladder and implantation via seeding from the urinary tract.
To determine the pathogenesis, DNA extracted from the original bladder TCC and vaginal TCC were analysed by single nucleotide polymorphism array to assess copy number variation and copy number neutral loss of heterozygosity (CN-LOH). This demonstrated a match between the metachronous tumours including gains of 3q, deletion of CDKN2A, CN-LOH of distal 7q and CN-LOH 9p.
Conclusion: Genetic analysis proved conclusively that this was a bladder metastasis. The likeliest mechanism of spread was implantation via the urine. We note that primary vaginal TCC is now no longer recognised within the WHO classification.

E-PS-11-035
Choriocarcinoma: case report
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Background & objectives: The choriocarcinoma may occur subsequent to molar pregnancy (50%), spontaneous pregnancy loss or elective termination (25%), ectopic pregnancy (2.5%), or normal pregnancy (22.5%), being the most aggressive form of GTD and characterized by premature vascular invasion and metastasis.
Methods: A 29-year-old patient who was diagnosed with hydatidiform mole in 2013, lost follow-up with menometrorrhagia and pelvic pain in October 2017, being diagnosed with an invasive spring initiating methotrexate chemotherapy. The patient had several clinical complications that led to a change in the therapeutic regimen resulting in fluctuations in the levels of beta-HCG.
Results: In February 2019, there was another increase in beta-HCG level, when a hysterectomy and removal of a lump from the bladder and a margin of the small intestine was performed. Histopathological examination showed Invasive trophoblastic neoplasm formed by syncytiotrophoblasts, cytotrophoblasts and intermediate trophoblasts with marked cytological atypia. Bladder nodule, bladder margin and small intestine margin also showed invasion. One month after hysterectomy the patient presented with pulmonary and cerebral metastasis.
Conclusion: Even though the patient has been followed in a specialized DTG centre, the diagnosis of choriocarcinoma was delayed. Hysterectomy was not planned as the first therapeutic option because the patient's desire to get pregnant. The knowledge of the diagnostic criteria of DTG and the clinical follow-up of the patient is critical for both gynaecologists and pathologists in order to prevent late diagnosis and advanced stages of the disease.

E-PS-11-036
Histopathological profile of endometrium among perimenopausal women with abnormal uterine bleeding
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Background & objectives: Abnormal uterine bleeding is important symptom of both benign and malignant diseases of endometrium. Until the underlying pathology is accurately diagnosed, proper therapy is hardly possible. To study histopathological patterns of endometrium among perimenopausal women with abnormal uterine bleeding and correlate with the endometrial thickness.
Methods: Hospital based cross sectional study carried out on 75 cases of hysterectomy and endometrial biopsy specimens of perimenopausal women with abnormal uterine bleeding, at Department of Pathology in CMS-TH, Bharatpur from January 2017 to June 2018. The specimens were grossed, processed and embedded using standard procedures, were stained with Haematoxylin and Eosin stain and were analysed using light microscopy.
Results: The mean age of patients was 45 ± 3.4 years and menorrhagia was the dominant clinical presentation. Histopathology of endometrium

revealed 17 (22.7%) proliferative endometrium, 13 (17.33%) secretory endometrium, 12 (6%) weakly proliferative endometrium, 8 (10.7%) endometrial hyperplasia without atypia, 7 (9.3%) disordered proliferative endometrium, 5 (6.7%) atrophic endometrium, 4 (5.3%) cases of endometrial carcinoma and both endometrial polyp and chronic endometritis were seen in 3 (4%) cases each.
Conclusion: Histopathological examination of endometrium can serve as a mirror for detecting causes of abnormal uterine bleeding. Study of endometrial histopathology helps in early detection of premalignant and malignant lesions, leading to early diagnosis and prompt treatment at appropriate time.

E-PS-11-037
The importance of anamnestic data and the collaboration of colleagues in the curious case of endometrial cancer
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Background & objectives: Ectopic splenic tissue can pose diagnostic problems, especially in the form of splenosis which can mimic malignancy. Splenosis is an acquired anomaly related to heterotopic autotransplantation of splenic tissue following abdominal trauma or splenectomy.
Methods: We present a 69-year-old woman with extensive bleeding after menopause and many exploratory curettages. Last curettage was in July 2018. with HP diagnosis “high grade” serous endometrial carcinoma. Tumour markers are normal. The patient's general condition is good.
Results: Radiological diagnostic examinations show tumour deposits in omentum, retroperitoneum, intestinal serosa. Colonoscopy examination shows extraluminal tumour compressions, without mucosal lesions. The patient is referred to diagnosis: Carcinoma corporis uterii FIGO:IIIC. Histological analysis of the obtained materials designated as tumour deposits shows tissue of the spleen, which is presented as diffuse, multiple deposits throughout the whole abdomen, imitating disseminated peritoneal carcinomatosis. We got important data about performed splenectomy 30 years ago, after traumatic splenic rupture, and we conclude the case as splenosis. The endometrium showed no atypical changes. Regarding the previous HP diagnosis of serous endometrial cancer, the patient is certainly advised to further follow up.
Conclusion: Splenosis frequently mimicking abdominal tumours, which could lead to unnecessary surgery. A correct diagnosis should be rendered, considering the main differential diagnoses, clinicopathological correlation with the collection of anamnestic data. The current report aims to raise the awareness of splenosis so that it may be appropriately recognized and differentiated from other pelvic findings.

E-PS-11-038
Sclerosing stromal tumour of the ovary: two cases report
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Background & objectives: Sclerosing stromal tumour (SST) is an extremely rare benign subtype of ovarian stromal neoplasm of the sex cord stromal category, occurring in young adults. We report clinical and histopathological features of two cases of SST of the ovary.
Methods: A 18 years old and a 23 years old females presenting pelvic mass. On gross examination, the neoplasm was solidocystic.
The neoplasm was pseudo-lobular growth pattern composed of both spindle and polyhedral cells charged with lipids and a characteristic ‘hemangiopericytoma-like’ vasculature. Nuclear atypia and mitosis were not seen.
Immunochemically, tumoral cells were positive to smooth muscular actin and calretinin.
Results: SST is a rare benign ovarian neoplasm, mostly occurring in younger women. The clinical symptoms are non-specific.
The gross appearance of SST of ovary ranges from small solid to large multicystic masses.
Microscopically, the tumour is pseudolobulated with cellular areas and hypo cellular areas of collagenous or oedematous tissue.
Immunohistochemically, the cells of SST are positive for vimentin, inhibin, SMA and CD199 but negative for S-100 and epithelial markers.
These tumours are benign and can be treated successfully by enucleation or unilateral ovariotomy.
Conclusion: Due to the rarity of this ovarian neoplasm it is difficult to predict the presence of this tumour preoperatively on the basis of clinical and sonographic findings.
A possibility of SST should be kept in young patients with ovarian mass.

E-PS-11-039
Unusual form of squamous cell carcinoma of the cervix extending in situ into the endometrium and the fallopian tube: one case report and review of literature
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Background & objectives: Cervical squamous cell carcinoma (SCC) that spreads superficially to the endometrium and the fallopian tube with carcinoma in situ is a very rare phenomenon.
Our case represents superficial spreading of SCC of the cervix to the endometrium and fallopian tube.
Methods: 80 years old female, suffering from vaginal bleeding and pelvic pain. Gross examination revealed a slightly bulky uterus. The endometrial cavity was dilated and the endometrium was atrophic.
Microscopically, the cervical lesion was SCC, moderately differentiated and extending up and over the endometrial surface which was totally replaced with squamous cell carcinoma in situ, right fallopian tube was also involved.
Results: An extensive survey of the literature revealed 31 reported cases of cervical carcinoma with endometrial surface involvement, 15 cases were of invasive cervical carcinoma, in six cases, the fallopian tube was also involved.
The molecular mechanism of the superficial spreading of carcinoma cells is not yet well understood.
As the data are limited, it is still difficult to determine the optimal treatment of this unusual form of superficial spreading SCC.
The prognostic significance is also lacking because of limited data.
Conclusion: Superficial spreading SCC of the cervix is a rare phenomenon and guidelines for the management of these cases have not been determined yet.
Since SCC in situ of the endometrium is rare, its diagnostic must induce to explore the cervix.

E-PS-11-041
Transcription factor E3 overexpressing malignant perivascular epithelioid cell tumour of the uterus: a case report
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Background & objectives: Malignant perivascular epithelioid cell tumour of the uterus (PEComa) with Transcription Factor E3 (TFE3) overexpression is an extremely rare entity with less than ten cases in the English literature.
Methods: An 80-year-old female presented with pelvic pain and vaginal bleeding. Ultrasound examination revealed that there was a mass with the greatest dimension of 7 cm. A hysterectomy with loss of integrity was received at the intraoperative examination. The clinicopathologic properties of the present case were analysed.

Results: Gross examination revealed a bulky tan-brown, solid intrauterine mass. The cut surface was pink to grey with yellow necrotic areas. Microscopic examination showed neoplasia with an infiltrative border, resembling a "finger-like" appearance, predominantly composed of spindle cells with severe nuclear atypia. Accompanying epithelioid cells with oval to round central nuclei, large eosinophilic to clear granular cytoplasm had a nested pattern separated by a delicate vascular network. Bizarre giant cells were observed. There were 10 mitoses in 10 high power fields. Lymphovascular invasion was evident. Immunohistochemically the tumour cells express HMB-45, melan-A, SMA, desmin, caldesmon, oestrogen receptor, CD10, p53, and strong diffuse TFE3. S100, myogenin, Myo-D1, beta-catenin were negative.
Conclusion: It is important to differentiate malignant PEComa from smooth muscle tumours of the uterus. Additionally, the distinction between TFE3 translocation associated and Tuberous Sclerosis Complex (TSC)-related PEComa has a therapeutic value. A further molecular genetic examination should be offered to patients. Resistance to mTOR inhibitors has been reported in TFE3-translocated PEComas.

E-PS-11-042
Invasive stratified mucin producing carcinoma and usual type endocervical adenocarcinoma of the cervix: a case report
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Background & objectives: Invasive stratified mucin-producing carcinoma(iSMILE) has invasive nests of stratified columnar cells with peripheral palisading and variable amounts of intracytoplasmic mucin, resembling its in situ counterpart which has high risk HPV associated carcinogenesis methods.
Methods: 43 year old female patient presented with intermittent vaginal bleeding and she underwent cervical biopsy. Biopsy diagnosis was carcinoma. She underwent radical hysterectomy. Macroscopically tumour was 4.5x2.5x2 cm with cream colour and small cystic cavities located in the exocervix and protruding towards the endocervix. Microscopically tumour had two components as iSMILE and endocervical adenocarcinoma of the usual type.
Results: The tumour cells had spherical nucleus, distinct and sharp cytoplasmic borders. In iSMILE component the tumour had abundant intracytoplasmic mucin . iSMILE component showed an infiltrative growth of tumour cell nests with a finger-like pattern of invasion. Irregularly shaped, angulated or fragmented glands with an adjacent desmoplastic stromal reaction were present in adenocarcinoma component. Immunhistochemically tumour cells were positive with p16("block-like"expression pattern),PAX-8,and CK7 and negative with HNF1beta,NapsinA,GATA3,Calretinin for both components.
Conclusion: The present data and those obtained from the literature suggest that iSMILE represent a distinct subtype of invasive endocervical adenocarcinoma, associated with high-risk HPV-infection carcinogenesis and may be seen together with usual endocervical adenocarcinoma component.

E-PS-11-043
Serous adenofibroma of the fallopian tube with coexistent ectopic tubal pregnancy
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Background & objectives: Serous adenofibromas of the fallopian tube are rare tumours considered to be analogous to their counterparts in the ovary. They are usually small and incidental finding during surgery.
We present a 34-year old patient with previous history of uterine bleeding.
Methods: The patient was misdiagnosed in another institution as miscarriage. Due to persistent elevation of the HCG serum levels (from 2350 IU/L to 5980 IU/L), ultrasound examination was performed, which led to suspected left ectopic tubal pregnancy. Five days after receiving methotrexate, the patient was again admitted to the hospital with abdominal pain and vomiting. Left fallopian tube was surgically removed.
Results: Histopathologic examination confirmed ruptured ectopic tubal pregnancy in the isthmic portion. Small, 4 mm firm yellow nodule was attached to the fimbriae. On microscopic examination, the nodule was well-demarcated and consisted of intersected fibroblasts and hyalinized collagen bundles with few slit-like or cystic spaces covered with benign epithelium. Stromal cells were focally positive for inhibin and CD10, whereas epithelial cells coexpressed vimentin and cytokeratin 7, as well as oestrogen receptor.
Conclusion: Ectopic pregnancy in this patient might have potentially been caused by the presence of tubal adenofibroma. Even though only few cases of coexistent ectopic tubal pregnancy and serous adenofibroma of the fallopian tube have been published in the literature, ectopic tubal pregnancy associated with other benign tumours, such as adenomatoid tumour, leiomyoma or mature cystic teratoma have been reported. These tumours might lead to partial obstruction of the fallopian tube or mimic ectopic pregnancy.

E-PS-11-045
Incidental primary extranodal ovarian diffuse large B-cell lymphoma (DLBCL): a case report
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Background & objectives: Ovarian lymphomas are usually secondary and indication of disseminated disease. Primary ovarian lymphomas are rare and the prognosis is better. We describe a primary ovarian DLBCL in a 57-years-old woman who underwent surgery for a cyst in the fallopian tube.
Methods: We received left fallopian tube measuring 6cm long and 0,5cm in diameter and ovary whose dimensions were 4x1,5x0,3cm. There was a paratubal cyst measuring 7cm in its greatest dimension. The frozen sections were negative (benign paratubal cyst). On permanent sections there were two lesions in the ovary measuring 0,5 and 1,3 cm respectively.
Results: The first one was a benign transitional (Brenner) tumour. The second one was composed of a diffuse proliferation of relatively large pleiomorphic cells with vesicular nuclei and often prominent nucleoli. The immunohistochemical survey showed: Vimentin(+), LCA(+), KerAE1/AE3(-), CD20(+), CD3(-), Bcl2(-), Bcl6(+/-), CyclinD1(-), CD10(-), CD68(-), CD10(-), absence of clonal light chains. The proliferation index was 60%. The diagnosis was DLBCL,NOS with a further note for additional tests to prove the origin. A bone marrow trephine biopsy was performed which was negative, as other diagnostic imaging techniques. So the final diagnosis was primary DLBCL, NOS. The patient received 8 circles of RCHOP, and she is free of disease, one year later.
Conclusion: Primary ovarian lymphomas are rare. Their prognosis is better than secondary lymphomas which have to be excluded clinically. In our case the patient is free of disease one year later.

E-PS-11-046
HPV profile of adenocarcinoma of the uterine cervix: a 10 year-histopathological review of 242 cases in a large prevention centre
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Background & objectives: Adenocarcinoma (AC) comprises 10-25% of all cervical carcinomas in developed countries, and 94% are associated with high-risk HPV. This study aimed to determine the epidemiology, morphology, and HPV profile.
Methods: A retrospective review between January 2008 and January 2019 was performed using the cancer registry database in a single reference centre for cancer prevention in Brazil.
Results: Two hundred forty-two patients were diagnosed with AC. The majority of the patients were in their forties (88 patients - 36%). Invasive cases comprised 47.5%, and 44.6% were "in situ" AC. Of these, 173 patients were treated with surgery. HPV profile was performed in 64 patients using real-time PCR (Cobas 480® platform, Roche, Basel). Twenty-nine were high-risk HPV positive. The most common phenotype was HPV 16. The overall mortality rate was 12%.
Conclusion: Unlike the literature, our study identified HPV 16 as the most common subtype. The age range was composed of younger women as compared to the literature.

E-PS-11-047
Hyperreactio luteinalis after delivery: a case report of a rare entity with literature review
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Background & objectives: Hyperreactio luteinalis is a rare condition characterized by bilateral cystic enlargement of the ovaries, mimicking malignancy, during pregnancy, post partum or ovulation induction .
The aim of this work is to analyse epidemiological, clinical and pathological aspects of this entity.
Methods: We present a case of hyperreactio luteinalis in 31 year old women collected in our institution in 2019.
Results: A 31 year old woman consults for distension and abdominal pains, 7 days after delivery of a healthy baby. Ultrasound shows bilateral cystic ovarian tumours suspect of torsion. A left oophorectomy and a right cystectomy were performed in an emergency.
Macroscopically , the left ovary was enlarged and replaced by multiple cysts with brownish content and thickened partitions without solid elements, the right cystectomy consist of multilocular cyst with translucent wall and yellowish content.
Histologically, ovarian cysts were lined by luteinized with abundant eosinophilic granular cytoplasm and round nucleus sometimes nucleated , resting on an oedematous stroma containing clusters of these cells.
Conclusion: There are only very few case report of Hyperreactio luteinalis occurring after delivery. This case highlights the confusion between this entity and ovarian malignancy and the importance of increased clinician awareness with hyperreactio luteinalis diagnosis to reduce unnecessary surgical procedures and prevent morbidity from surgery.

E-PS-11-048
A rare case of stromal luteoma of ovary: case report and literature review
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Background & objectives: Steroid cell tumours are rare sub-group of sex-cord ovarian tumours accounting 0.1% of all primary ovarian tumours. Symptoms differ depending the hormones secreted from the tumour cell. Stromal luteomas presents with hyper-estrogenic symptoms as irregular menses, mood swing and headache.
Methods: A 26-year-old female, married 4 years ago, presented with primary infertility, irregular menses, painful on and off left iliac fossa mass for 3 years. She had several dilate and curettages (D&C) and treated as hormonal imbalance without improvement. Preoperative transvaginal ultrasonographic examination revealed a 1.2cm left ovarian tumour, oophorectomy done and histology revealed stromal hyperthecosis.
Results: Steroid cell tumours account for 0.1% of all primary ovarian tumours, and classified as: stromal luteomas, Leydig cell tumours and steroid cell tumours not otherwise specified (NOS). A 26-year-old female, presented with primary infertility, irregular menses, painful left iliac fossa mass for 3 years.
Preoperative transvaginal ultrasonography revealed a 1.2 cm left ovarian tumour. Grossly specimen appeared yellow coloured, solid with clear borders, tumour sized 1.5x1.3 cm. Microscopic examination showed benign stromal hyperthecosis. To exclude Malignant melanomas as mimickers S100 and HMB-45 stained negative. With clinical and histopathological examination, patient diagnosed with stromal luteoma a benign tumours surgically treated without staging, as these tumours are seen very rarely.
Conclusion: Ovaries should be carefully examined with transvaginal ultrasonography to reveal any ovarian pathology in all age women presenting with irregular bleeding. Stromal luteomas presents with hyper-estrogenic symptoms as irregular menses, mood swing and headache. Stromal luteomas should be considered as one of the reasons though are rare and are confirmed through endometrial curettage and ovarian histology. Stromal luteomas are benign tumours surgically treated without staging.

E-PS-11-049
Endometrial carcinoma and Lynch syndrome in Botswana
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Background & objectives: Endometrial carcinoma is the sixth most common cancer in women. It is traditionally classified into type I and II. Type II usually arises in elderly women and carries a worse prognosis and Type I in younger women with better prognosis.
Methods: All cases of endometrial cancer seen at the National Health Laboratory, Gaborone, Botswana from 2012-2019 were reviewed. A select number of cases were screened for Lynch syndrome using the four immunohistochemical stains (MLH1, MSH2, MSH6, PMS2).
Results: 38 cases were included in the study. 15/38 (39.5%) of the women were diagnosed with Type I endometrial carcinoma whilst 23/38 (60.5%) were diagnosed with Type II endometrial carcinoma. 10/38 (26%) of the cases were tested for DNA mismatch repair gene mutations using the four panel immunohistochemical stains. 7/10 of these cases showed intact staining for all stains and 3/10 had indeterminate results.
Conclusion: This study shows that the burden of endometrial cancer in Botswana is largely attributable to Type II endometrial cancers which varies from the published literature which shows Type I endometrial cancers to be more common. A myriad of preanalytical factors have been shown to influence immunohistochemical staining patterns and many of these factors unfortunately plague our Anatomical Pathology laboratory.
Funding: BDIAP grant

E-PS-11-050
Elevated neurokinin 1-receptor expression in uterine products is associated with first trimester miscarriages
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Background & objectives: Miscarriage is a common complication of early pregnancy, mostly occurring in first trimester. The present study aimed to clarify the localization and expression for NK-1R in human retained products of conception, not known previously
Methods: NK-1R expression was assessed in products of conception and normal placental tissues by immunohistochemistry; protein expression was evaluated using the nuclear labelling index (%).

Results: Ten human products of conception tissues were studied by immunohistochemistry to demonstrate the localization of NK-1R. The expression of NK-1R protein was high in all the cases of POCs. NK-1R expression showed no notable differences among different cases of miscarriages irrespective of the mother's age and gestational age at which the event occurred.
Conclusion: Expression of NK-1R was similar in all the cases. It shows that dysregulation of NK-1R might be involved in miscarriages, abortions. It will open new avenues to investigate sudden perinatal deaths. Thus, the present study recommends that SP/NK1R system might, therefore, be considered as an emerging and promising diagnostic and therapeutic strategy against SIDS, SIUDS and miscarriages. Hence, we report for the first time, the expression and localization of NK-1R in products of conception.

E-PS-11-051
The oestrogen plasma level does not relate to fallopian tube epithelium differentiation
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Background & objectives: Non-uterine high-grade serous carcinomas are believed to arise from precursors in the fallopian tube. The distribution of epithelial cell types is not uniform and there is not sufficient evidence supporting hormonal regulation of their differentiation.
Methods: The study material consisted of 14 cases after total hysterectomy mostly for myomatosis of the uterus (women age 41 – 56 years). We evaluated oestrogen levels and compared with the percentage of secretory cells in the fallopian tubes. Oestrogen receptor (ER) and Bcl-2 protein expression was assessed immunohistochemically. Secretory/stem cell outgrowth (SCOUT) represented expansion of at least 20 secretory cells.
Results: Immunohistochemical stain for oestrogen receptor and Bcl-2 visualized secretory cells, distinct from ciliated epithelial cells with weak ER and no Bcl-2 expression. In 50% of cases we found SCOUTs regardless of age, without apparent location prevalence. It showed a positive correlation with increasing percentage of secretory cells in the mucosa. The histopathological findings did not correlate with oestrogen blood levels.
Conclusion: Despite of no correlation with oestrogen plasma levels, high expression of ER together with Bcl-2 in the secretory cells might participate at the formation of SCOUTs, the increased frequency of which is linked to serous carcinoma development.
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E-PS-11-052
Uterine mesonephric carcinoma: an uncommon carcinoma that must be distinguished from mesonephric-like carcinoma of endometrium
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Background & objectives: Mesonephric carcinomas (MC) of female genital tract are unusual neoplasms located on the lateral walls of uterine cervix although have also been reported in other gynaecological locations. The uterine origin is extremely rare, only few cases have been reported hitherto.
Methods: We report a 66 year-old woman with a background of vaginal bleeding. Magnetic Resonance image showed a uterine enlargement of 16 cm, involving all the wall thickness. With a diagnosis of uterine sarcoma, the patient was undergone a surgical radical hysterectomy. The tumour involved all entire uterine thickness, yet no intracavitary lesion was identified.
Results: The histology revealed a series of contorted papillae with non-stratified nuclei and fine chromatin giving a clear appearance. By immunochemistry (ICH) the cells expressed neither oestrogen nor progesterone receptors, whereas were positive for GATA-3 and CD10. The Ki 67 was high; >80%. On the contrary, the immunostain of cytokeratin CK7 only was patchy.
Conclusion: Myometrial depth involvement, where presumably mesonephric remnants can be present, is a requirement for diagnosis MC and must be distinguished from endometrioid mesonephric-like carcinomas (EMC) that are more frequent. Morphological and IHC both are indistinct, despite having the same histology and IHC. EMC are intracavitary tumours and use to be more aggressive. As the true MC is concerned, its behaviour is still unknown due to few number of cases reported.

E-PS-11-054
Endometrial lymphoepithelioma-like carcinoma – a very rare location
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Background & objectives: Lymphoepithelioma–like carcinomas (LELCs) are tumours with histological features similar to those of lymphoepithelioma of nasopharynx. They have been described in many organs including female genital tract. However, only few cases have been described in in the endometrium.
Methods: We hereby report a rare case of a 73-year-old woman, G4.P3.A1, presented with postmenopausal vaginal bleeding. She consulted the local doctor and she underwent endometrial curettage biopsy.
Results: The material from endometrial curettage consisted of small fragments of poorly differentiated carcinoma, showing focal area of necrosis. The tumour was composed of poorly defined nests of large syncytial cells. The tumour cells had eosinophilic to amphophilic cytoplasm with round to oval vesicular nuclei with prominent nucleoli and high mitotic index. The tumour nests were surrounded by dense lymphoplasmacytic infiltrate. Immunohistochemically, the tumour cells were strongly and diffusely positive for cytokeratins AE1/AE3 and Oestrogen receptors.
Conclusion: LELC arising in endometrium is an extremely rare tumour. Only seven cases of LELC have been reported in literature to date. Nevertheless, there are no association with Epstein-Barr virus and LELC in this location such as in nasopharyngeal lymphoepithelioma.

E-PS-11-055
Uterine adenosarcoma: analysis of 3 cases
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Background & objectives: Adenosarcoma or Mullerian Adenosarcoma represents 6% of uterine sarcomas. It is composed by two components, one benign epithelial and a low grade sarcomatous stromal component. Uterine corpus is the most common site but cervical cases are described in about 2%.
Methods: We reviewed all cases of uterine and cervix adenosarcoma from 2009 to 2019, at Centro Hospitalar e Universitário de Coimbra, an Universitary and tertiary centre.
Results: We found 3 cases, with a mean age of 53,3- years-old. Two cases were located in the corpus in patients both with 69 - years-old, and one in the cervix in a 22 - years-old. One case was an adenosarcoma with sarcomatous overgrowth, which is a rare variant in which the stromal component is a high grade sarcoma in at least 25% of the tumour. The

clinical presentation were abnormal vaginal bleeding and abdominal pain. Grossly the cervical adenosarcoma corresponded to a polyp. Our three cases had an average of 6 years disease-free survival, although adenosarcomas are known for having poor outcome.
Conclusion: Adenosarcomas are extremely rare, typically found in middle age women. Cervical adenosarcomas are even rarer usually found in women of reproductive age and mainly present as cervical polyps and can be misunderstood as benign lesions as seen in our case.

E-PS-11-056
Uterine leiomyosarcoma: a series of 7 cases
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Background & objectives: Leiomyosarcoma is the most common uterine sarcoma representing 1-2% of all uterine malignancies. Cervical sarcomas are extremely rare tumours accounting for 1% of the cases.
Methods: We reviewed all cases of uterine leiomyosarcomas from 2009 to 2019, at Centro Hospitalar e Universitário de Coimbra, an Universitary and tertiary centre.
Results: We found 7 cases, with a mean age of 59,6 years-old. Four cases were located in the corpus, one bifocal and three in the cervix. The clinical presentation was abnormal vaginal bleeding and abdominal pain. All the cases presented with a mass with a mean diameter of 10,5cm and were histologically classified as spindle cell leiomyosarcomas. High grade leiomyosarcomas, with more aggressive histologically behaviour, were located in the cervix, showed marked cellular atypia and more than 10 mitoses/10 high power fields. Leiomyosarcoma is associated with poor prognosis and our cases have an average of 5,4 years disease-free survival.
Conclusion: Although cervical leiomyosarcoma is a rare location in our series almost half of the cases were found in the cervix. Mores studies are needed to clear up the prognosis of leiomyosarcomas specially in cervical location.

E-PS-11-058
Intravenous leiomyomatosis pathology: case report
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Background & objectives: Intravenous leiomyomatosis (IVL) is a rare benign neoplasm of smooth muscle cells, usually arising from the uterus. It can develop directly from the smooth muscle wall of large veins, or is formed during intravascular invasion of the uterine leiomyoma.
Methods: We report the case of giant IVL located in the inferior vena cava. Female patient,38y.o, had a hysterectomy for a uterine cellular leiomyoma in her medical history. Now a tumour was removed from the inferior vena cava, continuing from the pelvis to the right atrium. Tumour samples were evaluated grossly, and then microscopic examination of histological slides was carried out.
Results: Gross examination revealed a cylindrical shape rubbery tumour, 50 cm long, 4 cm in diameter. Its surface was smooth, grey-pink in colour, covered with a thin translucent capsule. In the section, the tumour was fibrous, with severe oedema and multiple small cysts with a diameter of up to 0.2 cm. Cysts were filled with a slightly unclear grey liquid. Histologically neoplasm was represented by elongated spindle-shaped cells that formed solid fields. It had minimal cell atypia and rare mitotic figures. The stroma of the tumour was loose and swollen. Based on a morphological study, the diagnosis IVL with growth in the lumen of the inferior vena cava was made.
Conclusion: IVL is an uncommon tumour, it may extend intravascularly and reach the inferior vena cava, right atrium, and pulmonary arteries. Early diagnosis and complete tumour resection is important in treating the disease. The tumour material needs further thorough research, including immunohistochemical and molecular genetic studies to identify the causes, new diagnostic criteria. Morphological features and the differential diagnosis of this rare tumour in the light of the literature are discussed.

E-PS-11-059
Atypical papillary mucinous proliferations of the endometrium – diagnostic difficulties on curettage specimen
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Background & objectives: WHO Classification categorizes endometrial mucinous proliferations that display "confluent or cribriform architecture with even minimal atypia" in sampling specimens as carcinoma, and other features that aren't diagnostic of carcinoma as atypical mucinous glandular proliferations (AMGP).
Methods: We present a case of a 58 year-old woman with no relevant personal history and not under hormone replacement therapy, referred to consultation for postmenopausal metrorrhagia.
Ultrasound showed multiple uterine nodules in the myometrium and intracavitary. MRI scan demonstrated endometrial thickening of 11mm. Hysteroscopy revealed endometrial cavity filled with multiple digitiform projections with atypical vascularization, and curettage was made.
Results: Histologically there was a papillary glandular proliferation with complex ramified architecture, with morphologic characteristics resembling mucinous and eosinophilic metaplasia, multiple neutrophilic microabscesses, moderate pleomorphism, nuclear pseudoestratification and presence of macronucleolus, but without evidence of cribriform or confluent pattern.
Hysterectomy with bilateral adnexectomy was performed.
Macroscopy examination revealed an intracavitary 2,5cm creamy white tumour that appeared to invade the myometrium superficially.
Histological examination was consistent with mucinous carcinoma.
Conclusion: Although the aspects of the biopsy specimen were suspicious of malignancy, they didn´t fulfil all the morphologic criteria for carcinoma, mainly due to scarcity and superficiality of the sampling, and so it wasn't possible to sign it out as carcinoma.
AMGP of the endometrium are a rare and heterogeneous group that include lesions ranging from metaplasia to carcinoma. There are no definitive morphologic criteria nor immunohistochemistry to rule out malignancy.

E-PS-11-060
One of the rarest benign solid tumours of the ovary
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Background & objectives: Ovarian leiomyoma (OL) is a very unusual benign tumour, most often occurring in premenopausal women, and accounts for 0.5-1% of all benign ovarian neoplasia. Since Sangalli first described OL in 1862, fewer than 100 cases have been reported.
Methods: We present a case of a 50-year-old woman that was referred to gynaecology department for a mass incidentally found in her pelvic cavity. Computed tomography showed a soft tissue tumour inseparable from the right ovary. Biochemical tests and tumour markers were within normal ranges. Total hysterectomy with bilateral salpingo-oophorectomy was performed.
Results: Ovary measured 5.5x3.5x2.5cm with a solid, firm, oval mass. Outer surface was smooth and cut section revealed a well-circumscribed, homogeneous, grey-white solid mass with lobulated appearance, entirely within the ovary and measured 4.5 cm in diameter. Microscopic examination revealed interlacing fascicles of smooth muscles cells, without any

evidence of atypia, mitosis or necrosis. The histopathological diagnosis of OL was made on basis of histologic features.
Conclusion: OL is usually small and asymptomatic, mostly discovered incidentally during routine examination, surgery or autopsy. Precise histogenesis of OL is unknown. Microscopically areas of leiomyosarcoma should be excluded. Differential diagnosis includes other solid ovarian tumours such as fibroma, thecoma, low-grade endometrioid stromal sarcoma, as well as secondary involvement. After complete resection, OL rarely recurs and the prognosis is excellent.

E-PS-11-061
Unusual clear cell variant of papillary carcinoma in struma ovarii: a case report
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Background & objectives: Malignancy of ovarian struma is reported in less than 5% of cases. Papillary carcinoma, as in the thyroid gland, is more common here. We present a rare case of a clear cell variant of papillary cancer in struma ovarii.
Methods: A 68-year-old woman has been hospitalized for a painful palpable tumour of the left ovary. After salpingo-oophorectomy, the material was examined. Macroscopically, the ovary was enlarged as a tumour node 5.0 cm in diameter. The cut surface was brown, with multiple cysts filled with jelly-like contents and solid areas. Histological and immunohistochemical studies were performed.
Results: Microscopic evaluation of this tumour revealed a conventional type struma composed of typical small to medium sized follicles lined with cuboidal epithelium and filled with an eosinophilic colloid. In addition to this tumour there were areas significantly differed in structure. This thyroid-type tissue showed crowding follicles with irregular contours and papillary structures. They were composed predominantly of clear cells with optically empty cytoplasm. The nuclear alterations were close to those of conventional thyroid papillary carcinoma (oval shape, clearing, ground glass appearance, membrane irregularity, pseudoinclusions). Immunohistochemical staining was positive for TTF1, PAX8, Thyroglobuline. This tumour was diagnosed as a struma ovarii with a clear cell variant of papillary carcinoma.
Conclusion: Clear cell variant of malignant struma ovarii is an extremely rare lesion. The biological nature of this tumour and its behaviour are unknown. In this case, no metastases were detected. Long-term follow-up is necessary for developing an adequate treatment and prognosis.

E-PS-11-062
Hereditary leiomyomatosis showing deletion of 1p in multiple lesions: a case report
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Background & objectives: A 40 year old Para1 presented with a 4 month history of abdominal distension. Past history included a large vulval cutaneous leiomyoma. There was a family history of multiple leiomyomata in her mother and sister at an early age.
Methods: She underwent total abdominal hysterectomy, myomectomy and salpingo-oophorectomy for multiple large solid and cystic lesions. The largest was a smooth muscle tumour of uncertain malignant potential(STUMP) and the remainder were benign leiomyomata. This unusual presentation raised suspicion of Hereditary Leiomyomatosis and Renal Cell Carcinoma (HLRCC) which carries a risk of aggressive renal cell carcinoma. She was referred to clinical genetics.
Results: Sanger sequencing of the Fumarate Hydratase(FH) gene which is responsible for HLRCC was carried out which showed no evidence of a mutation at 1q43. SNP array analysis of 6 tumours including the cutaneous lesion and a leiomyoma from the proband's sister was carried out. No loss of heterozygosity at the FH locus was detected. However, deletions of 1p were seen in five of the tumours with retention of the same 1p haplotype. Deletions of 13q were seen in three. The results indicate the absence of a germline pathogenic variant in the FH gene which is associated with HLRCC. However, deletion of 1p is a recurrent but rare finding in leiomyomata.
Conclusion: Detection of recurrent 1p deletion with retention of the same haplotype in multiple lesions in the family is highly unusual and suggestive of a familial variant in a tumour suppressor gene in this region causing a dominant predisposition to leiomyomata and as yet unknown risk of renal cancers.

E-PS-11-065
Placental metastases of maternal anaplastic thyroid carcinoma: a case report
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Background & objectives: Metastatic malignancies in placenta are underreported despite their prevalence (~1:1000 pregnancies). We report a case of a 44-year-old female with anaplastic thyroid carcinoma with breast metastases who underwent a caesarean section on gestation week 33 and had placental metastases
Methods: For the microscopic study, we included several sections of the placental disc, membranes and umbilical cord. CKAE1/AE3, p53, cyclin-D1, TTF-1, Ki-67 and BRAF immunostains were made in order to identify and study tumoral cells.
Results: The placenta weighed 444 g and the macroscopic examination revealed several solid nodules, well delimited and non-capsulated, measuring from 0.4 cm to 1.7 cm. The umbilical cord measured 42 cm and showed no abnormalities. Microscopically, the tumours were composed of cells with marked atypia, eosinophil cytoplasm and pleomorphic nuclei with prominent nucleoli. The infiltrate was confined to the maternal space, occupying perivillous spaces, but no villous infiltration was identified. Immunohistochemically, tumoral cells were positive for CKAE1/AE3, cyclin-D1 and overexpressed p53. TTF-1 was negative. BRAF was mutated. Ki-67 proliferative index was 75-80%.
Conclusion: It seems that thyroid carcinoma metastases to placenta are very uncommon, although is highly recommended to do an exhaustive study of the placenta in cases of maternal cancer given its prevalence.

E-PS-11-069
A case of coexistence of uterine lipoleiomyoma, leiomyoma, endometrial polyp and early clear cell carcinoma of the endometrium, never described before
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Background & objectives: Uterine lipoleiomyoma is a rare variant of leiomyoma with considerable amount of adipocytes. It may have concomitant malignancy and abnormal oestrogen status. We report a case of coexistent uterine lipoleiomyoma, leiomyoma, endometrial polyp and clear cell carcinoma of the endometrium.
Methods: A 66-year old woman, was admitted in our hospital for surgical treatment. She was diagnosed with an endometrial polyp with focal complex atypical endometrial hyperplasia in D&C. She underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy.
Results: Macroscopic examination revealed a 2.5cm well-circumscribed soft mass, with a yellow cut surface, on the anterior surface of the fundus and one small intramural leiomyoma of 0.5cm. In the endometrial cavity there was a 2cm endometrial polyp, with an early clear cell carcinoma. Microscopically, the intramural tumour proved to be a lipoleiomyoma.

Conclusion: Lipoleiomyomas are found incidentally during surgery for other reasons. They are associated with hyperoestrogenic-related conditions. Our findings are in concordance with the ones referred in the literature, of concomitant gynaecologic malignancy. In conclusion the presence of adipocytes in an otherwise normal leiomyoma should lead to further detailed clinical and pathological evaluation in order not to overlook a coexistent gynaecologic malignancy. Although lipoleiomyomas have a favourable prognosis, the pathogenesis and clinical significance of these rare neoplasms remain to be clarified.

E-PS-11-070

Recurrent struma ovarii with incidental peritoneal inclusion cysts. A potential pitfall

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Background & objectives: Peritoneal inclusion cysts (PICs) is the formation of multicystic abdominal masses. They are associated with previous abdominal surgery. Struma ovarii can be accompanied by ascites and raised CA-125. We present a case of recurrent struma ovarii, associated with incidental PICs.
Methods: A 22 year-old woman was admitted to our hospital with ascites. She was diagnosed with a right ovarian mass and raised CA-125 (2761.3 U/ml). Her surgical history included a prior laparoscopic cystectomy, for struma ovarii, with preservation of the right ovary. The association of pelvic mass, ascites and elevated CA-125, was highly suspicious of malignancy. The woman underwent right salpingo-oophorectomy.
Results: The ovarian mass was a pure struma ovarii. Pathological examination of the cystic structures was consistent with IPCs.
Conclusion: IPCs are rare cystic structures that arise from the abdominal peritoneum and can mimic gynaecologic malignancies. Past histological diagnosis should always be reviewed. CA-125 can be elevated in both benign and malignant ovarian tumours, including struma ovarii. The coexistence of a second pathology, not diagnosed preoperatively, like IPCs should be borne in mind in cases of ascites after previous surgery.

E-PS-11-071

Microglandular hyperplasia-like mucinous adenocarcinoma of the endometrium. A very rare entity and a challenging diagnosis in curettage specimen

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Background & objectives: Microglandular hyperplasia (MGH) is a proliferation of endocervical glands, related to oestrogen stimulation, mainly occurring in the reproductive age group. The differential diagnosis includes endometrial adenocarcinoma with MGH-like pattern (MGA), a distinction that may be particularly problematic in curettage specimen.
Methods: A 57-year old, postmenopausal woman was admitted in our hospital for surgical treatment. She had been diagnosed with a uterine leiomyoma, after complaints of irregular vaginal bleeding. She underwent D&C and subsequent total abdominal hysterectomy with bilateral salpingo-oophorectomy.
Results: D&C were compatible with MGA. Histologically, a proliferation of small glands, without intervening stroma, with mucin production, accumulation of neutrophils in the gland lumen and stroma, mild nuclear atypia and rare mitoses, were seen. In the hysterectomy specimen, the endometrium was thickened, but without apparent tumour formation. On microscopic examination, a residual similar adenocarcinoma was seen in the isthmus and more conventional-of endometrioid type, in the rest of the endometrium.
Conclusion: MGH-like proliferation with mild cytologic atypia, detected in the endometrial curettage specimen of a postmenopausal woman, should alert pathologists for MGA of the endometrium. VIM, p16, ER, PR, CD10 and CD34 may help in the differential diagnosis.

E-PS-11-072

Squamous cell carcinoma of the uterine cervix associated with osteoclast-like giant cells: a case report

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Background & objectives: Cervical carcinoma is the most common malignancy of the female genital tract. Osteoclastic giant cells (OGCs) have been reported mainly in pancreatic and breast carcinomas. OGCs squamous cell carcinoma in uterine cervix is an unusual histological variant.
Methods: We present a case of a 79-year-old woman with a 4-month history of irregular vaginal bleeding. Colposcopy was performed and a cauliflower-like mass was identified at the front lip of the uterine cervix. Biopsy was performed.
Results: Microscopically the tumour was composed of infiltrative nests of poorly differentiated nonkeratinizing squamous cell carcinoma. Interspersed in between these tumour cells were numerous osteoclastic giant cells with abundant eosinophilic cytoplasm with devoid of nuclear atypia. Immunohistochemistry was performed using P63, cytokeratin (pankeratin-CK), Vimentin, CD68, CD20, and CD3. CK and P63 were strongly positive in the squamous component and negative in the OGCs, while Vimentin and CD-68 were strongly positive in the giant cell population and negative in the squamous component. Expression of CD20 and CD3 showed a reactive pattern of the lymphocytic areas.
Conclusion: The presence of OGCs in squamous cell carcinoma of the uterine cervix appears to be an indicator of poor prognosis. However, the type of primary tumour appears to be the main determinant of prognosis. Considering the age of the our patient, radiotherapy was administered. The patient succumbed due to brain metastasis of the tumour after eight months of follow-up.

E-PS-11-073

Angioleiomyoma of broad ligament of uterus: a case report

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Background & objectives: Uterine angioleiomyoma is an extremely rare neoplasm, which occurs in middle-aged women who commonly present with menorrhagia, abdominal pain, or abdominal mass. The lesions are either single or multiple and manifest as submucosal, intramural, or subserosal whorled nodules.
Methods: A 47- year- old woman presented to the Gynaecology outpatient department of our hospital with complaints of vaginal bleeding. The patient underwent total hysterectomy and bilateral salpingo-oophorectomy. Grossly, two circumscribed solid tumours measuring 2 and 5cm were found at the broad ligament of the uterus which showed worlly appearance after sectioning.
Results: The microscopic examination revealed circumscribed fascicles of spindled well-differentiated smooth muscle cells, with interspersed thick walled blood vessels. No hypercellularity, pleomorphism, mitotic figures, or necrosis was identified. Immunohistochemical study showed strong positivity to SMA, Desmin, PR, weak staining and focally positivity to CD10, negativity to HMB-45. The Ki67 labelling index was low (<1%).

Conclusion: Uterine angioleiomyoma is a rare variant of uterine leiomyomas. Preoperative diagnosis is extremely difficult because of the fact that there are no specific imaging findings . The treatment of choice is surgical excision and the differential diagnosis includes endometrial stromal nodule, angiomyofibroblastoma and perivascular epithelioid cell tumour. Also, it is important to recognize this entity and differentiate it from a malignancy.

E-PS-11-074

Primary strumal carcinoid of the ovary presenting with severe constipation

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Background & objectives: Strumal carcinoid of the ovary is an uncommon form of ovarian teratoma composed of a mixture of thyroid tissue and carcinoid. They account for approximately 0.5-1.7% of all carcinoids which are less than 0.1% of all ovarian malignancies.
Methods: We report a case of a 62 year old female patient who presented with progressive abdominal pain, distention and severe constipation over 5 years. CT scan showed a large left ovarian cystic mass suggestive of a cystic teratoma. On explorative laparotomy, there was little ascites and a total hysterectomy with bilateral salpingo-ophorectomy was done. The specimen was sent for histopathology analysis
Results: Grossly, the ovarian mass measured 34x10x5 cm and weighed 634g. It was soft, nodulated and encapsulated. On cut section, it had solid and cystic areas containing yellowish greasy material. On microscopy, H&E stained sections showed a neoplasm exhibiting features of both struma ovarii and carcinoid tumour characterized by solid areas of nests, trabeculae, cords, ribbon and cribriform patterns of carcinoid cells. Synaptophysin was diffusely positive in the carcinoid cells.
Conclusion: Strumal carcinoid of the ovary is a rare entity and these cases have only rarely been reported, although there may be many unreported cases.

E-PS-11-075

Stemness in high grade serous carcinoma of tubo-ovarian origin: a challenging immunohistochemical pitfall

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Background & objectives: Architecturally and/or cytologically diverse areas in high grade serous carcinoma of tubo-ovarian origin can cause diagnostic confusion. This case illustrates that clear cells and stemness in HGSC can cause multiple immunohistochemical pitfalls, thereby mimicking a dysgerminoma component.
Methods: A unilateral ovarian neoplasm of a 77-years-old lady was referred to an academic laboratory for further investigation. The reason for the referral included the presence of clear cell areas associated with a bizarre immunohistochemical staining pattern, evoking the diagnosis of a dysgerminoma. Additional immunohistochemical stainings and targeted next-generation sequencing were performed to establish the final diagnosis.
Results: A unilateral ovarian mass with prominent atypia, numerous mitoses and necrosis showed clear cells with associated CD117 and PLAP expression, and focal immunoreactivity for glypican-3 and podoplanin. The tumour showed diffuse expression of EMA, CK-AE1/AE3, PAX8 and WT1, without immunoreactivity for OCT4 and SALL4. The tumour showed a mutation-type p53 staining pattern and harboured a pathogenic TP53 missense mutation. This profile corresponded with a HGSC, and not with a dysgerminoma.
Conclusion: HGSC of tubo-ovarian origin is a malignant neoplasm with heterogeneous morphology, comprising various architectural patterns and diverse cytological aspects, which often coexist within a single tumour. Clear cell areas may mimic other tumour types, thereby causing diagnostic confusion. The expression of CD117, PLAP, glypican-3 and podoplanin in HGSC might indicate stemness, i.e. the tumour acquires pluripotency, probably indicating a more aggressive behaviour. Future studies should investigate whether stemness in HGSC identifies a patient subgroup with poor prognosis.
Funding: M.R. Van Bockstal received a grant (2019-089) from the Foundation Against Cancer (Brussels, Belgium).

E-PS-11-076

Vulvar Paget's disease – a case report

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Background & objectives: Paget's disease of the vulva is a rare tumour with the incidence below 2%, often combined with other malignancies.
Methods: Patient, age 77, complained of prolonged itching and redness of the vulvar skin. Due to resistance to applied therapy, lesion was biopsied, and a microinvasive Paget's disease was diagnosed. Complete excision was performed, and tissue was histologically processed using hematoxilin&eosin and immunohistochemistry (CK20, CK7, CEA, p16, survivin, S100, HMB45, Melan A).
Results: Tumour cells were larger than basal and parabasal skin cells, with large nucleuses and vacuolated cytoplasm due to intracellular mucus. Tumour cells were located in the parabasal area of the skin, but in few focuses they invaded under the basement membrane (maximal depth of 1mm), as single cells or small clusters. Tumour cells were positive to CK20, CEA, p16 and survivin, and negative to CK7, HMB45, S100 and Melan A.
Conclusion: Immunohistochemical analyses are valuable in diagnostic process for such a rare tumour like primary vulvar microinvasive Paget's disease. It is of great importance not only for proper diagnosis, but also for defining the primary site and prognosis. Thorough clinical examinations led to a diagnosis of colonic villous adenoma with high grade dysplasia. After 4 years, patient had relapsed, when immunoprofile of tumour cells was CK20 negative, CK7 positive. At that time, patient was diagnosed with nonmetastatic lobular breast carcinoma.

E-PS-12 Haematopathology

E-PS-12-002

Neurotropic mycosis fungoides causing a cryptic painful neuropathy

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Background & objectives: Neurolymphomatosis (NL) is a rare clinical entity of nerve infiltration by neurotropic cells in a known or occult hematologic malignancy. Peripheral nerve infiltration in T-cell malignancies is vanishingly rare. The diagnosis can be elusive in symptomatic patients without known lymphoma.
Methods: Neuropathic pain prompted a sural nerve biopsy. Transcompartmental infiltration of nerve fascicles by highly atypical lymphoid cells, with irregular convoluted nuclear contours. Immunohistochemistry denoted these to be CD4 expressing T-cells, clonal on T- cell receptor rearrangement PCR study. Skin biopsy from the putative eczematous lesions revealed interface centric, CD4 positive T-cell infiltrate. A diagnosis of Neurotropic Mycosis Fungoides was rendered.

Results: A histologic diagnosis of Neurotropic Mycosis Fungoides was rendered.
Conclusion: This singular case of a patient under dermatologic treatment for unclassified, eczematous like dermatosis of the back and left flank, intercurrently developing intense burning pain in bilateral posterior calves - illustrates that rarely mycosis fungoides, may demonstrate neurotropism, and neuropathic pain can be an obscure harbinger of a rare and pernicious proclivity of this lymphoma..

E-PS-12-003
Solitary extra nodal oesophageal recurrence of nodal Hodgkin lymphoma a decade after treatment
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Background & objectives: Oesophageal involvement by lymphoma is distinctly rare , representing only about 1% of the cases of lymphomatous involvement of the gastrointestinal tract - and Hodgkin lymphoma with primary oesophageal recurrence is unheard of.
Methods: Dysphagic patient underwent endoscopic oesophageal biopsy, with histopathology and comprehensive immunohistochemistry.
Results: Histomorphology and immunohistochemistry confirmed classical, mixed cellularity Hodgkin lymphoma, in the oesophageal biopsy, with no other local or systemic nodal or splanchnic disease on imaging.
Conclusion: This report of oesophagus as the solitary site of extra nodal recurrence of Hodgkin lymphoma, after a decade - is the first one in peer reviewed English literature. We describe this singular manifestation of recurrent Hodgkin's lymphoma, without concomitant nodal disease - diagnosed on an endoscopic mucosal biopsy.

E-PS-12-004
Augmented paradigm of gastric round cell neoplasms – primary ALK positive gastric anaplastic large cell lymphoma
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Background & objectives: The stomach is a common site of extra nodal lymphomas in adults, most of which are of B-cell origin. ALK and CD 30 expressing, primary gastric lymphomas are seldom reported.
Methods: We record here, one such case, in an elderly female, presenting with haemoptysis. The gastro-endoscopic examination showed mucosal irregularity and shallow ulceration of the antrum.
Results: Histology of the endoscopic biopsy was that of a quintessential round cell neoplasm, which was leucocyte common antigen and cytokeratin negative. Subsequent comprehensive, staggered immunohistochemistry was the cornerstone of analysis, funnelling into the final diagnosis of ALK + / CD 30 + anaplastic large-cell lymphoma. Radioimaging did not reveal any nodal disease or any other site of involvement.
Conclusion: This case illustrates the significance of having a judiciously divergent pathologic diagnostic differential, when faced with indifferent morphology, and immunohistochemistry results which is initially equivocal and noncommital.

E-PS-12-005
Proteomic and genetic aspects in a rare case of primary testicular lymphoma
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Background & objectives: Testicular lymphoma represents a distinct, rare and clinically aggressive form, usually being diagnosed in elderly patients. The aim of this study is to present the immunohistochemical and genetic assessment of the testicular tumour to establish the primary character.
Methods: We report a case of a young male patient with left orchiectomy. Further to the histopathological examination, immunohistochemical testing was mandatory by using the monoclonal antibodies (CD45, CD10, CD20, Bcl-2, Bcl-6, EBV and Ki67). Complementary, the FISH molecular cytogenetic technique was used to confirm the subtype of lymphoma.
Results: The expression profile of immunohistochemical markers (positive for CD45, CD10, CD20, and Bcl-6; the lack of both Bcl-2 and EBV expression) established the diagnosis of Burkitt-like diffuse large B-cell testicular lymphoma, with a high nuclear proliferation marker (Ki67 more than 95%).
Conclusion: The proteomic analysis of the presented case has confirmed the diagnosis and sets the guidelines for the therapeutic management, main characteristics being in this case both the age and tumour aggressiveness potential.

E-PS-12-006
Localised kappa restricted Russell body accumulation within germinal centres in lymph node without gammopathy or haematopoietic malignancy: a case report
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Background & objectives: Light chain restriction is very rare in benign or reactive processes. Until today a few case has been reported, most frequently in the GI tract of adults and rarely in paediatric age, without overt gammopathy or hematopoietic malignancy.
Methods: Our case, 33-year-old woman, admitted to hospital because of enlarged cervical lymph node. On systemic examination, there were no pathology with plasma cell. Serum immunoglobulin levels were normal. 2,5 cm diameter lymph node was resected doubt of lymphoma.
Results: Histologically, beside of common secondary follicles, limited accumulation of plasma cells and Russell bodies in the only two germinal centre was observed. They were positively stained with kappa, IgM, CD138, and MUM1 and negatively lambda, IgD, IgG, IgA. Russel bodies were positive for PAS in bright pink colour, negative for Congo red and crystal violet. Because systemic disease was not detected, we reported reactive kappa restricted plasmacytosis with Russell bodies
Conclusion: The real incidence and importance of Russell body accumulation within the germinal centre in lymph node is unknown because of rarity. So, presence of aggregates of plasma cells with Russell bodies demonstrating kappa or lambda light chain clonality should not be mistakenly interpreted as a tumour, especially with the absence of additional histopathological and clinical features.

E-PS-12-007
Kikuchi-Fujimoto disease: case report of two teenagers in Brazil
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Background & objectives: Kikuchi-Fujimoto's disease is characterized by lymphadenopathy, fever and typical histological features. Japan described it in 1972.The disease has been found worldwide, predominantly in Asia, but remains rare in the United States and Europe. We report two cases of Kikuchi-Fujimoto's disease.
Methods: The morphologic characteristics associated with immunohistochemical study were evaluated according to scientific literature.
Results: The 14-year-old male patient presented subclavicular mass, fever, joint pain, prostration and weight loss with the diagnostic hypothesis of tuberculosis. The 18-year-old female patient presented painful cervical

lymphadenomegaly, a history of contact with pigeons and cats and the diagnostic hypothesis of toxoplasmosis or lymphoma. Both had histopathological characteristics compatible with the diagnosis of Kikuchi-Fujimoto's disease, research for alcohol-resistant bacillus and negative fungi and benign evolution after diagnosis. The histopathological findings included nodal architecture distorted by areas of coagulative necrosis, with abundant carioretic debris, surrounded by histiocytes, T lymphocytes and plasmacytoid monocytes, in addition to the absence of neutrophils and eosinophils.
Conclusion: Differential diagnosis with lymphoma, inflammatory, autoimmune and infectious conditions is important when facing lymph nodes with these findings. Therefore, the pathologist's knowledge of this rare disease in the Western sites is important when correlating clinical and anatomopathological data for diagnosis.

E-PS-12-008
Rare presentation of Castleman disease – association of unusual angiolipomatous features in two cases
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Background & objectives: Castleman disease (CD) or angiofollicular lymph node hyperplasia is a rare benign lymphoproliferative disorder. Association of angio-lipomatous hyperplasia has only been reported in a few single cases, and may add complexity to the diagnosis of CD.
Methods: We present CD occurring in two male patients, aged 36 and 65. The first presented only with leukocytosis. A CT scan revealed a retroperitoneal mass at T12-L1 level.
The second patient presented with cough. A CT scan revealed an anterior mediastinal mass and multiple mediastinal adenopathies.
Tissue blocks were formalin-fixed paraffin-embedded. For the first patient immunohistochemistry was performed.
Results: The masses had a biphasic appearance: the centre was represented by a firm tan-grey tissue, while the periphery resembled adipose tissue. Microscopically, the tan-grey and reddish areas represented typical CD of hyaline-vascular type, presenting lymphoid follicles with atrophic germinal centres, occasionally penetrating vessels, a hyperplasic mantle zone and vascular proliferation of the interfollicular areas. The surrounding adipose tissue presented prominent blood vessels dispersed among mature fat cells and areas of fibrosis. The two components were distinct for the most part with areas of intermingling.
CDK4 and MDM2 stains were negative for the first patient.
Conclusion: The occurrence of typical CD within an angiolipomatous lesion has rarely been reported.
In this setting, Castleman disease is difficult to diagnose, especially on needle biopsy, where the adipose tissue may be mistaken for atypical lipoma or well differentiated liposarcoma.

E-PS-12-009
Pitfalls and perils of immunohistochemistry diagnostics in haematopathology practice
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Background & objectives: Lymphoma is often a diagnostic challenge. At diagnosis a balance between tissue availability and the size of the initial immunohistochemistry panel can be problematic, especially if the diagnosis is unexpected. In this context immunohistochemistry stains can be misleading.
Methods: We present three case studies encountered within the Oxford Haematopathology Service, illustrating pitfalls with interpreting immunohistochemistry stains in the setting of lymphoma diagnosis. The cases are supported by a literature review, on the role of immunohistochemistry in lymphoma diagnosis and known, along with the lesser known, lymphoma markers (Oct 3/4, Gata-3, Pax-8, CD79a, cyclin D-1, CD 45 and CD 99).
Results: There are numerous new monoclonal antibodies in use for immunohistochemistry diagnoses. They are particularly useful for tumour lineage distinction. But there are issues of sensitivity and aberrant expression in differential diagnosis e.g. cancer of unknown primary and as highlighted by three case studies, primary lymphoma. It is important for pathologists, especially sub specialists to keep up to date with specific antibody patterns to be able to appropriately interpret them.
Conclusion: Sensitivity of immunohistochemistry stains means they cannot be relayed on solely for diagnosis, morphology and clinical context still remain vital in the diagnostic process.

E-PS-12-011
Case report: small lymphocytic lymphoma/chronic lymphocytic leukaemia (SLL/CLL) coexisting with Langerhans cell histiocytosis
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Background & objectives: A 81 year-old male patient was admitted to our hospital due to allergic reaction with clinical history of probable spondylodiskitis. Fine needle biopsy (FNB) of lumbar spine showed no pathological findings.
Methods: Blood tests showed prominent eosinophilia, considered as a side effect of the antibiotic treatment. The antibiotics were changed, however eosinophilia remained. Further imaging studies revealed a cavity in the lung, inaccessible for FNB, and inguinal lymphadenopathy. Multiple testings for tuberculosis (quantiferon and bronchoscopy) were negative.
Results: Biopsy of bone marrow showed 8-9% infiltration by SLL/CLL (positive for CD20, PanB, CD79a, CD-23, bcl-2, weakly positive for CD5 and negative for Cyclin-D1, bcl-6 and CD30). Because of the persisting eosinophilia, a month later we received an inguinal lymph node, with partially disrupted architecture, diffuse infiltration of lymphoid cells, similar to those in the bone marrow, and aggregates of histiocytic cells with elongated nuclei, prominent nuclear grooves and folds and strongly positive for S-100 and CD-1a. The diagnosis of coexistent SLL/CLL with histiocytosis X was concluded.
Conclusion: Langerhans cell histiocytosis is usually presented in older children or young adults and is often coexistent with leukaemia. The age of the patient and the synchronous presentation of histiocytosis X and low grade lymphoma render our case extremely rare.

E-PS-12-012
Granulomatous dermatitis associated with chronic mielomonocytic leukaemia: a challenging diagnosis
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Background & objectives: Neutrophilic granulomatous dermatitis has been recently described in association with systemic processes, including hematologic disorders such as Chronic Mielomonocytic Leukaemia (CMML).
Methods: We present the case of a 58 y/o male with disseminated erythematous papules on the extremities and trunk, appearing over several months period. A skin biopsy (SB) was performed showing a non-necrotizing granulomatous dermatitis. A peripheral blood test showed a monocytosis of 23.3% and a bone marrow (BM) aspirate demonstrated slight hypercellularity with trilineage dysplasia and mild monocytic infiltration.

Results: By flow cytometry, monocytes represented 11% of the total white blood cell count, with expression of CD64, CD13 and CD14. Although a CMML was suspected, according to the WHO 2017 diagnostic criteria, follow up was necessary. Two more SB showed epithelioid histiocytes intensely positive for CD68, CD11c, CD15, MNDA and CD123, partially for CD1a and CD56 and negative for S100, MPO, CD34 and CD117. NGS in BM identified SRSF2 and IDH2 point mutations. Finally, a mutational analysis by pyrosequencing technique from a SB resulted with the same IDH2 base change as the one in the BM. Then, the patient was diagnosed with a MDS/MPN CMML type with secondary granulomatous dermatitis.
Conclusion: Cutaneous manifestation might be the first symptom of the CMML and it is mandatory to maintain a high index of suspicion. The presence of molecular alterations in bone marrow and skin may help to reach an early diagnosis.

E-PS-12-013
An unusual presentation of plasmablastic lymphoma: case report and literature review

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Background & objectives: Plasmablastic lymphoma (PBL) is a rare and aggressive lymphoma typically located in the oral cavity of HIV-positive patients. We present a rare clinical case of bladder PBL and a review of the literature on PBL over the last 5 years.
Methods: A 58-year-old HIV positive male, diagnosed in early 2019, presented to our hospital with haematuria, abdominal bloating and weight loss. Physical examination was normal. CT-scan showed a bladder polypoid and infiltrating lesion and a transurethral resection was performed.
Results: A histologic diagnosis of PBL was made, showing the classical morphology of this neoplasia. Immunostains revealed positivity for CD138, CD38 and MUM1, negativity for CD20 and HHV8 and a Ki-67 of 100%. In situ hybridization test for EBV was positive.
PBL most frequently presents in extranodal locations, in particular the oral cavity (44%), followed by the gastrointestinal tract (14%). Nodal involvement is found in < 10% of the cases. In the genitourinary system there are less than 30 cases reported (4%) none of them in the bladder (presentation).
Conclusion: PBL is seldomly reported in the genitourinary tract. Pathologists should be familiar with this diagnosis, even in highly unlikely locations such as the bladder, especially in the context of immunodepressed patients with rapidly proliferating tumours.

E-PS-12-014
Evaluation of naked eye single tube red cell osmotic fragility test in screening and diagnosis of beta thalassaemia trait carriers in a resource challenged country

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Background & objectives: Beta thalassemia major is a severe disease and places a huge economic burden on the health care setup especially in developing countries like Pakistan. Different screening techniques are available for detection of Thalassemia but most are expensive. Pakistan is a resource-poor country and every diagnostic laboratory is not well equipped to screen this disease. Naked Eye Single Tube Red Cell Osmotic Fragility Test (NESTROFT) is a reliable & cost effective screening method. Our study sought to evaluate the efficacy of NESTROFT as a screening tool for detection of beta thalassemia trait in Pakistani population.
Methods: All participants requesting a complete blood count were enrolled in the study. After obtaining informed consent, NESTROFT was performed using freshly prepared 0.36% buffered saline. Turbidity in the tubes indicated that the individual was positive for beta thalassemia trait. Haemoglobin electrophoresis was performed on all NESTROFT positive cases to confirm the sensitivity of the screening test NESTROFT.
Results: A total of 812 patients were enrolled in the study between January 1, 2017 and June 30, 2017. The mean age + SD of participants was 35.5 + 13.6 years. There were 351 (43.2%) male and 461 (56.7%) female participants. In the present study, NESTROFT was reported to be 100% sensitive claiming superiority over other evaluated parameters individually, besides being technically simple and cost-effective.
Conclusion: The present study revealed that NESTROFT is a highly sensitive, cost-effective, and a rapid screening test for the detection of carriers of beta thalassemia trait in our population.

E-PS-12-015
Gamma heavy chain disease associated with an Epstein-Barr virus (EBV) positive lymphoproliferation: a case report and review of the literature

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Background & objectives: Gamma heavy chain disease (γ-HCD) is rare, usually characterised by a neoplastic proliferation of small B cells demonstrating plasmacytic differentiation with heterogeneous clinical and histological features. We present a diagnostically challenging and very unusual case of EBV positive γ-HCD.
Methods: A right cervical lymph node biopsy from a 78-year-old lady with generalised lymphadenopathy was submitted to histopathology. Routine haematoxylin-eosin sections and a broad panel of immunohistochemistry were performed. In view of the histological findings serum protein electrophoresis and immunofixation was requested. Review of the clinical record did not identify features of auto-immunity or a cause for immunocompromise other than age.
Results: Histology showed diffuse effacement of node architecture by a malignant infiltrate of medium to large cells, many with evidence of plasmablastic differentiation. The tumour cell population was positive for CD79a, with very few scattered CD20 positive cells but a significant number of CD138 positive cells. The neoplastic cells were negative for CD5 , CD10, CD56, cyclin D1 and EMA. The tumour was positive for EBV and had a very high proliferation fraction. Serum electrophoresis revealed a broad monoclonal IgG band without associated light chains. The findings indicated a diagnosis of γ-HCD, either presenting with an EBV positive monomorphic morphology or as an EBV positive lymphoma with plasmablastic differentiation.
Conclusion: EBV positive lymphoproliferations with high grade plasmablastic features have not been described in association with γ-HCD. Previous reports suggest that EBV positive lymphoproliferations may occur in a distinct subset of patients with γ-HCD who are immunocompromised and warrants further investigation.

E-PS-12-018
A very rare case of type V inflammatory pseudo-tumour IGG4-related lymphadenopathy (IGG4-LAD)

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Background & objectives: IgG4-LAD can be the expression of IgG4-related disease. Unlike other organs, storiform fibrosis and obliterative phlebitis are not peculiar; 5 subtypes are described: multicentric Castleman's disease-like, reactive follicular hyperplasia-like, interfollicular expansion and immunoblastosis, progressively transformed germinal centre-type and inflammatory-pseudotumor-like IgG4.

Methods: We report the case of a 75 yrs old man with a painless and mobile 3 cm inguinal subcutaneous nodule, present for 2 years. Histologically it was entirely occupied by hyalinized fibrous tissue, with very few lymphocytes at the periphery and scattered plasmacells with an IgG4/IgG ratio of 1:1. ALK, S-100, CD34, Actin, EBV, Treponema and HHV-8 stains were negative.
Results: Our revised diagnosis was of a type V inflammatory pseudo-tumour IgG4-Related Lymphadenopathy, This is the least common type of IgG4 LAD, with only two cases reported in literature to our knowledge. The patient turned out to have elevated serum IgG4 level (1940 g/L) and monoclonal gammopathy IgMK. A systemic IgG4-related disease could also be suspected: the year before he was hospitalized for an acute hepatitis of unknown origin and many years before he was subjected to Wirsung-jejunostomy and cholecystectomy for chronic calcific unspecified pancreatitis with pseudocysts of the pancreatic head and chronic cholecystitis. A more correct clinical framework could now save costs and improve patient's quality of life.
Conclusion: Type V IgG4-LAD can mimic several benign and malignant lesions, in primis nodal inflammatory myofibroblastic tumour and other mesenchymal tumours such as schwannomas and solitary fibrous tumour. Because of its rarity, the natural course and prognosis are uncertain. An improper diagnosis can preclude the detection of a IgG4-related disease, leading to fibrous progression, mechanical obstruction or organ dysfunction and to delay in prompt treatment with glucocorticoid, immunosuppressive agents or other.

E-PS-12-019

A case study of prolonged febrile illness, diagnosed with a rare form of non-Hodgkin lymphoma, angioimmunoblastic T-cell lymphoma (AITL), after CT-PET scan and lymph node biopsy

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Background & objectives: A 64-year-old Caucasian male with a history of prostate cancer 8 years ago, presented with reported fever >38 oC and night sweats, which had started one month ago. Splenomegaly and palpable lymph nodes were not found.
Methods: During the hospitalization, the patient continued to have episodes of fever. Anaemia (hypochromic, microcellular) and a three-digit erythrocyte sedimentation rate were found.Laboratory tests for infectious,viral and autoimmune diseases,abdominal Ultrasound, thoracic and abdominal Computed tomography(CT), bone scan, endoscopic examination of the upper and lower gastrointestinal tract, biopsies of the temporal artery, liver and bone marrow were performed without abnormal findings.
Results: Finally, Positron Emission Tomography-Computed Tomography(PET-CT) scan was performed, which showed mild hypermetabolism in the axillary lymph nodes. Subsequently, based on the above finding, we proceeded to axillary lymph node biopsy, which revealed a Non-Hodgkin AITL. The patient received chemotherapy(cyclophosphamide, vincristine and mitoxantrone) and lymphoma was sent into remission. After 42 months, a relapse of the disease occurred and the patient died due to septic shock, as a result of an infection in the respiratory tract.
Conclusion: We point out the contribution of PET-CT scan to the diagnosis of prolonged febrile of unknown origin. This case is of particular interest, because of the rarity of the disease (accounting for only 2-4% of all lymphomas) and its atypical manifestation(non-palpable lymph nodes, without splenomegaly and without rash). We also underline the patient's survival beyond 19 months, which is the average life expectancy for this type of lymphoma.

E-PS-12-020

Follicular dendritic cell sarcoma with abundant lgG4-positive plasma cells arising in a lymph node near salivary gland mimicking lgG4-related lymphadenopathy

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Background & objectives: Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm arising in lymph nodes. Increased IgG4-positive plasma cells mimicking IgG4-related disease is reported in inflammatory pseudotumour (IPT)-like FDCS, a variant associated with Epstein-Barr virus (EBV), but not in a conventional FDCS.
Methods: The patient is a 73 year-old male with a one-week history of soft and non-tender mass in the left cervical region. Fine needle aspiration cytology and core needle biopsy were suggestive of sarcoidosis and lymphadenitis respectively, so the patient was followed-up. However, as the mass kept enlarging slowly, the mass was excised one year later.
Results: Macroscopically, the mass was 70-mm in size, well-circumscribed, and displayed yellow-white cut surface with focal haemorrhage. Histologically, neoplastic cells had round to ovoid vesicular nuclei with small conspicuous nucleoli aggregating in several foci and forming a multinodular mass. Lymphoplasmacytic infiltration was noted within the nodules but it was prominent especially between the nodules. In immunohistochemistry, neoplastic cells were positive for several follicular dendritic cell (FDC) markers such as CD21 and podoplanin. EBV was not detected in both neoplastic cells and lymphocytes by chromogenic in situ hybridization. The mass was diagnosed with FDCS. Despite the increase of IgG4-positive plasma cells, postoperative study showed no evidence of IgG4-related disease.
Conclusion: We report a case of FDCS with abundant IgG4-positive plasma cells involving a lymph node near salivary gland. Raising a suspicion for FDCS and applying several FDC markers are necessary even if the morphology fulfils the criteria for IgG4-related disease.

E-PS-12-021

Unusual presentation of a follicular lymphoma as two distinct tumours located in the mediastinum and retroperitoneum

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Background & objectives: Follicular lymphoma is typically a slow-growing or indolent form of non- Hodgkin B-cell lymphoma. It is characterized by diffuse lymphadenopathy, bone marrow involvement, splenomegaly and less commonly other extranodal sites of involvement.
Methods: We present the case of a 65-years-old female patient showing reduced appetite and weight loss (10kg in 6 months).
Abdominal CT-scan showed an extended retroperitoneal mass with bilateral paravertebral involvement and extension in the posterior mediastinum, enclosing the large vessel, extending into the mesentery, the head of the pancreas, the left adrenal gland and the left ureter with secondary hydronephrosis.
Results: The thoracic CT-scan showed a 10 cm tumour in the anterosuperior left mediastinum, closely related to the big vessels. A mediastinoscopy was performed and biopsies were taken.
The tumour biopsies showed a lymphoproliferation with big, uniform, closely packed follicles containing small cleaved cells without nucleoli (centrocytes) and few (<15/HPF) larger noncleaved cells with open chromatin and multiple nucleoli (centroblasts). The mantle zone was markedly attenuated and the germinal centres lacked tangible bodies.
On immunohistochemistry the tumour is CD20(+), Bcl2(+), Bcl6(+) and CD5(-) showing the centrofollicular origin of the B cell proliferation. Ki-67 index is low (10-15%). Final diagnosis was Follicular type non-Hodgkin lymphoma, Grade 1-2.

Conclusion: This is an exceedingly rare way of presentation of a follicular lymphoma as two separate lesions and this case highlights the need for the differential diagnosis and shows the importance of multidisciplinary communication.

E-PS-12-022

Involvement of cervix uteri by non-Hodgkin lymphoma: a case report

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Background & objectives: Involvement of female genital tract with lymphoma is a rare phenomenon. It can be seen in female genital tract during advanced stage of systemic disease.
Methods: 50-year-old female patient applied to the hospital with complaints of vaginal bleeding and abdominal swelling for a month. She underwent excisional biopsy with a suspicion of cervical carcinoma. Histopathologically, discohesive malignant cells with large, vesicular nucleus and one prominent nucleoli were present in solid pattern.
Results: Immunohistochemically, epithelial, mesenchymal and melanocytic markers were negative. The immunoprofile of the tumour showed positive staining for CD45, CD20 and Bcl-6, negative staining for CD10 and MUM1. These morphological findings and immunohistochemistry results supported a diagnosis of diffuse large B-cell lymphoma of germinal centre origin. Accompanied by these findings, PET-CT imaging identified multiple extensive lymph nodes throughout the body and intense hypermetabolic lesions in the colon, rectum, bladder and vagina.
Conclusion: Hematopoietic malignancies involving the cervix are commonly suspected to be epithelial neoplasms. Secondary cervical involvement of lymphoma, should be kept in mind for patients with systemic lymphoma.

E-PS-12-023

IgG4 related ophthalmic disease

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Background & objectives: IgG4-related diseases are immune-mediated, fibroinflammatory conditions that are characterised by affected organ enlargement, plasma cell infiltration (determined with IgG4-positive plasma cells) and serum IgG4 level elevation.
Methods: A 53 year-old man presented with right eye proptosis. He had painless swellings for both eyes for 20 years, and proptosis of right eye for 12 years. We received right orbital mass which had a feature of lenfoid tissue. A hyalinized-collagen ground is observed in nodulated focal areas starting from the capsule to make towards the centre of the lymph node.
Results: There are numerous reactive follicules with distinct germinal centres. A large number of plasma cells, histiocytes and sparse eosinophils with lymphocytes was observed. Because of the presence of collagen bands and mixed cellular population on the ground, we considered Hodgkin's Lymphoma as differential diagnosis, however there were no typical Reed-Steinberg cells or variant. Orbital mass showed local infiltration around neural tissue. There were large number of plasma cells in the ground and the lesion was accompanied by significant fibrosis. IgG4/IgG immunohistochemical staining showed a significant increase in favour of IgG4. The patient diagnosed as IgG4-related ophthalmic disease(IgG4-ROD).
Conclusion: Ocular adnexial tissues, such as the lacrimal gland, extraocular muscles, trigeminal nerve branches (cranial nerve V) and orbital fat, effected collectively in IgG4-RODs. Although diseases related to IgG4 are rare, ophthalmic localization should be kept in mind.

E-PS-12-024

A case of Erdheim-Chester disease

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Background & objectives: Erdheim-Chester Disease (ECD) is a rare histiocytic neoplasm. BRAF mutations have emerged as potential molecular markers of ECD, but diagnosis hinges on histological identification of infiltrative histiocytic proliferations in the appropriate clinical and radiological context of disseminated mass lesions.
Methods: Retrospective review of histology, immunohistochemistry and molecular results was undertaken, with correlation to ehealth records and radiology. The importance of clinical and radiological context in interpretation of cytology and histology, and the critical role molecular testing played in establishing the diagnosis of ECD are discussed.
Results: We present a 56yo female with clinical and radiological features of malignancy of unknown origin with mediastinal (including pericardial effusion), skeletal, abdominal and retroperitoneal disease. Two diagnostic samples were available: pericardial fluid, containing abundant large CD68-positive histiocytes in an otherwise inflammatory background, and retroperitoneal biopsies, containing a predominantly fibroinflammatory lesion with dispersed large histiocytes, initially interpreted as reactive. Clinical correlation raised the possibility of ECD, and both samples were re-examined revealing occasional atypical histiocytes and a single Touton giant cell within the pericardial fluid, and dispersed, single foamy histiocytes within the biopsy. Mutation testing demonstrated analogous BRAF mutations in both pericardial and retroperitoneal samples, supporting a diagnosis of ECD.
Conclusion: While a fibroinflammatory 'background' is frequently cited within prevailing histological descriptions, in this case our observation is of a predominant fibroinflammatory lesion with only dispersed, mildly atypical histiocytes that lacked the foamy cytoplasm or Touton giant cell forms reported to exemplify ECD. Our case highlights the necessity for appropriate clinical and radiological context, and the potential value of BRAF testing in diagnosis of ECD.

E-PS-12-025

Primary effusion lymphoma involving intrasinusoidal's liver and spleen

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Background & objectives: Primary effusion lymphoma (PEL) is one of the rarest subtypes of large B-cell neoplasm usually presenting as serous effusions in the setting of immunosuppression. It is associated with the human herpesvirus 8 (HHV 8).
Methods: A 52-year-old man HIV-positive with two-month history of fever, asthenia, hiporexia and liquid stools. An infection disease was ruled out. He underwent worsening of symptoms and a PET scan was done showing an hepatomegaly and a splenic pathologic increase in captation suspicious for lymphoproliferative disease. Due to the hepatomegaly a hepatic biopsy was performed while he was waiting for splenectomy.
Results: The hepatic biopsy showed mild changes in lobular space. Atipical cells were present in sinusoids being positive for CD30 and EBER. No additional stains were performed in this sample. The spleen weighed 560 grams. Microscopically, white pulp was preserved while red pulp did show large pleomorphic lymphoid cells, with irregular nuclei and prominent nucleolis and abundant basophilic cytoplasms. By immunohistochemistry, these cells show positivity for CD30, MUM1, HHV8 and EBER, as well as negativity for the rest of the panel performed (CD138, CD45, CD79a, CD20, PAX5, EMA, Bcl2, Bcl6, CD15, CD3, light chains and ALK).
Conclusion: PEL usually involves the pleural, pericardial and peritoneal cavities. Here we describe a unique case of PEL in an HIV-positive patient involving intrasinusoidal's liver and spleen.

E-PS-12-026

Experience and perception of patients, health professionals and health administrators regarding the management of acute leukaemia in Rwanda

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Background & objectives: Recent studies reported a lower incidence of acute myeloid leukaemia (AML) and acute lymphoblastic leukaemia (ALL) in Rwanda, than expected. The aim of this study was to explore barriers to timely diagnosis, therapy and prognosis of acute leukaemia in Rwanda.
Methods: We performed a qualitative study using a phenomenological approach that involved 41 participants including patients, patients' guardians and key-informants, such as physicians from district hospitals and specialists in from referral hospitals, as well as directors from Rwanda Biomedical Center (RBC). In-depth interviews were conducted and thematic analysis was employed to interpret results.
Results: We identified barriers to seeking healthcare such as (i) insufficient knowledge, occasionally making patients and their care-takers to first consult traditional healers and (ii) financial constraints that preclude payment of healthcare fees and transport costs to diagnosis and treatment sites. Barriers to timely diagnosis and therapy include (i) tedious referral system; (ii) primary diagnostic facilities which don't sufficiently capture the results of laboratory tests that would indicate the diagnosis of acute leukaemia. Chemotherapy is the only available for ALL in Rwanda, while palliation is the only available treatment for the vast majority of Rwandan AML patients.
Conclusion: ALL and AML are likely under-reported in Rwanda and diagnosis delayed, as explained by patient-related factors (poor knowledge, financial constraints), tedious referral system and suboptimal diagnostic resources.

E-PS-12-027

Synchronous chronic lymphocytic leukaemia and metastatic squamous cell carcinoma in a cervical lymph node

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Background & objectives: As the population of cancer survivors grows, is becoming more frequent the diagnosis of second primary malignancies (SPMs), specially for primary malignancies where patient outcomes are relatively good, like chronic lymphocytic leukaemia (CLL).
Methods: We report the case of a 76 year-old male, with a previous diagnosis of CLL, currently in remission, presenting with a newly noticed right laterocervical mass. The patient underwent PAAF, whose smear showed atypical keratinized squamous cells, suggesting a metastatic carcinoma as the first diagnostic possibility. The patient underwent parotidectomy and homolateral lymphadenectomy.
Results: The histopathological evaluation revealed multiple metastasis of keratinizing squamous cell carcinoma and a diffuse mature lymphoid infiltrate whose immunophenotype was CD79a, CD20, CD5, CD23, CD43, BCL-2 positive and CD10, BCL6, Cyclin D1 negative (consistent with CLL). A more in-depth evaluation of clinical history revealed a previous preauricular squamous cell carcinoma three years earlier.
There is a significantly high rate of SPMs in patients with CLL. Solid-organ cancers like lung/bronchus carcinoma and melanoma are the more frequent, but skin cancers as SCC are also reported. The aetiologies are not clarified and appear to be multifactorial, including prior chemotherapy, a dysregulated immune system, shared environmental and genetic risk factors.
Conclusion: In conclusion, although the coexistence of metastatic carcinoma and CLL/SLL in a lymph node is a rare event, the possibility of SPM must always be considered. For early detection of SPM, screening procedures like PAAF are useful to improve the outcome of those patients.

E-PS-12-028

Follicular lymphoma with prominent mott cell formation

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Background & objectives: The appearance of abundant Mott cells (hypersecretory, large plasma cells containing many Russell bodies) has been occasionally reported in low-grade B-cell lymphomas, but its association with follicular lymphoma (FL) is very rare.
Methods: Case Report
Results: The patient, a 77-year-old woman developed swelling of abdominal lymph nodes. Excisional biopsy of the lymph nodes demonstrated F, Grade 1-2, associated with a large number of Mott cells predominantly in the inter-follicular zones. The cytoplasm of Mott cells was immunoreactive for IgG and lambda chain but not for kappa chain. Cytogenetic studies demonstrated complex karyotypic abnormalities including trisomy 3, in addition to the characteristic translocation t(14;18)(q32;q21).
Conclusion: In the present case, the unusual and complex chromosomal abnormalities may have produced an accumulation of aberrant, non-degradable immunoglobulin within cisterns of rough-surfaced endoplasmic reticulum, which could have caused the transformation of FL cells into Mott cells.

E-PS-12-029

Mast cell sarcoma in a patient with a previous mediastinal mixed germ cell tumour: a case report

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Background & objectives: Mast cell sarcoma (MCS) is an extraordinarily rare form of mastocytosis characterized by destructive proliferation of mast cells and poor prognosis. Herein, we present a case of MCS in a patient previously diagnosed with a mediastinal germ cell tumour (GCT).
Methods: A 32 year old male with a diagnosis of mediastinal mixed GCT 7 years prior, treated with chemotherapy and subsequent surgery, presented with an expansive lesion on the right iliac bone on a follow-up CT-scan and with multiple other bone lesions suspicious of metastasis on PET scan. A biopsy of the iliac lesion was performed.
Results: Histologically, the bone marrow showed infiltration by eosinophils, plasma cells, lymphocytes and large cells with abundant clear cytoplasm, one or two irregular nuclei and inconspicuous nucleoli. These cells showed immunoreactivity for vimentin, CD117, mast-cell-tryptase and CD30. The diagnosis of MCS was made. The molecular analysis of the seminomatous component of the prior GCT disclosed the variant c.2459A>G p.(Asp820Gly) in the exon 17 of the Kit gene, whereas no pathologic mutations were unveiled on the same genetic region in the MCS. The patient has since started protein kinase inhibitor and remains clinically stable.
Conclusion: There are about 25 cases of MCS reported, with a single mention of another case with an associated mediastinal GCT, making this an extremely rare combination. The study of these cases might provide new insights on the molecular pathways and on the improved management of this type of disease.

E-PS-12-030

Low CD30 expression and negative for EBER detection in Hodgkin lymphoma patient associated with complete response therapy of ABVD regimen

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Background & objectives: More than 40% patient of Hodgkin lymphoma (HL) are chemoresistance. Epstein-Barr virus (EBV) associated with poor prognosis and CD30 associated with advanced disease stagesd in HL.
Objectives: Find association between CD30 and EBER1 in HL with ABVD regimen response therapy.
Methods: Cross-sectional study that was conducted at 3 hospitals in Bandung, Indonesia. Our study composed of 60 cases histopathologically diagnosed with Hodgkin's lymphoma. Therapy response were evaluated by RECIL criteria. Detection of EBER1 by real-time PCR and CD30 expression was immunohistochemical semi-quantitative evaluated were performed to all samples. All data were analysed using Chi-Square test with p-value <0.05 of significant level.
Results: There were 28 patients with complete response and 32 patients with no response to ABVD regimen. EBV present in 21 cases (35%), 6 cases from the complete response group and 15 cases from no response group. Low CD30 expression distribution (≤25%) dominate complete response group (68%), whereas high CD30 distribution (>25%) dominate nonresponse group (67,7%). The result showed a statistically significant of EBV infection (p=0.03) and CD30 expression (p=0.004) between complete response and nonresponse group.
Conclusion: In conclusion, the ABVD chemotherapy response of HL associated with CD30 expression and EBV Infection.
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E-PS-12-031

Plasmablastic lymphoma of duodenum – metachronous malignancy with plasma cell myeloma

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Background & objectives: Plasmablastic lymphoma (PBL) is a very aggressive lymphoma that represents less than 1% of that category. Usually, PBL is immunodeficiency-associated lymphoma localized in the oral cavity/gastrointestinal tract.
The 33-year-old woman was diagnosed with multiple myeloma in 2011 (Durie-Salmon 1, ISS-1).
Methods: The first line of treatment was CTD consolidated with high dose melphalan, followed by steam cells autotransplantation and a complete response (CR) was obtained. In 2015 multiple myeloma relapsed and the patient started 2nd line of treatment with 8 cycles of DVd – CR was achieved again. The patient has been receiving maintenance treatment with daratumumab every 4 weeks.
Results: In August 2019 the patient was admitted to the hospital due to severe anaemia (HGB 6,5 g/dl) without a history of bleeding. All staging results confirmed the complete response of multiple myeloma. The patient underwent gastroscopy/colonoscopy – isolated, pathological mass in the duodenum was detected.
The microscopical examination revealed infiltration with immunoblastic cells, a "starry-sky" appearance, focal necrosis, and a high mitotic rate. Immunophenotype of neoplastic cells was: pan-B markers(-),T-cell markers(-), pan-CK markers(-), MUM-1/IRF-4(+), VS38C(+), CD138(+), c-MYC(+), BCL-2 (+), BCL-6(-), CD30(-), CD56(-), CD10(-), EBV-LMP1(-), EBER-ISH(-), Ki-67(+) in nearly 100% of cells. The diagnosis of plasmablastic lymphoma was established. The clinical investigation excluded HIV, EBV and CMV active infections.
Conclusion: We present a rare case of PBL after multiple myeloma treatment. The patient was characterized by iatrogenic immunodeficiency following transplantation but was not related to EBV infection. The differential diagnosis required exclusion of gastrointestinal tract cancer (radiological imaging suggestion) or multiple myeloma progression (absent monoclonal protein, normal FLC ratio, negative serum, and urine immunofixation, no bone lytic lesions, immunohistochemistry of trephine biopsy revealed no infiltration of CD138+ cells).
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E-PS-12-033

Paediatric-type follicular lymphoma: a rare case report with cytohistopathological correlation and review of literature

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Background & objectives: The revised 4th edition of WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues has described Paediatric-type follicular lymphoma (PTFL) as a distinct clinicopathological entity. Here we report, a rare case of PTFL with cytohistopathological correlation and review of literature.
Methods: A 17-year old male patient presented with right submandibular region swelling for 3 months. Computerized tomography (CT) scan of the neck showed multiple bilateral necrotic lymph nodes. FNAC was done followed by surgical excision of the largest node.
Results: FNAC shows features of Non-Hodgkin's lymphoma. Biopsy showed effaced architecture with irregularly shaped lymphoid follicles having numerous large sized atypical lymphoid cells having round nucleus, vesicular chromatin, prominent nucleoli and moderate amounts of cytoplasm. Many tingible body macrophages noted. No Reed Sternberg cells seen. On IHC follicular cells were positive for CD20, CD 10, and BCL6 and negative for CD 30, CD 15, CD 3, CD 5. Ki 67 labelling index was approximately 70-80% in the follicles.
Conclusion: Based on morphological and immunohistochemistry findings, the case was diagnosed as PTFL. Very little literature is available about the patients with advanced stage of the disease. Due to the rarity of the disease, more detailed studies are required.

E-PS-12-034

A case of CLL/SLL with transdifferentiation to dendritic cell tumour and possibly a hybrid lymphodendritic cell neoplasm: the missing link?

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Background & objectives: Recent studies have shown evidence of cross-lineage transdifferentiation of B-cell lymphomas, such as low-grade follicular lymphoma and chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) to histiocytic and dendritic cell sarcomas, but the clonal relationship between the 2 neoplasms is still unclear.
Methods: Here, we report the morphologic, molecular and cytogenetic analysis of a unique case of CLL/SLL associated with indeterminate dendritic cell tumour and possibly a hybrid lymphodendritic cell neoplasm , using immunohistochemistry, electron microscopy, in situ hybridization and fluorescence in situ hybridization (FISH).
Results: A 48-year-old Chinese woman presented with left upper neck swelling. Blood examination revealed lymphocytosis. Microscopic

examinations showed the lymph node has effaced architecture, and has a very complicated, variegated appearance with three distinct components. Electron microscopy revealed the cells in the third component had short and thick bulges like dendritic cell. FISH analysis using CLL probes showed identical deletion TP53, ATM, and deletion 13q14.3 in all 3 components.
Conclusion: Our study provides evidence for transdifferentiation of CLL/SLL to dendritic cell tumour possibly via the intermediate linklymplymphodendritic cell neoplasm and suggests that EBV may play a role in this phenomenon.

E-PS-13 Head and Neck Pathology

E-PS-13-001
Tumour microenvironment, p16 staining and tumour budding in oral squamous cell carcinoma: a prospective study of 12 cases in a resource poor setting
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Background & objectives: Oral SCC is associated with HPV infection in our setting. The TME is well documented in oral cancer which leads to immunosuppression in favour of proliferation. Tumour budding at the invasive front has been reported as a promising prognosticator in SCC,
Methods: The clinical details, sex, age, site distribution, social habits and sexual partners were collected by means of a structured proforma. Sections were cut at 3μm and mounted on glass slides processed with haematoxylin and eosin (H&E). TME was accessed using CD3, CD20, CD45 and CD68. p16 IHC stain was used for HPV infection while AE1/AE3 was used for tumour budding.
Results: The age range of occurrence of oral SCC was 31-80±21.8 years. The buccal mucosa, palate and tongue were the commonest site for SCC. Six (50%) of the 12 cases of squamous cell carcinoma were positive for p16 IHC stain. CD3+ T cells and CD68+ were strongly expressed in p16 positive oral SCC. There is significant association between tumour budding and SCC with those with tumour buds associated with poor prognosis.
Conclusion: HPV 16 is one of the most common causes of oral SCC in our environment with tendency to affect young adults. Those with tumour buds tend to have poor overall survival. TME should be potential biomarkers in the future for immunotherapy.

E-PS-13-002
Analysis of lymphatic vessel and capillary vessel microdensities and mast cell density in lip squamous cell carcinoma and actinic cheilitis
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Background & objectives: The aim of this study was to evaluate capillary vessel and lymphatic vessel microdensities and their relation to the number of mast cells in cases of lip squamous cell carcinoma and actinic cheilitis.
Methods: Thirty cases of each lesion were included. The immunomarkers CD34 and Podoplanin (D2-40) were used to identify capillary and lymphatic vessels, respectively. Mast cells were identified with toluidine blue histochemistry. In addition, actinic cheilitis cases were analysed morphologically and divided into degrees, according to the criteria suggested by the WHO. The data obtained were compared using statistical analysis.
Results: Lip squamous cell carcinoma cases showed an average of 4.8 capillary vessels/mm2 and 1.98 lymphatic vessels/mm2, while in actinic cheilitis cases these averages were 4.29 and 1.69; however, this difference was not statistically significant. Regarding mast cell count, lip carcinoma cases had an average of 2.4 mast cells/mm2. For actinic cheilitis this average was 1.93 (p=0.02). Both microvascular densities and mast cell density were similar between degrees of epithelial dysplasia.
Conclusion: We observed that mast cell density is increased in cases of lip squamous cell carcinoma. This suggests that mast cells are involved in the progression of actinic cheilitis to lip squamous cell carcinoma and possibly in the regulation of neovascularization.
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E-PS-13-003
Adamantinoma-like Ewing sarcoma of the parotid gland, report of two cases and review of literature
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Background & objectives: Adamantinoma-like Ewing sarcoma is rare but has been increasingly reported in the head and neck. Morphologically, these tumours show nested proliferation of monotonous-cells with desmoplastic fibrous stroma. These tumours are immunoreactive to CD99,cytokeratins,p40, p63,neuroendocrine markers and consistently show EWSR1 gene-rearrangement.
Methods: We reported clinical, radiological and histopathological features of two unique cases of Adamantinoma-like Ewing sarcoma of the parotid gland.
Results: Microscopically, the tumour of both cases was composed of solid nests of monomorphic small round blue cells with a separating dense fibrous stroma. Both cases show CD99 positivity in addition to the expression of cytokeratins and neuroendocrine markers. EWSR1-FLI1 rearrangement was detected and confirming the diagnosis of ALES. The second case showed focal squamous differentiation which is not commonly encountered in this tumour.
Conclusion: In conclusion, although Adamantinoma-like Ewing sarcoma is rare and a recently described entity, this tumour carries a peculiar combination of epithelial and neuroendocrine differentiation, the recognition of this entity is important to guide appropriate management for those cases.

E-PS-13-005
Ghost cell odontogenic carcinoma: a rare case report
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Background & objectives: Ghost cell odontogenic carcinoma (GCOC) is a rare and aggressive malignant epithelial tumour with increased risk of local recurrence. Approximately, only 50 cases have been reported in the English literature to date. Herein, we report a new case of GCOC.
Methods: A 19-year-old male patient with complaint of a painless right maxillar giant mass which was present for 2 years but showed a rapid recent growth. Computed tomography scan showed a 123x98x96 mm ill-defined mass that has multilocular cystic and solid components destructing the maxillary bone, extending into the oral cavity and infiltrating the nearby subcutaneous fatty and muscular tissues.
Results: Histopathological examination of the incisional biopsy revealed neoplastic nests and sheets demonstrating the characteristic features of odontogenic epithelium, including an epithelial lining composed of a basal layer of columnar cells arranged in a palisading pattern and an overlying layer of stratified cells resembling stellate reticulum. The cells were uniform, small basaloid cells with round dark nuclei some with mitotic figures. Characteristic anucleated eosinophilic ghost cell clusters were seen in the hyalinized stroma. Immunohistochemical staining showed the tumour cells were strongly positive for p63, focally positive for p53 and negative for calretinin and cytokeratin 7. Ki67 proliferation index was %80. In ghost cell keratinization areas cytokeratin 5/6 and EMA were positive.

Conclusion: GCOC is a rare odontogenic tumour with aggressive rapid growth and destructive behaviour. The most probable mechanism in its development is suggested to be a malignant transformation from a pre-existing calcifying odontogenic cyst or a dentinogenic ghost cell tumour. As it is an extremely rare tumour stil with controversial therapeutic modalities and prognostic data, we decided to share this new case.

E-PS-13-006

Use of GFAP, B-catenin and DOG-1 in the differential diagnosis of benign biphasic basaloid salivary gland tumours

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Background & objectives: Cellular pleomorphic adenoma (PA) and basal cell adenoma (BCA) are benign biphasic basaloid salivary gland tumours that can pose differential diagnostic problems. We review the utility of GFAP, B-catenin and DOG-1 in this differential diagnosis.
Methods: We searched in our centre database cases of salivary gland tumours with a fine needle aspiration cytology diagnosis of "primary salivary gland tumour of the family PA/BCA". Histological diagnosis made on surgical pieces were reviewed and GFAP, B-catenin and DOG-1 immunohistochemistry (IHC) were performed on all retrieved cases.
Results: In our series of 20 cases, all PA showed a immunoprofile GPAF+/B-catenin-/DOG1-, and all BCA were GPAF-/B-catenin+/DOG1+. GFAP positive cases showed focal or diffuse cytoplasmic staining. Cases with focal staining tended to be in mesenchyme-like cells adjacent to epithelial nests. B-catenin positive cases had at least 3% positive nuclear staining. DOG-1 positive cases showed cytoplasmic staining in the basal cell component.
Conclusion: In our experience this IHC panel is useful in this differential diagnosis where even though both entities are benign, PA has a higher recurrence and malignancy rate, so a correct diagnosis has important prognostic implications. Besides, although some literature reports comment on the expression of these markers in different salivary gland tumours, to the best of our knowledge, there are no reports comparing its expression in PA and BCA.

E-PS-13-007

HPV related multiphaenotypic sinonasal carcinoma

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Background & objectives: HPV related multiphenotypic sinonasal carcinoma (HMSC) is recently described entity in the sinonasal region. A 43-year-old female with right sinonasal mass showing typical histological features of this entity is presented.
Methods: CT scan showed a heterogenous enhancing soft tissue mass in the right anterior nasal cavity infiltrating the nasal septum as well as the medial wall of right maxillary sinus.
Biopsies from the mass showed a tumour exhibiting predominantly solid areas with cribriform architecture. The tumour surrounded myxoid to hyalinized stromal material and true ductal spaces were seen.
Results: The cells contain round to oval irregular hyperchromatic nuclei, inconspicuous to discernable nucleoli and scant amounts of lightly eosinophilic cytoplasm. Scattered large markedly pleomorphic hyperchromatic nuclei were seen. Frequent mitoses were present with occasional atypical mitoses. Overlying stratified squamous epithelium showed atypia with enlarged nuclei and prominent nucleoli. CD117 was positive in the solid areas with focal luminal accentuation. P63 and p40 highlighted the predominant abluminal/myoepithelial component. S100 was negative.
Conclusion: Immunostaining for p16 showed positive nuclear and cytoplasmic staining of >80-90% tumour cells including the surface epithelium. Further testing for Human Papilloma Virus [HPV E6/E7] RNA in Situ Hybridisation (ISH) studies was positive.
HMSC should be considered in the differential diagnosis of sinonasal tumours with morphology resembling adenoid cystic carcinoma. Limited follow up with these apparent high grade cases show favourable behaviour.

E-PS-13-008

Teratocarcinosarcoma of the sinonasal tract: a case report with review of literature

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Background & objectives: Sinonasal teratocarcinosarcoma is a highly aggressive malignant neoplasm with combined histological features of teratoma and carcinosarcoma, but lacking malignant germ cell components. We report a new case of this very rare entity, almost exclusively observed in adults, around 60 years.
Methods: A 51 year-old woman presented a rapidly progressive recurrence of a sinonasal tumour, of doubtful histological initial diagnosis. CT-scan and MRI showed a 60mm tumour invading the nasal fossa, maxillary, ethmoidal and sphenoidal sinuses, the cribriform plate, coming in contact with the meninges. Pet Scan showed no metastases. After debulking of the tumour, chemotherapy, endoscopic resection and radiochemotherapy were performed.
Results: The histological material came from the debulking performed before chemotherapy. The tumour was necrotic and showed heterogeneous features: a predominant round blue small cell component with numerous mitoses, some pseudo-rosettes and true rosettes; spindle cells on a myxoid matrix and a nest of cartilage; an epithelial component, glandular, and squamous with a "foetal" appearance.
The small round cells were positive for Synaptophysin, CD56 and Chromogranin A. PS100 was negative, but highlighted in some areas a network of sustentacular cells. A few cells were desmine and myogenin positive. Cytokeratin AE1/AE3 was positive in the epithelial component and in dispersed small round cells. Proliferative Index (Ki67) was 70%, with hotspots of 100%.
Conclusion: Sinonasal teratocarcinosarcoma is a very rare tumour, thought do develop from somatic pluripotent stem cells of the olfactory neuroepithelium. Although challenging, it's important to perform the diagnosis of this tumour, because of its highly aggressive behaviour and poor prognosis.

E-PS-13-009

High-grade transformation of adenoid cystic carcinoma with retained morphologic features of conventional adenoid cystic carcinoma

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Background & objectives: High-grade transformation of adenoid cystic carcinoma (AdCC-HGT) confers poorer prognosis than conventional AdCC, with frequent early metastases and significantly shorter median survival time. Due to the significantly increased proliferation, AdCC-HGT may be receptive to systemic chemotherapy. The high-grade component is reported to morphologically resemble poorly differentiated adenocarcinoma, undifferentiated carcinoma and only rarely high-grade myoepithelial carcinoma. We report a case of AdCC-HGT where the transformed area retains some architectural features of conventional AdCC, potentially mimicking conventional high-grade AdCC.
Methods: A 67-year-old woman presented with right-sided paraesthesia of the anterior mandible and poor fitting dentures. Radiological imaging showed an ill-defined mass extending from the right sublingual gland to

the midline of the mandible with destruction of the alveolar bone. Anterior mandibular resection confirmed a widely infiltrative mass of the right sublingual gland with bone invasion.
Results: Histopathologic findings showed a 4.6 cm mass predominantly composed of irregular, frequently cribriform tumour islands containing basaloid cells with marked nuclear atypia, limited cytoplasm and brisk mitotic and apoptotic activity. Several foci of necrosis were identified. A distinct transition zone and a minor component of conventional low-grade AdCC was present. Immunohistochemistry revealed loss of the biphasic (luminal/abluminal; CD117/p63) pattern, diffuse CD117 expression and approximately 70% nuclear labelling with Ki-67.
Conclusion: AdCC-HGT may be composed of cribriform islands of basaloid cells; features allowing separation from conventional AdCC include marked nuclear atypia, loss of biphasic pattern, necrosis and increased proliferative activity. High proliferative activity of AdCC-HGT may influence response to systemic chemotherapy.

E-PS-13-010
IDH2 mutations in sinonasal tumours: are they restricted to SNUCs? A case report and review of the literature
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Background & objectives: IDH2 mutations have been described in different types of poorly differentiated sinonasal tumours but the nosology is still unclear. We report a case of poorly differentiated sinonasal tumour with IDH2 R172G mutation and areas of high grade Olfactory Neuroblastoma (ONB).
Methods: A 52 years old man presented with a skull base tumour involving the ethmoid sinus and the lamina papyracea. Biopsies were performed, allowing an extensive pathological and molecular investigation.
Results: Biopsies highlighted a heterogeneous tumour made of lobules and nests of atypical cells with a moderately abundant cytoplasm, round to ovoid nuclei and a clear chromatin. In some areas atypia were more severe. Immunohistochemistry showed quite a diffuse expression of keratins, a focal expression of 3 neuroendocrine markers and the presence of focal sustentacular S100 positive cells. A targeted DNA sequencing panel showed an IDH2 R172G mutation.
IDH2 mutations have initially been described in Sinonasal Undifferentiated Carcinoma (SNUC). They were then reported in tumours displaying frank neuroendocrine immunophenotype, i.e. LCNEC or ONB. This case brings new arguments to the presence of IDH2 mutations in tumours other than SNUCs.
Conclusion: IDH2 mutations are not restricted to SNUC. They can occur in poorly differentiated sinonasal tumours showing some degree of neuroendocrine differentiation and notably Large Cell Neuroendocrine Carcinoma or high grade ONB. To clarify the nosology of those sinonasal tumours, IDH2 mutation should consistently be evaluated in poorly differentiated sinonasal tumours, LCNECs and high grade ONBs.

E-PS-13-011
A pulsatile mass behind tympanic membrane
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Background & objectives: Glomuvenous malformation or glomangioma (GVM) are rare lesions accounting for approximately 0.5-1.5% of soft tissue neoplasms, can rarely be found in head and neck region and present in two forms: sporadic (solitary lesion) or familial (multifocal lesions).
Methods: We report an exceptionally rare case of a GVM stemming from the middle ear space in a 69 year-old woman that was referred to consultation for bilateral otalgia and progressive hearing loss. Otoscopic examination revealed a reddish pulsatile mass behind tympanic membrane. Ear computed tomography showed a 4 mm lesion in the middle portion of the right tympanic membrane.
Results: Patient underwent surgical resection via postauricular approach. The tympanic membrane was reconstructed with temporalis tissue.
Histological examination revealed a neoplasm composed of thin-walled dilated vascular structures surrounded by round cells, with sharply defined cell borders, eosinophilic cytoplasm and centrally placed nucleus without atypia; immunohistochemistry studies revealed positivity of the tumour cell for smooth muscle actin and CD34. A GVM was diagnosed, with free resection margins.
Conclusion: GVM are slow-growing benign vascular lesions representing the most common primary neoplasms of the middle ear. Pathologically, they may be misinterpreted as haemangiomas or venous/arteriovenous malformations depending on the degree of vascular proliferation. Complete surgical excision is the treatment of choice; they're usually encapsulated and may show irregular borders leading to the possibility of recurrence if the nodule is not completely excised. Our patient had a full recovery.

E-PS-13-012
Malignant extrapleural solitary fibrous tumour of the parotid gland: an uncommon condition worth surveilling
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Background & objectives: Extrapleural solitary fibrous tumours represent a rare type of mesenchymal neoplasms that can arise in any location, including the head and neck. Some of these lesions have malignant potential, hence the importance of accurate diagnosis and surveillance.
Methods: We present a case-report of a 77 year old woman who presented with a 10cm mass on her left parotid gland. Aspiration cytology specimens were evaluated, being diagnosed with undetermined significance moderate atypia. Magnetic resonance imaging was consistent with a possibly malignant lesion. Surgical resection was performed.
Results: The surgical specimen was sent to the pathology department for evaluation. The macroscopic examination revealed an encapsulated, white and homogeneous lesion, with calcifications and necrosis, measuring 6,5cm.
The microscopic examination showed an encapsulated tumour with epithelioid, atypical cells, counting fifty-six mitosis per ten high power fields, within a collagenous stroma with staghorn vessels, perivascular hyalinization. The morphology and immunohistochemical study were consistent with an extrapleural malignant solitary fibrous tumour.
The clinical behaviour of these neoplasms can be unpredictable. Although most are benign, 10% behave aggressively, with local our distant recurrence. The criteria for aggressiveness vary, but malignant histology, such as high mitotic rate, remains the best indicator of poor outcome.
Conclusion: This case-report highlights the importance of careful evaluation of this type of lesions, since it may require different clinical approaches. Hence, it is important to correctly diagnosing this group of tumours in order to give patients the best possible follow-up.

E-PS-13-014
Analysis of the casuistry of small round and blue cell tumours of nasal cavity in the pathology department at the Clínico Universitario Lozano Blesa Hospital 2015-2020
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Background & objectives: Malignant sinonasal tract tumours comprise less than 1% of all neoplasms. Small and blue round cell tumours are rare,

representing 2-3% of all sinonasal tumours. We report the number of cases in the last 5 years in our hospital
Methods: A review in the PATWIN computer program database of CULBH January 2015- January 2020 in which we identified three cases; two of which correspond to olfactory neuroblastomas (ON) and one to small cell neuroendocrine carcinoma (SCNC). We present the morphological and clinical characteristics of the cases identified
Results: We found three cases, two male and one female between 49 and 67 years of age. In all cases, biopsy were made. Morphologically an important fibrovacular component and cell nest with hyperchromatic, small and monotonous nuclei. Frequent mitosis in neuroendocrine carcinoma and scant in olfactory neuroblastoma. In none of the cases were rosettes or pseudo- rosettes observed. Immunohistochemically they showed expression for CD56, synaptophysin, BCL2, B-catenin, elevated ki67 and s100 positive sustentacular cells, in ON. A variable stain for CKAE1-AE3 were observed. CD45, CD99, EMA were negative. ON patients has had a torpid evolution with early relapse and aggressive local behaviour. SCNC patient died a month after diagnosis
Conclusion: The morphological similarity and the uncommon of these lesions represents real difficulties of diagnosis. The late presentation makes the tumours locally advanced at the time of diagnosis. In ON the correlation between morphological grade and patient evolution is not clear

E-PS-13-015
Parotid oncocytosis, FNA findings with histology correlation
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Background & objectives: Diffuse oncocytosis of parotid gland is rare with <20 cases reported since its first description in 1982. FNA is a real challenge for cytopathologists as oncocytic cells are common. Our aim is to present FNA finding & histological correlation of one case.
Methods: A 73 years old female with a painless mass in right parotid dating 2 years treated as sialolithyasis. Parotid CT with contrast showed some nodularity but no stones. FNA and total parotidectomy performed intra-operative assessment of superficial and deep lobe involvement. One year after surgery the patient has no signs of recurrences or metastases.
Results: The FNA showed cohesive clusters of oncocytic cells with abundant, granular & eosinophilic & round nuclei with prominent nucleoli. Background was poorly cellular with occasional lymphocytes. Cytology report was: Warthin tumour. Histology showed deep and superficial parotid lobe totally replaced by oncocytic cells in all acini & ducts without intervening normal acini. There were no, fibrosis, capsule formation or papillae to confirm Warthin tumour. The histological diagnosis was: diffuse oncocytosis.
Conclusion: Our case confirms the challenges of FNA diagnosis and the rarity of oncocytosis. In 1982, an extensive review of 7000 cases from the salivary gland tumour registry in Hamburg found 2 cases only (2/7000). In 2002 Capone at al. in a review of oncocytic lesions of salivary glands over 16 year period found 28.5% of both multifocal and diffuse oncocytosis. In all published cases diffuse oncocytosis was "discovered" on parotidectomy specimens

E-PS-13-016
Hemangiosarcoma of the nasal cavity and paranasal sinuses – a diagnostic challenge
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Background & objectives: We present two cases of hemangiosarcoma with misleading initial morphology.
Methods: Case 1: A 67-year-old male patient presents with pain of the right face. A polypoid mass is detected in his paranasal sinuses. Due to his history of melanoma it is suspected for metastasis. An excisional biopsy is interpreted an organized hematoma.
After surgical removal of the whole mass diagnosis of hemangiosarcoma with lymph node metastasis was conducted.
Results: Case 2: A 73 years old patients presents with an ulcerated multinodular mass of the nose. The first biopsy is interpreted as an ulcerated haemangioma. The clinically suspected diagnosis of a squamous carcinoma is given histopathologically the second excision.
Finally, an hemangiosarcoma in the ablatio nasi specimen is diagnosed. The patient dies three weeks later, most likely due to his atrial fibrillation.
Conclusion: The morphological diagnosis of hemangiosarcoma of the nasal cavity and paranasal sinus may be challenging.
Massive haemorrhage and siderosis masked the tumour cells in Case 1. In Case 2 the pseudoepitheliomatous hyperplasia was misinterpreted as squamous cell carcinoma. Mild atypia of the vascular tumour resulted in the erroneous assessment of malignancy.

E-PS-13-017
Sclerosing polycystic adenosis of the minor salivary gland: case report
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Background & objectives: Sclerosing Polycystic Adenosis (SPA) is a relatively new entity. It is a rare entity mostly seen in the parotid & submandibular glands, rarely in minor salivary glands. It histologically resembles breast fibrocystic disorders and is a clonal process hence neoplastic.
Methods: A 59 year old male presented with a mass in the buccal mucosa which had been present for 40 years. An incisional biopsy was hence performed and sent for histopathology analysis and specialist review.
Results: Histopathology showed a well circumscribed lesion with varying sized tubules surrounded by fibrosis and showing dilatation. A few of the tubules contained eosinophilic and amorphous secretions. There was focal ductular proliferation with apocrine metaplasia. No atypia was noted.
Immunohistochemistry showed positivity for CK7, S100, mammaglobin and androgen receptor whilst the cells were negative for CK20, CK5/6, DOG1 and calponin.
Conclusion: A diagnosis of SPA was made and as the lesion was seen reaching the margin, an excision was advised. SPA is a difficult diagnosis to make and although it is a rare entity it should be considered in the differential diagnosis even in minor salivary glands.

E-PS-13-018
Thyroid cancer in children: about 6 cases
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Background & objectives: Thyroid cancers are rare malignant tumours in children. They are dominated by well-differentiated tumours: papillary and vesicular. The prognosis is generally favourable. Herein, we report the clinicopathological particularities of thyroid cancer in children.
Methods: It is a retrospective study on paediatric thyroid cancer diagnosed in the Pathology Department, Farhet Hached Hospital, Sousse (Tunisia), during 2005-2014.
Results: Two girls and four boys were included. The mean age was 12.5 years. Hypothyroidism was found in one case. Ultrasound and thyroid scintigraphy showed nodules whose structure was hypoechoic in 5 cases, and heterogeneous in one case. Lymph node aspiration was positive in 3 cases. Surgical treatment was performed in all patients. Extemporaneous examination was in favour of malignancy in 4 cases. The final

histopathological examination concluded in papillary carcinoma (4 cases) with nodal metastasis and in vesicular carcinoma with minimal invasion without nodal metastasis (2 cases). They all had adjuvant therapy with radioactive iodine and hormone therapy. The evolution was favourable for all patients

Conclusion: Thyroid cancers are rare tumours in children with a generally favourable prognosis, even in cases of initial extension or after local relapse. Therapies targeting angiogenesis and the mutations frequently encountered in this type of cancer constitute a new tool aimed at eradicating the disease and minimizing morbidity especially among young patients.

E-PS-13-019

Mucoacinar carcinoma – a putative variant of mucoepidermoid carcinoma

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Background & objectives: A rare variant of mucoepidermoid carcinoma displaying acinic differentiation was first reported in a case series of five cases presented in an USCAP abstract in 2017 (Mod Pathol 2017 vol.30 p.322 abstract #1294). We present another instance of this entity.

Methods: MAML2 Fluorescence In-Situ Hybridization (FISH) analysis was performed using break-apart probes (Empire Genomics, Williamsville, New York).

Results: A 52-year-old man presented with a two year history of slowly growing, asymptomatic, superficial left parotid tumour with no lymphadenopathy. CT appearance was benign and a local excision was performed. The tumour was composed of goblet cells, clear epidermoid cells, and scattered cells with basophilic, granular cytoplasm containing multiple PAS+ granules. Tumour cells were positive for p63, keratin 5, keratin 19, vimentin, CD117, and Sox10, and negative for DOG1, actin, SMMS and mammaglobin. MAML2 break apart FISH showed complex rearrangement pattern with 66% of cells showing one copy of rearranged MAML2 with a deletion of its 5' segment. The diagnosis of mucoepidermoid carcinoma with acinic differentiation (mucoacinar carcinoma) was made.

Conclusion: We present a new case of a rare variant of mucoepidermoid carcinoma with acinic differentiation, previously termed mucoacinar carcinoma. Our case adds to the five previously reported cases of this rare entity.

E-PS-13-020

Significance of cytomorphological studies in the diagnosis of salivary gland diseases

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Background & objectives: Adenomas comprise from 70 to 80% of all epithelial tumours of the salivary glands. The most common are pleomorphic adenomas, Adenolymphoma, oncocytomas, basal cell adenomas. Adenolymphoma makes up 1.7–10.1% of all benign tumours of the salivary glands and takes the second place in frequency of occurrence after pleomorphic adenomas. Histological examination of the tumour is currently the most accurate method of differential diagnosis to compare the data of the macroscopic picture with the histological types of Adenolymphoma of the parotid glands.

Methods: Retrograde results of examinations and treatment of 19 patients with a clinical diagnosis of Adenolymphoma from 2015 to 2018. An analysis of the description of macro drugs and data of postoperative histological diagnosis is carried out.

Results: In 9 cases, the formation was described as having a thin shell, having a lobed structure. Histologically corresponded to 2 subtypes.6 patients had a cystic mass. Histologically, this corresponded to subtypes 3 and 4. In 2 cases, there was a cystic formation with liquid contents and a soft tissue component, and in 3 cases, soft tissue content with a cavity component. Histologically, this corresponded to subtypes 1 and 2.

Conclusion: There is a direct relationship between the macroscopic structure of the tumour and its histological structure.

E-PS-13-023

Proliferative activity of recurrent inverted papilloma cells

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Background & objectives: In 8-10% of inverted papillomas IP in situ, papillomavirus DNA(HPV) is detected. Aim. Identification of immunohistochemical criteria for pathological transformation of cells of the mucous membrane of the nasal cavity(NC) in case of recurrent IP using expression of Ki-67 .

Methods: Ki-67 & HPV-positive cells were determined in the mucosa of NC. As an indicator of proliferative activity, the Ki-67 proliferation index was used, which was determined in each row of cells by fractions of stained nuclei, expressed in %.

Results: Most immunopositive cells were localized in the second row of cells, with recurring IP Ki-67-positive cells were found in the basal and parabasal layers. HPV-positive immunostaining was detected in individual nuclei of infected cells of the basal and parabasal layers. HPV elements were detected in actively proliferating basal and parabasal IP layers and their relapses.

Conclusion: HPV elements in IP and their relapses were identified. This indicates their role in the formation and relapses of nasal cavity IP. In all studied preparations, pronounced Ki-67 expression was observed in the nuclei of proliferating cells.

E-PS-13-024

A rare variant: adenomatoid ameloblastoma with dentinoid

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Background & objectives: The ameloblastoma in the epithelioid group of odontogenic tumours is classified according to its radiological, histological and behavioural characteristics. However, some types of ameloblastoma that may contain several of these definitions outside the classification as hybrids are also described in the literature.

Methods: A 58-year-old male patient presented with a complaint of mass in the left lower jaw and gingival region, which has been around for 6 months. A 40x25 mm sized lesion was observed in the anterior left half of the mandible, which thinned the bone cortex. With these findings, the patient underwent a curettage biopsy for diagnosis.

Results: Excisional material's total size was 1.5x1.5x0.4 cm. In histopathological examination, the lesion was observed as solid in places and forming adenoid/duct-like areas. Basophilic mucoid material, stellate reticulum cells and mesenchymal elements are seen in these spaces. Peripheral cells exhibiting prominent palisading of the basal cells nuclei with reverse polarity with ameloblast-like pattern.

The immunohistochemical findings;CK19,CK14,PanCK focally and strongly positive,CK7 negative,p16 focally cytoplasmic and nuclear positive, P53 focal positive, Ki-67 was found about %15-20.

Conclusion: Adenomatoid odontogenic tumour(AOT) and adenoid ameloblastoma with dentinoid distinction can be problematic. Adenoid ameloblastoma with dentinoid has duct-like structures without palisading cells, ameloblastomatous areas, stellate reticulum-like cells.

The most important feature of this lesion is its local recurrence when compare with AOT. Evans et al. and Ide et al. had described their cases of a recurrent lesion that was initially diagnosed as adenomatoid odontogenic tumour after the recurrence and after reviewing all histologic findings, they named it adenoid ameloblastoma with dentinoid.

E-PS-13-025
Schneiderian type papilloma of the middle ear
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Background & objectives: Schneiderian type papillomas are benign neoplasms that develop from the sinonasal tract mucosa. Due to embryological and anatomical closeness, it can develop in different localizations: pharynx, lacrimal sac, middle ear.
Methods: 63 year old female patient. She applied with unilateral hearing loss, otorrhea and otalgia. The lesion was excised in the patient whose lesions were detected in the middle ear.
Results: Excisional material with a total size of 1.5x1x0.4 cm was sent for histopathological examination. Hematoxylin and eosin stained slides examined. When we looked at the microscopic findings; lesion has a papillomatous appearance. The surface of this lesion has columnar cells and also included goblet cells. Chronic inflammatory cells and oedema were observed in the submucosa.
Conclusion: Schneiderian type papilloma of the middle ear is a rare tumour. The first case was described by Stone et al.in 1987.
The excision of the lesion is sufficient in the treatment of these cases, there is no clear information in terms of recurrence or malign transformation since the total number of reported cases is around 30. In this respect, it is necessary to follow up the cases. This case is in second month of follow-up.

E-PS-13-026
Oral focal mucinosis of tongue
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Background & objectives: Oral focal mucinosis is the name given to the oral form of cutaneous focal mucinosis. This lesion generally appears smooth round asymptomatic elevation from around. This lesion's aetiology is unknown but probably cause is overexpression of hyaluronic acid by fibroblasts.
Methods: A 64 year old female patient presented with a lesion on the tip of tongue. The lesion was approximately 7mm in diameter and round in shape, firm and sessile. The mucosal surface of the lesion was smooth, not ulcerated and showed no colour change. Excisional biopsy was performed.
Results: Macroscopically, the diameter of the lesion was 0.6 cm. Hematoxylin&Eosin and Alcian blue & Periodic acid–Schiff(PAS) stained microscopic slides are examined. On H&E slide, lesion surface was stratified squamous non-keratinized epithelium and the underlying connective tissue stroma was composed of loose fibro-myxoid stroma with fibroblasts. Alcian blue and periodic acid–Schiff (PAS) staining of the mucinous part of the tissue demonstrated a positive reaction with Alcian blue and a negative reaction with PAS.
Conclusion: Oral focal mucinosis is a very rare case on tongue; reported cases are less than 10. Histopathological distinction is necessary from diseases with a myxomatous stroma: Myxoma, mucocele, nerve sheath myxoma, focal myxedema, and mucoid degeneration of fibrotic lesions. Clinically, these lesions cannot be distinguished, so excision is recommended.

E-PS-13-027
Solitary fibrous tumour of the thyroid
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Background & objectives: Solitary fibrous tumour (SFT) rarely arises in the thyroid. We report a case of SFT of the thyroid which showed usually infiltrative growth pattern with entrapment of many thyroid follicles within it and simulated desmoid-type fibromatosis.
Methods: Case report
Results: The patient was a 61 year-old man, who presented with a painless mass of about 4 cm in the right lobe. The resected mass was grossly yellowish white, and microscopically consisted of a diffuse growth of fibroblast-like, bland spindle cells which were embedded in a large amount of collagen fibres. The mass was relatively well-circumscribed but contained many thyroid follicles within it. Tumour cells were immunoreactive for STAT6 and CD34.
Conclusion: In our case, SFT of the thyroid showed production of abundant extracellular collagenous matrix and an infiltrative growth with entrapment of follicles, thus closely stimulating desmoid-type fibromatosis. Immunohistochemistry for STAT6 and CD34 was effective for the differentiation from desmoid-type fibromatosis.

E-PS-13-028
The effect of sodium thiopental and fentanyl on mast cell degranulation in the mesentery in rats when modelling septaplasty
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Background & objectives: Surgical lesion leads to general inflammatory reactions. The role of anaesthesia in septoplasty in these reactions remains unstudied. Objective.to study the effect of sodium thiopental and fentanyl on mast cell (MC) degranulation in the mesentery in rats when modelling septaplasty.
Methods: Wistar rats were simulated with septoplasty using fentanyl (1group, 5 rats) and sodium thiopental (2 group, 5 rats). 5 rats were a control group (CG). After surgery, rats were sacrificed on 2nd day and the mesentery was stained with toluidine blue. MC with varying degrees of degranulation (0-3) were counted in 20 fields of view.
Results: In 1&2groups, type0 MC number was significantly less(22.267 ±2.45&29.5±6.73, respectively)than in the CG(40.45±6.2)($p<0.001$).In 1group, type0 MC number &type1(22.31±3.48) prevailed, over 2types(2.04±0.33)& 3(1.18±0.24) ($p<0.001$), but type2 TC was greater than 3rd($p<0.01$).In 2group, there was an increased content of 1type TC(43.76±7.99), compared with other types of TC degranulation in 2group($p<0.001$). 2type(1.22±0.22)as well as in the 1group prevailed over 3type(0.67 ± 0.13)($p <0.001$). Comparing the groups, a higher degree of TC degranulation was revealed in 1group.
Conclusion: Modelling of septoplasty under general anaesthesia with fentanyl causes more pronounced phenomena of general inflammation and higher mast cell degranulation activity in the mesentery in rats than with sodium thiopental. Also, septoplasty itself provokes not only local inflammatory reactions, but also a systemic inflammatory response

E-PS-13-029
Nasal septum histological changes in modelling septoplasty at rats
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Background & objectives: Modelling of septoplasty in rats leads to changes in behaviour in the autonomic nervous system and the appearance of dark neurons in the hippocampus. Purpose: to study the local effect of septoplasty modelling in rats during nasal septum scarification.
Methods: In 10 male rats of the Wistar strain of the experimental group (ExpG), the mucous-perichondrium layer of the nasal septum was scarified. The control group consisted of 5 male rats. Animals were slaughtered 3 days after surgery. After decalcification of the facial skeleton of rats, histological sections were stained with H&E. For statistical analysis of the results, the Mann-Whitney test was used.
Results: In ExpG, at the sites of nasal septum scarification, the leukocyte shaft was 45.43±1.07 μm. The average values of this indicator for each rat in ExpG did not differ ($p<0.001$). There was oedema, hyperaemia and diapedetic haemorrhage in the submucosa. Focal periductal mononuclear

infiltrates in the gland. A narrowing of the common nasal passages was noted due to oedema, which covered the nasal septum adjacent to the damage zone.
Conclusion: Scarification of NS in rats is accompanied by characteristic inflammatory phenomena, both in areas of direct damage and in areas close to them. This method of damage to the nasal mucous simulates inflammation after septoplasty in humans.

E-PS-13-031
Carcinoma showing thymus-like element (castle) of the submandibular gland: report of an extremely rare case
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Background & objectives: CASTLE is rare but a well-established thyroidal tumour as "intrathyroidal thymic carcinoma". Recently, one case of CASTLE arising in the parotid gland was reported (Head Neck 2017: 40: E1-E4). We reported herein one extremely rare case of salivary CASTLE.
Methods: We collected "basaloid/myoepithelial carcinoma" from a pathology file during 2009-2020. We re-estimated it, histologically, and immunohistochemically. The patient was 47 years-old female, involving the sense of incongruity at her left neck. MRI indicated an ill-defined mass in the left submandibular gland. The submandilectomy was performed. Sequentially, the late lymph node metastasis was found. After 3 years, distant metastases were found.
Results: Histologically, the tumour showed the nest-like or sheet-like pattern of short-spindle or basaloid atypical cells with hyalinous stroma. Stromal lymphoid cell infiltration was scanty. The tumour cells showed clear nuclei with short spindle-shaped cytoplasm and one swollen nucleolus, and focally squamous metaplasia. Immunohistochemically, the tumour cells were positive for CK5/6, p63, CD5, c-kit and EGFR, whereas they were negative for CK14, aSMA, NCAM, and synaptophysin. Ki-67 labelling index is 52%.
Conclusion: We finally diagnosed it as salivary CASTLE, due to CD5 positivity and negativity for both neuroendocrine markers and myoepithelial markers, except for p63/p40 and CK5/6. To the best of our knowledge, this is the first case of CASTLE arising in the submandibular gland. The origin of salivary CASTLE remains unknown. We discuss the differential diagnosis of salivary CASTLE from myoepithelial carcinoma, lymphoepithelial carcinoma or basaloid carcinoma of the salivary glands.
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E-PS-13-033
Aggressive neoplasia in the maxillary sinus in women in the eighth decade of life - case report and literature review
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Background & objectives: The sinu-nasal tract is an infrequent site of primary malignancy. Adenoid cystic carcinoma (ACC) is the most common salivary gland tumour in the sinus tract. The aim of this case is to identify the clinical-pathological features of sinus-nasal ACC.
Methods: Patient (60years) who debuted with left periorbital asymmetric facial tumour, with decreased visual acuity associated. In CT a tumour with a greater diameter of 47 mm was found with intense heterogeneous enhancement in the left maxillary sinus extending anteriorly to the subcutaneous cellular tissue and posterolaterally to the buccal space, eroding the walls of the sinus and without adenopathies.
Results: Under the optical microscope, this tumour is characterized by the presence of small, round cells of uniform appearance that are grouped into cylindrical structures, in which several lights containing hyaline or mucous material can be observed. The immunohistochemical: CK19, c-kit, CK5/6, EMA (luminal), p40 and p63 (basal) positive. ACC is a malignant tumour with a poor prognosis, very rare in the maxillary sinus with respect to other head and neck locations, but with a high recurrence rate. In contrast, the rate of metastasis appears to be lower than that observed for tumours of the salivary glands.
Conclusion: Predictors of survival in SNACC include age, comorbidity status, grade, and stage. Surgery is associated with improved survival and remains the mainstay of therapy, whereas the roles of radiation therapy and chemotherapy require future investigation, where pathology has the main perspective.

E-PS-13-034
A rare case of metastasis of breast carcinoma to buccal mucosa mimicking acinic cell carcinoma
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Background & objectives: Metastatic lesions to the oral cavity from distant tumours are rare, amounting to only 1% of all oral cavity malignancies and only occasional cases of metastasis to the buccal mucosa has been reported. A case is presented here.
Methods: A PubMed search was carried out for previous cases, using the reference terms "buccal mucosa", "breast metastasis" and "acinic cell carcinoma". A 62-year-old woman was referred to oral-maxillo-facial outpatient department for evaluation of an ulcerated left buccal mucosal lesion.
Results: The biopsy from the ulcerated lesion of the buccal mucosa revealed a tumour arranged in acinar/cribriform pattern with papillary like structures and some glandular structures. The features are reminiscent of acinic cell carcinoma. However, with DOG1 negativity, ER/PR positivity with QS of 8/8 for ER and 4/8 for PR and past medical history of ypT2 yN1 invasive ductal carcinoma, the diagnosis of metastatic breast carcinoma was made.
Conclusion: Diagnosis of a metastatic lesion in buccal mucosa is challenging histologically since it can mimic primary salivary gland tumours. Our case is complicated by the long interval of time (6 years) from primary breast tumour detection. Most of the reported cases have an interval of 2 years. The combination of medical history and a panel of immunohistochemical stains and interest in both breast and salivary gland pathology are key to achieve the correct diagnosis as shown in our case.

E-PS-13-035
Lichen sclerosus et atrophicus – an extremely rare diagnosis of the oral cavity
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Background & objectives: Lichen sclerosus et atrophicus (LSA) is an uncommon inflammatory dermatosis predominantly affecting the anogenital region. Extragenital manifestation is uncommon and LSA affecting the oral tissues in isolation is exceedingly rare, with only a few reported cases in the English literature.
Methods: We present the clinical and histological findings of a rare case of oral LSA with discussion of the management.
Results: A healthy Asian male presented with 15mm heterogenous ulcerative lesions in the left buccal mucosa and the gingivae above the upper right premolar teeth. There were no identifiable causes of ulceration and no extra-oral involvement. Clinical suspicion of syphilis was raised due to the resemblance with snail-track ulcers.
Incisional biopsies demonstrated atrophic epithelium, significant basal cell loss and prominently hyalinised connective tissue showing sclerosis; consistent with a diagnosis of LSA.
Conclusion: This case highlights a rare and interesting case of LSA affecting the oral mucosa. The aetiology and pathogenesis of LSA

remains largely unknown, although it is thought to be multifactorial with evidence to implicate genetic, hormonal, infective, traumatic and autoimmune-related factors.

E-PS-13-036

Radiation-induced osteosarcoma involving the mandible – report of a rare diagnosis

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Background & objectives: Irradiation can have adverse effects on bone. Late complications include osteoradionecrosis, radiation-induced osteitis and osteosarcoma. The latter are malignant tumours of undifferentiated connective tissue of bone and exceedingly rare in the jaw (incidence 0.7 per million) with only 10% radiation-induced.
Methods: We report the rare case of a radiation-induced jaw osteosarcoma.
Results: A Caucasian male patient presented with severe trismus and marked left lingual alveolus expansion which had caused deviation of the tongue. Four years previously he had radical radiotherapy (70Gy) and chemotherapy for a p16 positive T1N2cM0 squamous cell carcinoma of the left tonsil with a positive left level II node.
The patient had extractions in the lower left quadrant one year previously, with delayed healing. Initial bone biopsies of the left mandible showed a bony sequestrum suggestive of osteoradionecrosis with presence of abnormal osteoid suspicious for an osteosarcoma. Imaging demonstrated an abnormal exophytic bone forming lesion in the left body of mandible and parasymphysis and ruled out a metastatic lesion.
Conclusion: Following local and national multidisciplinary discussions, the patient underwent a bilateral neck dissection, left mandibulectomy with fibula flap reconstruction and full thickness skin graft. Due to the rarity of this lesion in the jaws and its slow-growing and painless nature, it is often diagnosed late. A diagnosis should be considered if changes are seen in previously stable irradiated bone with bony destruction and a soft tissue mass.

E-PS-13-037

Laryngeal basaloid squamous cell carcinoma with sarcomatous component and osteosarcomatous differentiation: an unusual histologic variant

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Background & objectives: Basaloid squamous cell carcinoma (BSCC) with spindle cell component is an uncommon aggressive variety of squamous cell carcinoma. Only few cases are reported in the larynx. The aim is to analyse epidemiological and clinic-pathological aspects of this rare entity.
Methods: We present a case of laryngeal BSCC with sarcomatous component and osteosarcomatous differentiation in 66-year old man. To our knowledge, it's the second case reported in the literature.
Results: A 66-year-old man, with a 40 pack-year smoking history, presented dysphonia and dysphagia. Laryngoscopy showed a glottis exophytic tumour. Diagnosis given on biopsy was moderately differentiated squamous cell carcinoma with sarcomatous component. The patient underwent partial laryngectomy with bilateral neck dissection. Macroscopically, it was an ulceroproliferative tumour involving the right vocal cord. Histologically, it presented several components: basaloid region, of which tumour cells have hyperchromatic nuclei, scanty basophilic cytoplasm and showed peripheral palisading, comedo necrosis and hyalinized stroma; conventional keratinizing squamous component and highly undifferentiated sarcoma; there were focal osteosarcomatous differentiation. All margins were negative. Multiple ipsilateral lymph nodes were metastatic. An adjuvant radiotherapy was preconised.
Conclusion: Overall, given the rarity of this diagnosis, few conclusions can yet be drawn about its risk factors, treatment approach or prognostic significance.

E-PS-13-038

Cervical ganglioneuroma - case report and literature review

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Background & objectives: Ganglioneuromas can appear anywhere but only 28 cervical ganglioneuromas have been reported. Because of non-specific radiological findings and wide differential diagnosis, pathological examination may be the only way to diagnose them. Its rarity and clinicopathological characteristics could justify its presentation.
Methods: We report a 41 years-old female patient with pain, tumour and redness in paramandibular region with clinical diagnosis of cellulitis. Through physical examination, an ovoid ipsilateral cervical mass was detected and radiology revealed a 5.1x3.5x2.1 cm homogeneous hypointense lesion. Fine-needle aspiration was performed but was insufficient for diagnosis. Therefore, surgical treatment was planned and morphologic description was performed.
Results: Grossly, it is a well-defined nodular-oval brownish white tissue fragment with whitish cut surface and elastic consistency. Microscopically, it is a circumscribed lesion with schwannian stroma and large dispersed cells with small eccentric nuclei and wide granular cytoplasm. It showed positivity for S100, neurofilament and synaptophysin. A final diagnosis of "Cervical ganglioneuroma" was made.
Conclusion: Although cervical ganglioneuroma is a rare entity, it should be taken into account in differential diagnosis of cervical soft tissue neoplasms.

E-PS-13-039

Rare case of a neuroendocrine carcinoma of the tongue

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Background & objectives: Neuroendocrine tumours are a heterogeneous group of tumours. The tongue is an extremely rare site for neuroendocrine carcinomas. Due to the paucity of studies, satisfactory classification and treatment protocols have been established for these tumours in the oral cavity.
Methods: A 69-year-old male was admitted to hospital with a tumorous mass on the left edge of the tongue, with a palpable resistance on the left side of the neck along sternocleidomastoid muscle. CT examination revealed lymphadenopathy in neck region and liver metastases. The patient underwent resection of the affected tongue area, cervical lymphatic nodes and a salivary gland.
Results: Macroscopically there was a sharply demarcated, superficially ulcerated nodule on the tongue surface with the size of 32x22x20mm, composed of multiple lumps, pale yellow to whitish colour, solid consistency. Microscopically the tumour had trabecular growth pattern with solid nests, oval to polygonal cells with nuclear chromatin of "salt and pepper" appearance, with multiple mitoses. Immunohistochemistry demonstrated expression of neuroendocrine markers (chromogranin, synapthophysin, CD56), positivity for AE1/3, negativity for CK17, strong proliferative index (Ki-67 >80%).
Conclusion: Neuroendocrine carcinoma of the tongue is a rare tumour, with an aggressive behaviour according to the published cases. The conclusion of the case was a primary, poorly differentiated G3 neuroendocrine carcinoma of the tongue with multiple metastases.

E-PS-13-040

Lymphadenoma of salivary gland - cytological and histological challenges

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Background & objectives: Sebaceous&non-sebaceous lymphadenomas of salivary glands are rare. The clinical, histological&cytological characteristics are obscure. In the largest review of 33tumours, a pre-operative diagnosis was impossible. We present 3cases of lymphadenoma from parotid gland where the pre-operative diagnosis didn't reflect the histology.
Methods: Patient1: A 72yr female presented with right parotid lump. FNA was consistent with cyst.
Patient2: A 49yr female with lump in the lower pole of parotid had a cytology diagnosis of intraparotid lymph node.
Patient3: A 57yr male with a lump in the left parotid underwent core biopsy. Following a diagnosis of malignancy surgery was performed.
Results: Subsequent surgical specimens showed similar features. A well circumscribed cystic and solid lesion surrounded by lymphoid tissue. The cyst was lined by squamous and oncocytic type of cells and multiple islands of non-keratinising squamous epithelium were identified within the lymphoid tissue. A second opinion was sought for patient one. The other two cases were assessed by a pathologist with an interest for salivary gland disease.
Conclusion: Our cases confirm:
a)The clinical-cytological and pathological difficulties in reporting lymphadenoma of salivary glands,
b)Possibility of misdiagnosis on FNA&core biopsy as there are no remarkable features that distinguish lymphadenoma from other parotid tumours. -Pathologists, to consider lymphadenoma in the differentials.

E-PS-13-042

The rare oncocytic variant of mucoepidermoid carcinoma (OMEC): a case report with clinical, immunohistochemical and morphological features

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Background & objectives: Recognition of OMEC is important because most other salivary gland lesions with oncocytic features are benign. Here we report a case of OMEC of right soft palate, which is considered as a rare site compared to other major salivary glands.
Methods: An excisional biopsy of the right soft palate was performed at one of the tertiary care hospital. The specimen was submitted for histology. After fixation in formalin solution, and inclusion in paraffin, 3–5 μm sections were stained with H&E for conventional evaluation. Morphologic features such as presence of mucin containing cells, and >60% population of the oncocytic cells were assessed.
Results: Permanent sections stained with H&E revealed a neoplasm that had replaced a wide area of the right soft palate. Morphological features included nests, trabeculae and aggregates of polygonal shaped cells. These cells had moderately pleomorphic nuclei, focally prominent nucleoli, and abundant amount of granular eosinophilic cytoplasm. OMEC must accounts for >60% of the oncocytic cell population. Occasional cells containing intracytoplasmic mucin which were highlighted by special stain mucin.
Immunohistochemical stains were performed and demonstrated cytokeratin-7 strong positivity. There was patchy positivity of p63 and p40 in the neoplastic cells. Thus, the final diagnosis was that of salivary gland neoplasm with extensive oncocytic change and admixed mucocytes favouring oncocytic mucoepidermoid carcinoma.
Conclusion: Mucoepidermoid carcinoma composed of exclusive oncocytes and rare mucocytes is a rare morphologic variant. Oncocytes are large epithelial cells that contain bright eosinophilic, granular cytoplasm & can potentially be confused with oncocytoma or oncocytic carcinoma. Diagnosis of all oncocytic lesions is important for correct treatment. A pathologist must remain aware of the rare diagnosis of OMEC of the palate which has a good prognosis according to the recent studies.

E-PS-13-043

Eosinophilic ulcer of the tongue: a case and confusing clinical entity

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Background & objectives: Eosinophilic ulcer of the tongue is a rare self-limiting chronic and benign ulcerative lesion often misdiagnosed as oral malignancy. Its etiopathogenesis is not clear, but trauma plays an important role in the development.
Methods: Here we report a case of eosinophilic ulcer in 74- year old woman, which presented with a symptomatic ulcer on the right lateral border of the tongue. Clinically, the lesion manifests as an isolated ulcer with indurated borders and a yellow fibrinous floor. A biopsy is indicated to rule out malignancy.
Results: We received a fragment measuring 1.4x0.7cm. Histopathological examination showed an ulcerated surface of the lingual mucosa. The background of this ulceration is characterized by the presence of fibrino-leucocytic exudate associated with a dense and pleomorphic inflammatory infiltrate with several eosinophils with sheets of lymphocytes, plasma cells and neutrophils extending deep into the mucosa and submucosa, underlying muscle. No cellular atypia was observed. The diagnosis of eosinophilic ulcer of the tongue was retained.
Conclusion: Eosinophilic ulcer of the tongue is a rare chronic benign ulcerative lesion often misdiagnosed as oral malignancy. Its histogenesis remains controversial. Generally surgical excision resolves it spontaneously within few weeks. Histopathological evaluation is essential for its definite diagnosis.

E-PS-13-044

Plasmatocytoma of the right tonsil. A case report with a short review of the current literature

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Background & objectives: Extramedullary plasmacytoma (EMP) is a rare neoplasm that occurs outside of the bone marrow. EMP usually occurs in the head and neck region (80%), with the nasopharynx and sinonasal cavities being the most common. Involvement of the tonsil is unusual.
Methods: A 58-year-old man presented with a history of discomfort during swallowing of 10 days duration. On clinical examination there was a firm swelling in the right tonsillar area. His medical history was unremarkable. A biopsy of the right tonsil was performed.
Results: Histologic examination showed a monotonous infiltrate composed of discohesive plasma cells characterized by eccentrically placed round nuclei. Immunohistochemical staining revealed reactivity for CD138, CD56, CD79a, EMA, bcl-2. Tumour cells were CD20, CD30, bcl-6, CD5, CD 10, CD15, AE1/AE3 negative. A diagnosis of extramedullary plasmacytoma was made.
Conclusion: The exact incidence of EMP is unknown, but they are rare, accounting for only 3%-4% of all plasma cell malignancies. The diagnosis of tonsillar EMP is important not only because it is a rare neoplasm but also because it mimics many reactive lesions and malignant neoplasms at this site. FNA may provide inconclusive results. Immunohistochemistry played a crucial role in differentiating it from other conditions involving plasma cells. Solitary EMP is managed with radiotherapy, surgery, or both.

E-PS-13-046

Primary malignant melanoma of the mandible: a rare entity

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Background & objectives: Primary malignant melanoma of the jaw is a rare neoplasm and it occurs more frequently in the oral mucosa of the maxilla. We present a case of a thirty-six year old woman diagnosed with melanoma in the mucosa of mandible.
Methods: A specimen of partial mandipulectomy 10.5x8x5.7 cm with four teeth and the surrounding soft tissue, was received. On macroscopic observation, a non-circumscribed dark-coloured lesion covering a surface area of 3x2.7cm at the retromollar fossa was described. All margins were coloured with various inks. The tissue was fixed in 10% buffered formalin, routinely processed, 2–4 μm sections were stained with H-E.
Results: Invasive oral melanoma composed of sheets of epithelioid pleomorphic cells with distinct nucleoli and geographical necrotic areas was observed. Atypical giant cells, melanin pigment and ulceration of the mucosa were also identified. The neoplastic cells invaded the submandibular bone and the soft tissue of the oral cavity. The excisional margins were negative. Mitotic rate was estimated 11 mitoses/mm2. Immunohistochemistry confirmed the diagnosis of malignant melanoma: S100 (+), MelanA (+), HMB-45 (+), p16 (+), C-KIT (+).
Conclusion: Based on the fact that no melanoma was reported either in patient's medical history or during clinical examination, all findings favoured the diagnosis of Primary Malignant Melanoma of the jaw.

E-PS-13-047

Adenoid cystic carcinoma in unusual sites: case reports

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Background & objectives: Adenoid cystic carcinoma (ACC) is a rare form of adenocarcinoma that commonly arises in the major and minor salivary glands of the head and neck. It can also occur in the breast, Bartholin gland or other locations in the body.
Methods: Three cases of adenoid cystic carcinoma, arising from the breast, Bartholin gland and external auditory canal were studied . Based on H&E features, further IHC studies, comprising AE1/AE3, p63, S100, CK7 and CD117 were carried out. Additional IHC markers, ER, PR and HER2/NEU were performed for the breast lesion. All the cases were reported digitally using Aperio Image Scope.
Results: The tumour element was seen arranged around cyst-like spaces, containing basophilic mucinous content and lined by uniform, monotonous appearing cells, with centrally placed nuclei. Focal areas of cribriform pattern and tubular differentiation streaming through a fibro collagenous framework were noticed in all the three lesions. Very occasional mitotic figures were observed.
Epithelial cells were strongly positive for AE1/AE3 and CK7. S100 and p63 highlighted the myoepithelial element. CD117 showed strong positivity for both the cribriform and the tubular component. ER, PR and HER2/NEU were negative for the tumour cells in the breast lesion.
Conclusion: It has to be stated that though rare in occurrence, a primary adenoid cystic carcinoma arising in unusual sites like the vagina, originating from Bartholin gland or from the breast or from the external auditory canal have been documented in literature. This should be considered in the differential diagnosis of malignant lesions of vagina, breast and external ear canal for proper management protocols.

E-PS-13-048

P16 positive basaloid carcinoma of tonsil: a case report

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Background & objectives: Basaloid squamous cell carcinoma (BSCC) is an uncommon, aggressive variant of squamous cell carcinoma. Tonsils are an uncommon site of occurrence of BSCC. p16 positive basaloid carcinoma of tonsils is rare and not many cases have been documented in literature.
Methods: A 38- year old male presented with a 2-month history of enlarged, fungating right tonsil along with right cervical lymphadenopathy. Multiple biopsy bits of the tonsil, measuring 9mm in aggregate was received. Based on H&E features, further IHC studies, comprising 34βE12, p63, p16, CK5, BCL-2, and Ki-67 were carried out and the slides were reported digitally using Aperio Image Scope.
Results: A severe degree of erosion of the surface, along with prominent malignant basaloid element arising from the stratified epithelium was noted. Individual basaloid cells with enlarged nuclei, dense in nature without prominent nucleoli were observed, along with scattered mitotic figures. Underlying lymphoid tissue shows evidence of lymphoid hyperplasia with formation of germinal centres in many foci. IHC showed intense positivity for p16, 34βE12, CK 5, BCl-2 and p63 for the basaloid cells in the epithelium and subepithelial tissue. Ki-67 showed a high proliferative index of 60%.
Conclusion: Expression of p16 in basaloid variant of tonsillar carcinoma is very rare and denotes an aggressive behaviour due to HPV association. The prevalence and association of p16 has been well documented in oral squamous cell carcinoma. HPV serology in such cases can throw further insight to the type of HPV involved.
p16 analysis of tonsillar carcinoma is warranted in all cases for effective management.

E-PS-13-049

Myositis ossificans of masseter muscle: a rare case report

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Background & objectives: Myositis Ossificans is non-neoplastic, dystrophic calcification followed by heterotopic ossification of an intramuscular connective tissue, predominantly associated with trauma. Its involvement of the masticatory muscles is rare. The present case elaborates the histopathology of myositis ossificans and its clinical correlation.
Methods: This study is about a 32-year-old-male presenting with trismus and past history of trauma. Clinical examination revealed a well-defined, tender, hard swelling over the right cheek. Contrast enhanced CT scan suggested ossified right masseter muscle.
Results: Gross examination showed multiple grey-white, firm to hard tissue bits. Histopathological study revealed residual degenerated muscle fibres undergoing diffuse fibrosis surrounded by spicules of woven bone, along with focal areas of lamellated, uncalcified bone. Spicules of lamellar bone with well-formed medullary cavity containing haematopoietic elements were also noted. The diagnosis was given as myositis ossificans of masseter muscle.
Conclusion: Myositis ossificans of masseter is a rare entity causing trismus and reduced oral hygiene, leading into reduced quality of life. A detailed histopathological examination can confirm the diagnosis and improve prognosis.

E-PS-13-050

Analysis of P16, CDK4 and PTEN immunoexpression in oral melanocytic nevi and melanomas

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Background & objectives: This study aimed to investigate the immunohistochemical expression of p16, CDK4 and PTEN proteins in oral melanocytic nevi and oral melanomas.
Methods: Immunohistochemistry studies for the proteins p16, CDK4 and PTEN were conducted in 42 samples of oral melanocytic nevi and five cases of oral melanoma. Immunoexpression was evaluated semi-quantitatively and stratified into scores: 0 (negative expression), 1 (<5% positive cells), 2 (6-50% positive cells), 3 (>50% positive cells). To compare variables, appropriate statistical tests were used ($p < 0.05$ was considered significant).
Results: CDK4 exhibited nuclear expression score 2 in 20 (47.6%) cases of oral melanocytic nevi and score 3 (> 50%) in 22 (52.4%) cases. In oral melanomas, this expression was categorized as score 3 (> 50%) in all cases. p16 showed low nuclear immunohistochemical expression in cases of oral melanocytic nevi, with 2 cases (4.8%) being completely negative and 40 cases (95.2%) showing score 1. In the cases of melanoma, the immunohistochemical expression of p16 was notably higher, with all cases showing a score of 2. PTEN showed high cytoplasmic expression (score 3) in 41 (97.6%) of cases of oral melanocytic nevi. All cases of oral melanoma showed PTEN score 3.
Conclusion: In conclusion, CDK4 and PTEN proteins show high immunohistochemical expression in melanocytic nevi and oral melanomas. Whereas p16 protein shows low immunohistochemical expression in oral melanocytic nevi and moderate expression in oral melanomas.

E-PS-13-051
Combined squamous and small cell carcinoma of the larynx
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Background & objectives: We report a case of a combined squamous and small cell carcinoma (CSCC) of the larynx, which is extremely rare and a diagnostic challenge.
Methods: Clinical history, radiological exams, macroscopic and histological features have been reviewed.
Results: 69-year-old man, heavy smoker, presenting with 6-month history of hoarseness/haemoptysis. Laryngeal mass biopsy revealed a basaloid squamous cell carcinoma (SCC). Endoscopic resections were performed. Pathological examination showed a tumour composed of small round cells containing finely granular, hyperchromatic nuclei, inconspicuous nucleoli and scant cytoplasm, distributed in nests/sheets; mitotic count was high. These cells expressed neuroendocrine markers (synaptophysin and NSE); Ki67 >80%. Additionally there was in situ and invasive SCC (p63 and cytokeratin 5/6 positive). The diagnosis of combined squamous and small cell carcinoma was rendered. Neck dissection revealed one metastatic lymph node with both components. No distant metastasis was found. The patient underwent radiotherapy.
Conclusion: Laryngeal CSCC has been rarely reported. Diagnosis depends on pathological and immunohistochemistry markers. Should be distinguished from atypical carcinoid, basaloid squamous cell carcinoma, amongst others. Accurate diagnosis of the histological nature of these tumours is imperative to ensure optimal therapy.

E-PS-13-052
Molecular profiling of salivary duct carcinoma (SDC) reveals a novel HMGA2 – SMR3B fusion – a case report
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Background & objectives: SDC is a rare salivary gland malignancy of dismal prognosis without effective systemic therapy or predictive biomarkers. SMR3B encodes saliva-isolated opiorphin involved in pathogenesis of triple-negative breast cancer.
We present a case of SDC ex pleomorphic adenoma harbouring HMGA2-SMR3B fusion.
Methods: 54-year old male presented with palpable submandibular nodule for 4 weeks. MRI revealed polycyclic tumour of 55mm, adjacent to deep lobe of parotid gland. Lung metastases where detected by PET-CT. The patient underwent parotidectomy and surgical biopsy of a lung nodule.
FFPE tissue was used for targeted NGS using FusionPlex Comprehensive Thyroid&Lung(CTL) Kit and FusionPlex Sarcoma Kit sequenced on MiniSeq(Illumina).
Results: Macroscopic examination revealed partially encapsulated tumour of the parotid with calcification and necrosis. Microscopically, peripherally located ductal structures embedded in a hyalinized parenchyma corresponded to pleomorphic adenoma histology with focally atypical features (carcinoma in situ). Centrally, classic SDC morphology with comedonecrosis and highly atypical apocrine cells could be observed. Abrupt spindling of carcinomatous component and gradual transformation to sarcoma were histologically and immunohistochemically apparent.
Metastatic focus in the lung corresponded to the sarcomatous component. A novel fusion HMGA2[3]–SMR3B[3] was detected using panel FusionPlex® Sarcoma Kit. The presence of HMGA2 genetic alteration confirmed pleomorphic adenoma origin. Analysis with panel FusionPlex CTL Kit didn't reveal any potentially targetable genomic abnormalities.
Conclusion: Dedifferentiated SDC should not be confused with sarcomatoid SDC or carcinosarcoma for treatment purposes.
The significance of SMR3B rearrangement in salivary gland malignancies warrants further investigation to determine its possible role as a potential prognostic biomarker of dedifferentiation and/or poor outcome. Due to molecular similarities between SDC and predominantly triple-negative apocrine breast carcinoma, investigation of the latter might generate useful hypothesis for the former.

E-PS-13-053
Giant laterocervical sialolipoma: an unusual case of a very rare benign tumour
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Background & objectives: Sialolipoma is a recently described benign tumour of the salivary glands composed of a proliferation of mature adipocytes within normal salivary parenchyma. It a rare variant of salivary lipoma as there are just around 60 cases reported to date.
Methods: Sialolipoma can affect both major and minor salivary glands and is more frequently reported in older male patients. The aim of our study is to gain further insight into this very rare entity by evaluating localization, histopathological characteristics and differential diagnosis with other head and neck tumours.
Results: We report the case of a 62 year old male with a a giant laterocervical lipomatose mass. The ultrasound suggested a benign fatty tissue tumour which was then surgically removed. However, on histopathological examination, the diagnosis of sialolipoma was established.
Conclusion: Sialolipoma is usually located in the parotid gland, followed by the palate for minor salivary glands. Major gland sialolipoma occurs more frequently in males while minor gland sialolipoma is more frequent in females and is usually less than 2 cm in diameter. Therefore a male with 8x5x3 cm laterocervical sialolipoma probably arising from a minor salivary gland is extremely unusual for a tumour that is particularly rare anyway. Histopathology remains the only means of establishing the diagnosis in such cases.

E-PS-13-054

Primary sinonasal malignant melanoma: a case report

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Background & objectives: Malignant melanoma of the sinonasal mucosa is a rare tumour, and is more aggressive than its cutaneous counterpart. Primary malignant melanoma of nasal cavity arise from melanocytes located in the mucous membrane and only 0.5% arises in nasal cavity.
Methods: A 65 year-old female patient presented with epistaxis at the ENT Department of our hospital. The CT scan revealed a polypoid mass in the left nasal cavity extending to the nasopharynx. The mass was excised surgically.
Results: Gross findings consist of multiple brown-black soft tissue pieces together measuring 5,7x1,7 cm. Histologically, the epithelioid, variable sized tumour cells were arranged in nests and pseudopapillae, had prominent nucleoili, intracytoplasmic granules of melanin and high mitotic activity. Areas of necrosis were also recognized. Immunohistochemically the tumour cells showed positivity to S100p, Melan A, SOX10, MITF and negativity to HMB45, BRAF, AE1/AE3, CD34, GFAP and Synaptophysin. Postoperative radio-therapy was given to the patient but some months later liver metastases were found.
Conclusion: Rarity of this lesion warrants its mention and emphasizes the importance of considering malignant melanoma among the differential diagnosis of tumours of nose and paranasal sinuses. The prognosis is extremely poor and nodal and distant metastases are common, so early diagnosis and surgical treatment offer the only possible hope of survival and therefore, attention must be paid to the minor nasal symptoms at the earliest.

E-PS-13-055

Neuroendocrine carcinoma of tonsil-case report

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Background & objectives: The diffuse neuroendocrine system (DNES) is composed of cells with neuroendocrine secretory granules. Members of the DNES commonly express neuroendocrine markers by immunohistochemistry and may express a variety of peptide hormones.
Methods: The small cell variant of poorly differentiated neuroendocrine carcinoma, WHO grade 3 of the tonsil is extremely rare. The prognosis is poor. We present a 67-year-old male with symptoms of swallowing difficulty and pain in the right tonsil. After clinical examination right-sided tonsillectomy was performed.
Results: Pathohistological examination showed the presence of high grade malignant cells and with positive immunohistochemical markers related to neuroendocrine differentiation. The final diagnosis was small cell variant of poorly differentiated neuroendocrine carcinoma WHO grade 3 of the tonsil.
Conclusion: Although rare, neuroendocrine carcinoma (NEC) of the tonsil may occur with respect to the distribution of DNES. Poorly differentiated carcinoma with high nucleus to cytoplasm ratio suggest importance for immunohistochemistry analysis for neuroendocrine markers for final diagnosis.

E-PS-13-056

An unusual finding in a pleomorphic adenoma – a case report

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Background & objectives: A 49 year old female without any significant medical history presented with a 1cm nodular lesion in the right upper lip. Following excision, the lesion was sent for histopathological examination.
Methods: Histology showed lobules of bland plasmacytoid cells with a hyalinised and amorphous background in keeping with amyloid. Focally, muco-myxoid stroma, myoepithelial cells, and bilayered ductal structures in keeping with a pleomorphic adenoma appearance were seen.
Results: Immunohistochemistry showed diffused staining for AE1/AE3 and variable positivity for CK7 and CK5/6. SMA and p40 highlighted myoepithelial cells in this region. S100 was diffusely positive in the plasmacytoid cells but restricted to the abluminal cells within the bilayered areas. The hyalinised and amorphous background stained positive with Congo red and showed strong and diffuse birefringence under polarised light. The Ki67 proliferation index was less than 5%.
Conclusion: A definitive diagnosis of a pleomorphic adenoma with amyloid deposition was made. Only a few cases have been reported in the literature. Our case highlights this rare diagnosis and the importance of clinicopathological correlation to rule out systemic amyloidosis.

E-PS-13-057

A case of pleomorphic adenoma of the parotid gland in a patient of nodular sclerosis classical Hodgkin lymphoma

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Background & objectives: Hodgkin lymphomas are group of lymphoid tumours where as pleomorphic adenomas are benign mixed salivary gland tumours. Malignant lymphomas have a frequent appearance in the head and neck region, however malignant lymphomas of the parotid region is relatively rare.
Methods: Representative specimens were sent from Neck mass/parotid swelling and enlarged neck nodes from right and left side of neck. Gross sectioning and subsequent microscopic examination was performed.
Results: Sections examined from Parotid gland(left side primary tumour) shows a neoplastic lesion composed of epithelial component in a myxoidy background consistent with pleomorphic adenoma. Sections examined from Left Neck level lymph nodes' reveal lymph nodes exhibiting effaced architecture. The lymphoid population is predominantly composed of lymphocytes, histiocytes, plasma cells and occasional eosinophils and neutrophils. Scattered large atypical mononuclear cells and few Reed Sternburg like cells are also seen. Areas of sclerosis and occasional fibrous septae are also present. These cells were positive for immunohistochemical stains CD30 and CD15. These findings were consistent with Nodular sclerosis classical Hodgkin lymphoma.
Conclusion: We report a rare case of Pleomorphic adenoma in a patient of Nodular sclerosis classical Hodgkin lymphoma; Large scale surveillance studies are suggested to truly establish and quantify the risk for development of Pleomorphic adenoma in patients suffering from Nodular sclerosis classical Hodgkin Lymphoma.

E-PS-14 History of Pathology

E-PS-14-001

Gusman Bella Solomonovna - the founder of the school of childhood infectious pathology in Russia

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Background & objectives: Gusman Bella Solomonovna (12/11/1921–08/01/1983)-leading pathologist of the Soviet Union. Head, Laboratory

of Pathanatomy of Childhood Diseases, Institute of Human Morphology, USSR Academy of Medical Sciences (1976–83). Under the guidance of Academician A.I.Strukov, she defended her doctoral dissertation on the topic "Immunomorphology of some childhood infections"(1970).
Methods: In our research we used historical data and student memories.
Results: B.S. Gusman demonstrated for the first time that the reaction to the development of a tumour in the central nervous system proceeds in two phases: in phase 1,activation of the thymus, lymph nodes and spleen; subsequently, during blastomogenesis in the central nervous system, there is an inhibition of the reaction of immunogenesis organs. She studied the issues of paediatric pathology, experimental pathomorphology of some infectious diseases (ornithosis, infection with L-forms of bacteria: mycoplasmosis). B.S. Gusman is the author of more than 120 scientific papers, including two monographs, several chapters in the manual "Pathological anatomy of diseases of the foetus and child" and guidelines for the diagnosis of acute respiratory infections in children.
Conclusion: Under the direction of B.S. Gusman defended 4 doctoral and 15 master's theses. A distinctive feature of B.S. Gusman was a combination of a thoughtful erudite researcher and scientist, a charming woman and a friendly teacher.

E-PS-14-002
Diagnostic re-evaluation of wet and dry specimens of aneurysms from the pathology museum of Turin
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Background & objectives: The Pathology Museum of Turin houses dry and wet specimens of vascular pathology dating back to the end of XIX century and the beginning of the XX century. A study of these cases was carried out to re-evaluated the diagnosis.
Methods: Among the wet specimens of the Pathology Museum of Turin there are 9 cases of aneurysms, most of them of aorta. Among the 23 dry specimens of the collection two recently restored cases of aortic aneurysm were selected. The macroscopic study of wet specimen was carried out. Histological study was also performed in selected cases. Dry specimens were studied radiologically.
Results: The original diagnosis of wet specimens was confirmed in all cases. One of the dry specimen was confirmed to be a case of tuberculous abscess instead of an aneurysm, as hypothesized in a previous study.
Conclusion: These cases show particularly severe old aneurysms, now no longer observable for medical advances. Therefore these specimens are a
historical heritage important to preserve for didactical purpose.

E-PS-14-003
Activity of the soviet pathologist Vladimir Gerasimovich Molotkov during the Great Patriotic War
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Background & objectives: This work is dedicated to one of the most outstanding pathologists of the Smolensk region (USSR) - Vladimir Gerasimovich Molotkov.
He was born on 28/06/1903 in Vitebsk province.
Methods: After graduation from the Medical faculty of Smolensk University he worked at the Department of Pathological Anatomy. MolotkovV.G. headed laboratory No.3776 in the Western front in 1941-1944 as the Chief Pathologist of the front. Then in 1944-1945 he performed the same duties in the 3rd Belorussian front. V.G.Molotkov participated in the exhumation and post-mortem examination of Lieutenant General M.G.Efremov.
Results: He performed autopsy of the 3rd Belorussian front Commander General I.D. Chernyakhovsky. V.G.Molotkov was engaged in identifying of self-harming soldiers, who intentionally damaged their hands to leave the front. The study of a combat hand injury with rejection of the stereotype that a victim with a similar injury is a potential self-harmer has significantly improved the quality of medical care provided to them and reduced the percentage of subsequent disability.
Conclusion: V.G.Molotkov is the author of the Chapter "Pathological anatomy and pathogenesis of nephritis" in the 22nd volume of the book "the Experience of Soviet Medicine in the Great Patriotic War of 1941-1945".
V.G.Molotkov was dismissed from the armed forces as a Lieutenant Colonel of the medical service. For services to the Fatherland he got many significant military awards. Since 1946 he became the Head of the Department of Pathological Anatomy of Smolensk State Medical Institution till his death on 14/02/1976.

E-PS-14-004
Contribution of N. I. Pirogov in the development of pathological anatomy
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Background & objectives: Nikolai Ivanovich Pirogov - the great Russian doctor of the XIX century, was multilaterally developed specialist: surgeon, anatomist, teacher, public figure. He made an equally great contribution to the development of pathological anatomy.
Methods: Study of data from various Russian medical and historical archives.
Results: In Derpt in 1828-1833 N.I. Pirogov during experimental studies and autopsies drew attention to the variety of pathological processes in the body. In 1829, Pirogov published a work devoted to the anatomical and pathological description of the femoral-inguinal region, in this work a description of clinical and pathological disorders resulting from ligation of the abdominal aorta is given. During a business trip to Berlin and Göttingen(1833-1835) N.I. Pirogov produces a large number of autopsies, while he believed that German doctors and surgeons of that time were little acquainted and not sufficiently interested in the most basic pathological processes. In 1852, N.I. Pirogov in his "Anatomical and Pathological Lecture" notes the existence of various forms of tuberculosis and the presence of multinucleated cells.
Conclusion: In the Anatomical and Pathological Lecture (1852), Pirogov told about shock, bleeding, purulent processes, the consequences of gunshot injuries.
N.I. Pirogov attached great importance to the study of biopsies. These his judgments were given in the works of 1849-1855, before the cellular pathology of R. Virkhov. Literally every clinical work of N.I. Pirogov is inlaid with morphological data in order to create a complete picture of the pathological process and reveal its pathogenesis.

E-PS-14-005
The history of development of histochemistry and electron microscope in the world in USSR and RF
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Background & objectives: Histochemistry and electron microscopy occupy a worthy place among doctors and biologists for diagnostics and solving fundamental problems.
Methods: Work with archive, materials, textbooks and monographs.
Results: The development of histochemistry in USSR (Bukhvalov I., Korzhevsky D.) and Russian Federation (Petrov S. and Raikhlin N.,

Frank G., Atyakshin D.) has a specific value. First Russian electron microscope was created in 1942 in Leningrad, USSR. The laboratory of electron microscopy of Blokhin's Oncological centre (Raikhlin N., Bukhvalov I.) made an important contribution in development of this direction. Now the laboratories are working at Kazan Federal University, Belgorod State University and a number of others.
Conclusion: The histochemistry and electron microscopy can solve problems in oncology, virology and bacteriology, transplantology and in some other directions.

E-PS-14-006
The questionnaire portraits of four Russian pathologists
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Background & objectives: This work has the purpose to collect and systematize the biographical data for Academician Innokentiy Vasilievich Toroptsev, Academician Alexey Ivanovich Abrikosov, Professor Mikhail Mikhaylovich Averbakh and Professor Vsevolod Dmitrievich Tsinzerling.
Methods: According to the questionnaires prepared by me.

Questionnaire portrait of the Russian pathologist, scientist and educator, academician of the Academy of Medical Sciences of the USSR, Professor Innokentiy Vasilievich Toroptsev (14.09.1907–22.10.1985)
Results: Born at the station Slyudyanka of the Krugobaikalskaya Railway in the family of a railroad employee. After the Civil war he studied in the Soviet labor school and graduated in 1926; graduated from the Tomsk Medical Institute (TMI) (1931). Since the 4th course became interested in the issues of pathological anatomy and in their free time actively involved in practical work of pathologist.
Conclusion: Defense of the master's thesis on "Sclero-pigmentary nodules in the spleen" under the leadership of Prof. V.P.Mirolubov (1937), doctoral defense – on the topic "Materials to the problem of bactericides of plant origin (phytoncides)" (1947). Assistant (1932–40), associate Professor (1940–47), Head (1947–84), Department of Pathological Anatomy, TMI; Rector, TMI (1958–1974); Head, Tomsk regional pathoanatomical Bureau; retirement (1984). The first time he had been given the morphological characteristics of magnetobiological effects identified serious structural changes and functional changes in various body systems under the action of constant, variable and pulse magnetic fields of varying intensity. Research interests: Oncopathology, the study of the biological actions of magnetic fields of different intensity, the morphological characteristics of magnetobiological effects, etc. The author of more than 134 works, including 5 monographs and 60 inventions. Distinctive trait: Possessed impeccable technique of post-mortem autopsies, wide erudition, demanding to himself and his employees. Hobbies: Music, painting, literature, hunting. Died in Tomsk at the 79th year of his life.

Alexey Ivanovich Abrikosov - outstanding Russian pathologist, scientist and educator (18.01.1875– 09.04.1955)
Results: He was born in Moscow in a family of large entrepreneurs. Married for the second time. Wife: Abrikosova (Wulf), Faina Davidovna. Children: Alexey (academician of the Academy of Sciences of the USSR; winner of the Nobel prize in physics; died March 29, 2017 in the USA), Maria; Ivan and Andrey from the 1st marriage. He graduated from a private gymnasium, with honours from the Medical Faculty of Moscow University and continued his studies in clinics in Europe.
Conclusion: The defense of his doctoral dissertation on topic "On the first anatomical changes in lungs at the onset of pulmonary tuberculosis" brought him world fame. Head of Pathology Department of 1st Moscow State University, etc. Professor, academician of the Academy of Sciences of the USSR, Hero of Socialist Labor and was awarded various domestic and foreign awards. He participated in autopsy of body of V.I. Lenin, as well as other high-ranking figures of country. Scientific interests: Issues of morphology of pulmonary tuberculosis, allergies, wound infections, diseases of the oral cavity and teeth, military and oncopathology, etc. He is author of more than 100 scientific papers, including a number of monographs, manuals and textbook. Distinctive feature: Exceptional culture, simplicity, personal charm, benevolence, excellent technique of microphotography, as well as the production of histological and museum preparations. He died in the 81st year of his life and was buried at Novodevichy cemetery in Moscow.

Mikhail Mikhaylovich Averbakh – known Russian phthisiopathologist (14.02.1925–06.01.1995)
Results: He was born in Moscow in a family of hereditary doctors on the paternal line. His grandfather, M.I.Averbakh was an outstanding Russian ophthalmologist, academician of the Academy of Sciences of the USSR, founder of the Central Ophthalmological Institute of the Ministry of Health of the RSFSR. Married. Spouse: Ringel-Sementsova Evgeniya Nikolaevna. Children: Mikhail, Andrey. He graduated from high school, the Medical Faculty of 2nd the Moscow Medical Institute with a specialty in "medical business" with honours and full-time postgraduate study at Pathology Department.
Conclusion: Defense of the candidate's dissertation on topic "On the issue of breast cancer in the light of its the hormone therapy" (1953), doctoral dissertation on topic "Pathological anatomy, pathogenesis and classification of pulmonary tuberculomas (based on resection materials)". Junior, Senior Researcher, Head of Laboratory of Experimental Surgery and Pathology, Deputy Director for Scientific Work of Central Research Institute of Tuberculosis of Academy of Medical Sciences of USSR. Professor, Honoured Worker of Science of the RSFSR. Scientific interests: Study of pathogenesis, immunomorphology, immunology and immunogenetics of both tuberculosis and other lung diseases. He is author of more than 350 scientific publications, including 10 monographs. Member of the Board of All-Union Scientific Medical Societies of Pathologists and Phthisiatrists, etc. Distinctive feature: Kindness, politeness, and decency. He died at age of 70th year of life from exacerbation of coronary heart disease and was buried at Vvedenskoye cemetery in Moscow.

Vsevolod Dmitrievich Tsinzerling – well-known Russian pathologist, scientist, and educator (20.09.1891-16.02.1960)
Results: Born in St. Petersburg. Studying at the Military Medical Academy (MMA), during which he showed great interest in scientific work, actively engaged in the circle at the Pathology Department, where performed 2 scientific works, one of which was awarded the Academy Gold Medal. The award allowed him to set up a histological laboratory at home. Expelled from the IV course due to the temporary closure of the MMA after a student riot. During a short vacation passed the tests at Tartu University and received a senior doctor with honours.
Conclusion: Awarded the degree of Doctor of Medical Sciences without defending a dissertation. Drafted into the army as a Junior resident of the 1st infirmary of the 23rd infantry division. Dismissed "in the primitive state" and worked only as a pathologist, combining activities in both medical and research institutions. Arrested as a "socially dangerous element" and sentenced to exile, but thanks to vigorous petitions to various instances of colleagues, the sentence was cancelled. Chief Pathologist of the Northwest and Leningrad Fronts. Head, Pathology Department, II Leningrad Medical Institute. Research interests: Alimentary dystrophy, atherosclerosis, pneumonia, infectious diseases and wartime pathology. He died in Leningrad at the 69th year of his life from lung cancer.

E-PS-15 Infectious Diseases Pathology

E-PS-15-001
Immunocompetent sphenoid mucormycosis

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Background & objectives: The infections caused by fungi, like a mucormycosis, are uncommon, but are significant due to their aggressive nature, for the challenge of diagnosis and high mortality (40 - 100%), despite the antifungals and medical therapy currently available. It should be considered a differential diagnosis of synovial diseases in immunocompromised patients and an appropriate histopathological investigation should be performed. The article aims to describe and discuss case of sphenoid mucormycosis in immunocompetent patient.
Methods: Male, 62 years old, shows frontal, pulsatile and daily headache. Cranial tomography (CT) suggests inflammatory sphenoid sinusopathy associated with fungi. Unspecified clinical treatment was performed. Five years later, headache returns. CT shows continuous expansive infiltrative formation at the base of the skull. Transsphenoidal surgery was performed, using the chordoma hypothesis. Anatomopathological: fungal colonization, suspected mucormycosis. After investigation, immunocompetence was confirmed.
Results: Mucormycosis is an invasive, rare and severe fungal infection. Acquired with inhalation of microorganisms of the order Mucorales present in the decomposing organic material. It presents with invasion of paranasal sinuses, common jaw, sphenoid changes, cavernous sinus, orbits and cranial cavity. Uncommon in the immunocompetent. As signs and symptoms can be observed: fever, nasal ulcer, periorbital or facial oedema, decreased visual acuity, ophthalmoplegia and headache.
Conclusion: Mucormycosis has an atypical presentation in individuals without immune compromise. Requires early diagnosis and immediate treatment due to high mortality. Association between surgical and clinical therapy is decisive for the prognosis.

E-PS-15-002
Rare case of mucosal leishmaniasis simulating peritraqueous recurrence of squamous cell carcinoma of the larynx

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Background & objectives: Mucosal leishmaniasis(ML) appears after the healing of cutaneous leishmaniasis. We report a case with ulcero-infiltrative lesion in the tracheostoma area 10 years after laryngectomy due to laryngeal squamous cell carcinoma (SCC), whose biopsy was negative for neoplasia and amastigotes were identified.
Methods: A 59-year-old man from Manaus (North of Brazil) underwent laryngectomy and tracheostomy for glottic SCC in 2007.In 2017, he presented an ulcero-infiltrative lesion, bleeding in the peritraqueostoma region adjacent to the tracheoesophageal prosthesis. Incisional and endoscopic biopsy was performed, which showed subacute inflammation and absence of neoplasia. Due to suspected recurrence, the tracheoesophageal prosthesis was removed and a new biopsy was performed.
Results: ML in North of Brazil is caused by Leishmania braziliensis and represents the reactivation of a parasitized macrophage metastasized to the cartilage during primary infection. Differential diagnosis includes neoplasm and granulomatous diseases. Tumour recurrence in the tracheostoma area after resection of SCC of the larynx is a serious complication. The analysis of the histological preparations obtained from the biopsy showed pseudoepitheliomatous hyperplasia, sections of ulceration with formation of granulation tissue and, in the chorion, the presence of isolated or aggregated Leishmania amastigote forms within some macrophages. Thus, the diagnostic conclusion was ML. The samples were negative for neoplasia. Patient was treated with liposomal amphotericin and is well, with no evidence of disease.
Conclusion: Rare case of ML simulating tumour recurrence demonstrates the need for the clinical-epidemiological diagnosis and laboratory confirmation of the disease in order to establish the diagnosis and enable adequate treatment of the patient, as demonstrated in the reported case.

E-PS-15-003
Gastrointestinal basidiobolomycosis in a young adult patient: a case report

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Background & objectives: Basidiobolomycosis is a rare infection caused by the fungus Basidiobolus ranarum. It usually affects the subcutaneous tissue. Gastrointestinal involvement is rare with few reported cases. It typically affects immunocompetent patients. Diagnosis may be delayed due to non-specific clinical presentation.
Methods: The disease may mimic malignancy with mass formation, intestinal mural thickening or ulceration. Disseminated angioinvasion is extremely rare and is usually fatal. We report here a case of an angioinvasive gastrointestinal basidiobolomycosis in a 20-year-old male who had fatal outcome. Increased awareness of this entity will help to enhance early diagnosis and treatment.

E-PS-15-004
Tubal schistosomiasis in a sub-Saharan female: an incidental and unusual finding

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Background & objectives: Schistosomiasis is the second in endemic parasitic diseases in the world and as cause of death after paludism in tropical countries, but numbers are increasing. It also affects travellers and infection of the female genital tract is less frequently described.
Methods: A 25-year-old Malian female desiring a tubal ligation underwent bilateral salpingectomy making use of a caesarean delivery due to a risk of loss of foetal well-being. She lives in Spain since 2015 and she had another caesarean section in 2015 and later she had an eutocic delivery in 2018.
Results: One of the fallopian tubes showed cystic and basophilic oval structures, occasionally calcified, with small nodular formations inside. There was a granulomatous reaction with multinucleated giant cells in the periphery of these structures.
She had no symptoms neither laboratory findings. She denied any suspectful clinical symptoms before, but they treated her anyway with Praziquantel and they discharged her.
Conclusion: Schistosomiasis is a pathogenic helmintiasis that can be contracted by contact with fresh water containing larvae which penetrate human skin. It can prompt infertility or ectopic pregnancies due to the granulomatous reaction leading to mechanical obstruction or tubal fibrosis caused by occlusion of the blood vessels by the eggs of the parasite. Histopathologic examination has shown that eggs can be found most commonly in cervix and vagina but rarely tubal.

E-PS-15-006

Splenic leishmaniasis

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Background & objectives: Leishmaniasis is an infectious disease caused by protozoa that live inside macrophages in mammals. Visceral leishmaniasis (VL) is the severest form of leishmaniasis and fatal if left untreated. In Mediterranean countries, like Spain, it usually occurs in rural areas.
Methods: We present the case of a 71-year-old man from a village in the mountains, who presented with hepatosplenomegaly and pancytopenia. In clinical and radiological examination no other adenopathies were found. Initially, a bone marrow biopsy and aspirate were performed, which showed plasmacytosis with no light chain restriction and absence of parasites, respectively. Flow cytometry showed no monoclonal peak.
Results: Due to the worsening of hypersplenism syndrome, constant fever and progressive weight loss an urgent splenectomy was performed. histological examination of the spleen showed a loss of the normal architecture: disrupted lymphoid follicles sometimes replaced by hyaline deposits, white pulp atrophy, not feasible distinction between red and white pulp and presence of numerous plasma cell aggregates in the red pulp. Intracytoplasmic Leishmania amastigotes were observed with Hematoxilin-Eosin and Giemsa stains, and a polymerase chain reaction confirmed the diagnosis. The patient was treated with amphotericin B showing continuous improvement.
Conclusion: It is important to keep in mind that a negative result in bone marrow aspirate is not definitive to exclude a diagnosis of VL, in fact some studies conclude that splenic aspiration in experienced hands has higher sensitivity compared to bone marrow aspiration. Also, some reports suggest that splenectomy may contribute to the cure of patients with chronic relapsing VL.

E-PS-15-007

An unexpected passenger in a hemithyroidectomy

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Background & objectives: Human muscular sarcocystosis is rare, with fewer than 100 cases reported, a majority from Southeast Asia. Here we report muscular sarcocystosis as an incidental observation in a thyroidectomy specimen in an asymptomatic patient from the United Kingdom.
Methods: A 37-year-old female was referred to the Ear Nose and Throat service with a new right-sided neck lump. She was otherwise asymptomatic. Ultrasound investigation identified a 3.5 x 2.5cm, well-circumscribed nodule in the right lobe of the thyroid, which on fine-needle aspiration cytology revealed features consistent with a follicular neoplasm. The patient went on to have a hemithyroidectomy.
Results: Histopathological examination confirmed a diagnosis of follicular thyroid carcinoma but also identified several sarcocysts in skeletal muscle fibres adjacent to the pyramidal lobe. The patient's travel history was reviewed, which revealed she had visited Tioman Island, Malaysia, in 2010, where the largest outbreak of muscular sarcocystosis reported to date occurred between 2011-2012. Review of 502 muscle biopsy specimens in the Department of Neuropathology, Glasgow, did not identify any additional cases.
Conclusion: Confirmed cases of muscular sarcocystosis are rare. Prevalence in western countries is low and infection in this case was probably acquired in Tioman Island. Symptoms may include myalgia, muscle weakness, fever, and headache, but infection can be asymptomatic. Definitive diagnosis relies on identifying sarcocysts in a muscle biopsy, which should prompt a detailed travel history, if encountered incidentally. There is no vaccine or proven antiparasitic therapy, but anti-inflammatory drugs may offer symptomatic relief.

E-PS-15-008

Visceral leishmaniasis with bladder extension: a human case report

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Background & objectives: Leishmaniasis is a tropical disease caused by an intracellular parasite transmitted to humans by the bite of a sandfly, mainly Phlebotomus and Lutzomyia. It is endemic in circumscribed geographic areas and represents a health problem with a potentially fatal outcome.
Methods: We report the case of an Spanish 49 y/o female, affected by multiple sclerosis and homozygous thrombophilia, that had been diagnosed of systemic leishmaniasis in August 2019, after an insidious clinical picture of fever and anaemia. CT-scan imaging revealed an slightly enlarged liver, moderate splenomegaly and a blurry focal thickening in anterior bladder wall. Cystoscopy and biopsy were highly recommended.
Results: Histologic examination showed groups of transitional cells organized in trabeculae and glandular spaces, with an accompanying chronic inflammatory infiltrate arranged around. There were also frequent intracellular particles that suggested the presence of leishmania in bladder mucosa. The biopsy was referred to the Spanish National Microbiology Center, that confirmed the infection by Leishmania infantum.
Conclusion: Human bladder affectation in systemic leishmaniasis is an extremely rare condition, with few cases described worldwide in the literature. In visceral forms, the diagnosis is usually performed with high sensitivity by observing protozoans through the microscope.

E-PS-15-009

Coinfection of pasteurella multocida and Chikungunya: an autopsy report

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Background & objectives: Pasteurella multocida is a very common pathogen in animals, it has rarely been recognized as an infection of man. Chikungunya fever regarded as a benign disease with infrequent severe manifestations. Report a coinfection by Pasteurella multocida and Chikungunya fever.
Methods: A 32-year-old man, farmer with previously contact with birds on his family farm one year before the symptoms, when there was a massive death of about 150 birds .He started with frontal headache ,retroorbital pain and high fever with eight hours of evolution. He presents rapid clinical worsening, with dyspnoea, hypersecretive airways, hyposaturation, hypotesion and death Autopsy was made.
Results: At the autopsy, cloudy-looking cerebrospinal liquor, bilateral pleural effusion, pulmonary oedema, congestion, and heart with thin echinotic stippling on the surface. Microscopy, lumen of the alveoli with bacteria, macrophages and fibrin, some lymphocitis in septum, hyaline membrane in some alveolis and vessels with thrombus. The pathogen was identified as P. multocida by the culture from liquor. Immunohistochemistry, positivity for Chikungunya vírus. The diagnosis was septic shock with focus of infection, pneumonia.
Conclusion: In summary, P. multocida is an important pathogen in humans, where it can cause serious life-threatening infections and obtaining a detailed patient history about animal exposure is of paramount importance for the diagnosis of infections due to Pasteurella spp. Coinfection between P multocida and Chikungunya may been a determining factor for the severerity of the disease. It´s important to carry out studies to better elucidate this mechanism of interaction.

E-PS-15-010

Infective endocarditis due to actinomyces odontolyticus and penicillium chrysogenum: case report and review of the literature

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Background & objectives: The objective of this report is to present an extremely rare case of tricuspid valve Infective Endocarditis (IE) with a background of perimembranous ventricular septal defect (VSD). *Actinomyces odontolyticus* and *Penicillium chrysogenum* were cultured from the valvular vegetations.
Methods: 55-year-old male with hematemesis. Emergency Medical Services was called. The patient lost consciousness and went into asystole. He was taken to the ER where he was pronounced dead. Past medical history remarkable for VSD in 2002. An autopsy was performed and samples from the vegetations were sent for bacterial and fungal cultures. Special stains were performed on tissue sections.
Results: Examination of the heart revealed a large perimembranous VSD and two smaller adjacent VSD's. Multifocal vegetations were present on the chordae tendinae of the tricuspid valve, extending to the papillary muscle. Samples of the vegetations were sent to the microbiology laboratory. Matrix-Assisted Laser Desorption/Ionization-Time of Flight (MALDI-TOF) analysis identified the bacterium as *A. odontolyticus*. Fungal cultures were positive for *P. chrysogenum.* Special stains (Gram, PAS-D, Silver stains and AFB) revealed bacterial and fungal organisms consistent with the morphology of the reported isolates. Additional findings included pulmonary arterial hypertension, acute and organizing bronchopneumonia, chronic pericarditis with a large effusion and congestive heart failure.
Conclusion: This is the first case reported in the medical literature of IE due to two extremely unusual bacterial and fungal organisms, *A. odontolyticus* and *P. chrysogenum*, respectively. The most important risk factor for IE in this case is VSD. Complications of IE included acute and organizing bronchopneumonia and chronic pericarditis with a large effusion that eventually led to cardiac tamponade and the patient's demise.

E-PS-15-011

Histological diagnosis of opisthorchiasis: an accidental finding

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Background & objectives: A diagnosis of opisthorchiasis represents a clinical problem due to the absence of pathognomonic signs of disease and not informative duodenal juice microscopy (MAb-ELISA). Histological diagnosis allows objectifying clinical diagnosis, even in cases when parasite detection is a morphological finding.
Methods: We report a case of acute opisthorchiasis in a man (age 65). The diagnosis was established during a histological examination of a colon biopsy in a patient with an alleged clinical diagnosis of opisthorchiasis. The patient complained about discomfort in the upper left quadrant of the abdomen and diarrhoea. The pain was regulated by painkillers.
Results: The patient underwent a full examination, but the results of the physical examination were normal. All stool samples were negative. However, the results of the MAb-ELISA test were positive (May 15), so the patient was treated with anti-parasitic drugs (May 23-25). Two weeks after a colonoscopy was performed, and the doctor took tissue samples for biopsy (June 5). Histological examination of a colon revealed fragments of adult flukes, which confirmed the diagnosis of opisthorchiasis. An analysis of the clinical manifestations of opisthorchiasis and the results of laboratory tests indicated acute opisthorchiasis, caused by O. viverrini. The features of this case included moderate pain, diarrhoea, and weight loss of 20 kg.
Conclusion: The infection proceeded according to the type of acute enteritis and colitis, although usually acute opisthorchiasis caused by O. viverrini is asymptomatic or reminds of acute cholecystitis. Fragments of adult flukes were found in the colon mucosa. The foci of reactive inflammation of the mucosa during endoscopic examination reminded a polyp.

E-PS-15-013

Chronic Q fever - a rare disease diagnosed by molecular methods

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Background & objectives: Chronic Q fever is a rare disease caused by Coxiella burnetii and develops months or years following initial Q fever infection. C. burnetii is a fastidious pathogen which cannot be routinely cultivated, thus microbiological diagnosis is challenging.
Methods: Specimens from fistula secretions were evaluated via cytology and culture-independent, panbacterial PCR resolved with next-generation sequencing (16S rRNA gene sequencing).
Results: We report on a case of a 9-year-old female operated because of a valvopathy with pulmonary stenosis in her first year of life. Heart surgery required the use of prosthetic material and the procedure was performed in Kazakhstan. Since the surgery a chronic fistulating mediastinitis was present which did not respond to any therapy and no infectious agent could be identified. However, 16S rRNA gene analysis of specimens from the purulent secretions of the fistulas showed high loads of C. burnetii DNA. This was confirmed by C. burnetii specific PCR from the serum of the patient and C. burnetti specific serology.
Conclusion: We identified a rare case of chronic Q fever in association with prosthetic material after cardiac surgery. C. burnetii has a tropism to thoracic organs (lungs, heart) and normally infection occurs via inhalation of infectious dust or direct contact with C. burnetii carrying animals (goat, sheep). In our case, however, the pathogen was most probably acquired during surgery. Noteworthy, accurate microbiological diagnosis could only be achieved via molecular methods.

E-PS-15-014

Histologic and molecular manifestations of cardiac failure due to Puumala virus infection - an autopsy study

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Background & objectives: Puumala virus is the causing agent of nephropathia epidemica (NE) and has a tropism to endothelial cells. Although acute cardiac failure has been described in Puumala virus infection, a histologic and/or molecular proof of heart infection is lacking so far.
Methods: We report on 2 autopsy cases which were performed because of acute cardiac failure in the setting of Puumala virus infections. Histologic and molecular (RT-PCR) studies from tissues including the heart were performed.
Results: Histology showed the typical interstitial haemorrhages in the medulla of kidneys, a hallmark lesion in Puumala virus infection. In addition, a prominent perivascular lymphomononuclear inflammatory infiltrate was seen surrounding small vessels and capillaries in the myocardium, as well as in the lungs and kidneys. Endothelial cells showed prominent attenuation suspicious of virus mediated endothelial cytotoxicity. No histologic changes of myocarditis, such as immune mediated myocyte damage, were evident. Semiquantitative analysis via RT-PCR showed the highest viral load in the myocardium compared to kidneys and lungs. Interestingly, also multifocal ischemic changes of the myocardium were evident on histology.
Conclusion: Our findings suggest that Puumala virus infects also myocardial vessels (endothelia) to a large extend. The corresponding prominent immune response directed against the infected endothelia might lead to multifocal ischemic damages of the myocardium, thereby leading to the clinically seen sudden cardiac failure.

E-PS-16 IT in Pathology

E-PS-16-001
A survey on digital pathology and safe workplace station awareness amongst histopathology registrars in the West Midlands Deanery - England

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Background & objectives: A badly set up workstation can lead to Computer and visual display terminals syndrome. Histopathology trainees across the west midlands deanery were asked if they were aware of the ergonomics of the digital workstation to prevent repetitive stress injury.
Methods: A survey was sent to west Midlands histopathology registrars, who have been in training for at least 1 year (ST2 till ST6), via google form. ST1 were excluded from the survey as they would not have had enough time to be exposed to digital pathology.
Results: There was a 50 % response rate with the majority 63.6% being uncertain or unaware of the ergonomics of the digital workstation. 54.5% felt they would need support with the workstation set up. A similar percentage of trainees were unsure whether regular occupational health checks would help them to embrace digital pathology.
Conclusion: Workstation setup can be explained during local induction to increase awareness of the risks of repetitive stress injury. Standard operating procedures on workstation set up should be made available to trainees. Regular audits or surveys can help monitor whether trainees are working at a properly set up workstation.

E-PS-16-002
Macro and microscopic image collections as diagnostic aid tool in pathology, based on pattern recognition

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Background & objectives: Digital pathology has raised new opportunities to assist pathology diagnosis. Artificial intelligence offers different approaches in pathology diagnosis based on pattern recognition of lesions or entities. The source of machine learning procedures should be a well-documented collection of images.
Methods: Over the last ten years we have progressively collected images macro and microscopic in .jpg format of all the cases studied in our hospital, currently reaching a total around 800.000. Microscopic images are taken by pathologists at the moment of diagnosis selecting the most representative areas that lead to the diagnosis and allow by themselves to identify the lesional categories.
Results: To retrieve the image information we initially designed a search engine based on a MySQL database, presenting collections of thumbnails of the images linked to the diagnosis, introduced from the queries typed in a web form. Later the IT team in our hospital developed, based in a open source algorithm (Phase Stretch Transform) for image recognition, a solution to identify images among our collection, of similar features as those selected by the pathologist in the same way through a web form. The concordance is not yet perfect, but similarities to the original image bring in most instances an answer with a thumbnail collection of cases with the same diagnosis.
Conclusion: Daily practice in pathology allows to collect a huge number of images of the diagnosed cases. They can be used later to help diagnosis of complex cases or in the training of young pathologists. Nowadays recovery algorithms improve continuously.

E-PS-16-004
Digital pathology & artificial intelligence – developing a survey of ethical, governance and legal considerations

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Background & objectives: Digital pathology (DP) presents challenges for handling, storage and use of data/information, which must be implemented securely, ethically, and legally. In this study, we aimed to develop a pilot questionnaire, to understand potential ethical, governance and legal challenges.
Methods: We developed a pilot questionnaire focusing on gauging the current understanding of 3 consultant histopathologists and 1 academic clinical fellow of the legal, governance and ethical aspects of DP, specifically within the research setting. The questionnaire comprised of 10 questions, using open and closed format, developed following a literature review.
Results: All respondents were experienced with DP in research and clinical settings. The questionnaire comprised of 3 sections; background, knowledge and understanding the law. Pathologists describe key issues being data sharing with industry, patient understanding of the potential use of data and pathologists not necessarily understanding with confidence the ethical and legal frameworks governing use of scanned slide images in research (1/4 felt not at all confident and 3/4 felt only somewhat confident).
Conclusion: The DP community needs to be mindful of the legal and ethical considerations of this fast-growing field, not only to be legally compliant but ensuring transparency and protecting the trust of the public. Pathology specific resources and training may help.

E-PS-16-005
Automated classification of cancer from fine needle aspiration cytological image use neural networks: a meta-analysis

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Background & objectives: The role of retrospective analysis has been evolved greatly in cancer research. We undertook this meta-analysis to evaluate retrospectively the diagnostic value of Neural networks (NNs) in Fine needle aspiration cytological image (FNAC) of cancer.
Methods: Cytologicdiagnosis of 396 publications from Cochrane, PubMed and EMBASE related to NNs was retrieved. After screening, a total of 7 literatures were included in Meta-analysis. Data was comprehensively analysed by RevMan and Meta-Disc software.
Results: A total of 1660 cases were extracted from 7 literatures. Among them, 698 cases were in the cancer/abnormal group and 962 cases in the benign/normal group. The pooled estimates for the NNs cytology diagnosis were Area under ROC curve(AUC): 0.99, Sensitivity: 0.87(95% CI:0.84-0.90), Specificity: 0.97(95% CI:0.96-0.98), Positive Likelihood Ratio(LR): 24.23(95% CI: 9.20-63.38), Negative Likelihood Ratio(LR): 0.05(95% CI:0.00-0.50), and Diagnostic odds ratio (DOR):546.30 (57.46-5194.34).
Conclusion: To some extent, NNs Automated Classification algorithm can facilitate the diagnosis of FNCA in cancer confirmed by Meta-analysis.

E-PS-16-006
Utilisation of a diagnostic digital pathology platform for sharing of educational cases - opinions and attitudes of histopathology trainees

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Background & objectives: Use of digital pathology (DP) in the diagnostic setting offers opportunity for histopathology trainees and educators to share educationally valuable cases. We present a pilot study assessing attitudes to sharing of educational cases on the digital platform in this manner.
Methods: Educational cases on the diagnostic DP platform were identified by a consultant histopathologist, and links circulated by email. Cases included 'spot diagnoses' and more complex exam-type cases. Trainees were invited to submit an 'answer' by email to the educator or through an anonymous online survey. Educational comments were subsequently circulated by email to all. Trainee feedback was collected using SurveyMonkey(R).
Results: Feedback was provided by 7/9 participants. All had prior diagnostic exposure to the digital platform. All agreed that this teaching format was appealing, and that remote educator feedback enhances educational value. However, trainees also noted that simple signposting of cases by an educator without additional feedback could be helpful. Specific comments included that multiple trainees could access the digital cases simultaneously, that it offered provision of easy access to teaching cases without potentially making them unavailable for multidisciplinary team meetings, and that it offered useful exposure to cases across specialties. Potential collation of educational comments alongside cases was suggested to be of value longer term.
Conclusion: Diagnostic digital images are a promising resource for facilitating and enhancing histopathology education, allowing cases to be shared in a timely manner with multiple trainees. Educational experience is enhanced by educator feedback which can be specific to trainee needs, but simple signposting of cases is also valuable. It allows regular exposure across specialties in specialist centres and provides opportunity for educators to teach in a more time-flexible manner.

E-PS-16-007
International PathArt Photomicrography Contest: artistic reflections of pathologists' colourful daily lives through the microscope and introducing pathology to the public
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Background & objectives: As pathologists, we play an important role in the patient management which creates a stressful daily life and usually we are not fully understood nor appreciated. We aimed to bring together the artwork of the pathologists from all around the world.
Methods: In collaboration of Turkish Journal of Pathology and The Federation of Turkish Pathology Societies, we have started a science and art activity initiative in 2017.It has now become a tradition for the last 3 years. The contest was announced and voted online and the contest jury which consisted of members of the social media commission made the final decision.
Results: During the 3 years of the contest the participation has increased noticeably. There were 27 participants from 7 countries with 49 photos in 2017, 40 participants from 11 countries with 53 photos in 2018 and 50 participants from 16 countries with 103 photos in 2019. The winners of the competition were announced on the journal's website and their photos appeared on the cover page of the journal's next issue. Selected artwork was printed and exhibited at that year's national congress and there was also a public art gallery exhibition not only for doctors but also for all of the art lovers.
Conclusion: What started as an attempt to describe our profession through art has attracted much attention, inspired other pathology communities internationally, helped increasing the publicity of pathology and made everyone else be able to look at our profession from a different angle.

E-PS-16-008
The implementation and application of a fully digital pathology workflow in combination with ai tools in large general hospitals
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Background & objectives: Digital imaging associated with artificial intelligence applications for effective diagnosis are not yet routinely incorporated in practice, especially in large general hospitals. We have done a lot of practical work about digital pathology workflow in combination with AI tools.
Methods: Slides were digitized by three high-throughput scanners(250/360/1000) every day. In order to increase the efficiency of digital scan, we optimized the process from section to scan. We also designed a storage scheme to store and manage whole slides. We also investigated and researched how the AI systems assist pathologists work efficiently in cervical liquid-based cytology test and Ki67 quantification.
Results: The establishment of digital pathology diagnosis platform was completed, AI systems had been integrated the workflow into the digital pathology diagnosis platform, then making it easy to use for pathologists. The efficiency of digital scan was optimized in many ways, for example, auto-identifying labels. Digital whole slides were stored in the private cloud that we built. Hologic TIS system combines with AI system improved the efficiency and quality of cytology screening. The performance of the Ki67 AI assisted system is more objective and repeatable. With help of the Ki67 AI assisted system, pathologists corrected 2 mistakes in 200 checks timely.
Conclusion: Digital pathology diagnosis platform can be used for creating high quality pathology database and embedding AI tools for effective and accurate diagnosis. With the help of AI tools, digital workflow becomes practical and convenient and solves the shortage of pathologists.

E-PS-16-009
Hibiscus sabdariffa natural stain: an alternative to haematoxylin for human breast cancer diagnosis
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Background & objectives: Breast cancer is a heterogeneous disease. Considering the environmental aggression of hematoxylin, this research introduces an alternative natural dye, derived from Hibiscus sabdariffa as a substitute for hematoxylin in the histological technique.
Methods: 58 blocks from breast samples were previously diagnosed for breast cancer 29 cases of positive and 29 were negative ones. For testing, histological sections were stained with H. sabdariffa and eosin. All samples were also stained in H&E for controlling.
Results: In order to compare possible ecotoxicity effects of stains, an antiproliferative assay was carried out in Allium cepa experimental model. Onion roots were exposed to H&E and H.sabdariffa stain for 48 hours at 10%, 1%, and 0.1%. Root tip was prepared, and 1000 cells were counted for mitosis in each concentration. H.sabdariffa stain promoted a high affinity to nuclear structures, such as conventional H&E. Comparing diagnosis, it was revealed a high concordance (κ=0.613) of results from both stains. Mitotic indices of onion root tips were lower for exposition to H&E than H.sabdariffa in all tested concentrations. This reveals than the alternative stain should present a lower ecotoxicological effect than hematoxylin.
Conclusion: It was concluded that the staining with H. sabdariffa presented a significant result for nuclear staining, being an efficient substitute

for hematoxylin in the conventional H&E staining technique for diagnosis of breast cancer.

E-PS-16-010

Adapting the Gail model to breast cancer risk for the Brazilian reality

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Background & objectives: Breast cancer is the second most frequent neoplasm in female Brazilian patients, then becoming an important public health issue. To translate, culturally adapt, validate breast cancer risk assessment tool, and make an application to calculate the risk of developing breast cancer.
Methods: A prospective observational study conducted through an interview using a standard form of the questionnaire made available on NCI-USA. Patients with a previous history of Lobular or Ductal Carcinoma in situ were interviewed, as well as those with a mutation in the BRCA1 and BRCA2 suppressor genes and other hereditary syndromes associated with an increased risk of breast cancer.
Results: The risk calculated through the tool in the eligible patients was 1.3% in the next five years (Standard Deviation ± 0.86) and 12.41 (Standard Deviation ± 8.72), with no difference compared to the general population. The application for Android platform is in the testing phase.
Conclusion: The tool has been translated, culturally adapted and validated according to international protocols for tool validation. Based on reliable epidemiological data, which reflect the reality of miscegenation, public resources initiatives and individualized actions of the professionals in possession of this new tool lead to the best use of available resources and adequate intervention at the individual level.

E-PS-16-012

Digital pathology reporting in Malaysia: an overview

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Background & objectives: Digital pathology reporting has become a reality in many countries. One of its main advantages against traditional microscopy, is distance reporting. In an era of increased workload, case complexity, and staffing shortages, digital pathology in the laboratory is a necessity.
Methods: Clinipath Pathology, Malaysia acquired the much advanced Aperio AT2 slide scanner in 2018 and incorporated routine digital pathology reporting. An initial validation study was carried out for a three-month duration. More than 5000 surgical cases including Non- gynae cytology have been reported so far. An average of 40 histological samples, including big resected specimens are reported every day.
Results: Digital pathology reporting is as accurate as conventional microscope reporting, and in a few instances more advantageous. With an integrated lab setup, all types of surgical specimens and EUS FNA have been reported without resorting to the conventional microscope for a review. The response and acceptance from the clinical faculty has been over whelming. Measurements of extremely small malignant lesions coupled with digital photography has made the system more rewarding. Due to constant practice, the system has become more dependable, robust and accurate than conventional microscope reporting. IHC analysis with comparison of various IHC markers in a single view is a prolific outcome of digital reporting.
Conclusion: Digital pathology reporting should be incorporated as a regular diagnostic procedure in all institutions. The accuracy and effectiveness are very advantageous for the current demand of histopathology in many laboratories. A constant practice of digital images makes the system very robust and the images can be shared for expert second opinion in complex cases. This is the future of diagnostic pathology and artificial intelligence (AI).

E-PS-16-013

Assessing the biochemical features of breast cancer using Raman spectroscopy

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Background & objectives: Raman spectroscopy (RS) offers real-time, non-destructive, optical identification of tissue components through molecular vibrations, not requiring dyes. It was already proved effective in evaluating early melanocytic lesions. Raman Microspectroscopy may detect and identify breast cancer on surgical margins.
Methods: The analysis of three sets of human breast tissue samples collected through breast conserving surgery and classified by control histopathology as containing (1) invasive carcinoma, (2) in situ carcinoma, or (3) "healthy" breast tissue. RMS probing of 10 μm thick, digitally dewaxed tissue sections to detect and identify the composition and distribution of molecular biomarkers specific to each tissue set.
Results: According to a Principal Component Analysis, Raman Microspectroscopy probing successfully distinguished the three sets of samples, and further identified biochemical traits specific to each tissue set, namely its distinct content and distribution of proteins, lipids, and nucleic acids.
Conclusion: Improving clinical outcomes for breast cancer patients requires faster, more objective diagnostic tools, particularly within the operating room. One promising approach is in loco tissue analysis for biochemical differences, potentially much faster and more specific than conventional histopathology. Spectral histopathology, as an adjunct to conventional histopathology, may provide non-invasive, real-time, highly accurate information about the presence of malignant tissue on surgical margins, even for highly heterogeneous biospecimens.

E-PS-17 Molecular Pathology

E-PS-17-001

Aberrant expression of neuroendocrine markers in mucosal malignant melanoma of the nasal cavity; case report highlighting a potential diagnostic pitfall

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Background & objectives: Melanomas show morphological heterogeneity and are thus challenging to diagnose on H&E. Melanocytic markers are effective in their identification. However aberrant expression of non-melanoma markers remains a pitfall. The authors document the expression of neuroendocrine markers in a mucosal melanoma
Methods: A right maxillary antral mass in a 77yr old male showed on microscopy sheets of malignant epithelioid and spindle cells with enlarged, pleomorphic nuclei and basophilic cytoplasm. Differential diagnoses were sinonasal neuroendocrine carcinoma, and olfactory neuroblastoma. Immunostaining was performed with a panel including but not restricted to epithelial [AE1/AE3, EMA], neuroendocrine [synaptophysin, NSE] and melanocytic [S100,melanA and HMB-45] markers.
Results: The tumour cells were positive for all three melanoma markers and negative for cytokeratins, hence excluding a neuroendocrine

carcinoma. The characteristic lobularity and sustentacular cells of an olfactory neuroblastoma were absent, hence ruling out this entity. In the light of the aforementioned positive expression of melanocytic antibodies, a diagnosis of a sinonasal melanoma was made. However, expression of synaptophysin and NSE was observed in up to 50% of the tumour cells.
Conclusion: With regard to cancers of unknown origin/primary, melanomas should be included in the differential diagnosis of tumours expressing neuroendocrine markers. The co-expression of both melanocytic and neuroendocrine markers, as well as the loss of melanocytic markers are possible and seemingly frequent scenarios in melanomas and should be considered to avoid diagnostic and hence management errors.

E-PS-17-002
Development of an expanded microsatellite instability panel with automated data analysis
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Background & objectives: Microsatellite instability testing has been used to study Lynch Syndrome and in immuno-oncology research. However, clinical researchers have indicated that current solutions to detect MSI have limitations, including insufficient markers for applications across multiple tumour types and cumbersome data analysis.
Methods: To facilitate further clinical research on MSI, Thermo Fisher Scientific has developed the Applied Biosystems™ TrueMark™ MSI assay. This multiplex fluorescent PCR panel consists of eight markers used historically in Lynch syndrome and MSI identification as well as five novel quasi-monomorphic homopolymers. Two human identification satellite tandem repeats are included for sample traceability.
Results: Fourteen of the 15 amplicons are less than 180 base pairs in length to maximize robustness in degraded FFPE samples. This 15-plex fluorescent PCR fragment analysis assay is performed via a standard capillary electrophoresis workflow and requires low input DNA (2ng). The included software automatically detects unstable microsatellite markers and sample contamination or mix-up. To demonstrate the utility of the expanded panel and software solution, we performed a retrospective study using FFPE research samples derived from colon, gastric, and endometrial cancers. This assay produced high concordance with immunohistochemistry and fewer ambiguous results relative to the Promega MSI assay due to the expanded marker set.
Conclusion: The combination of our expanded marker set and automated data analysis software constitutes an important tool for studying microsatellite instability. For research use only. Not for use in diagnostic procedures.

E-PS-17-003
Inhabitual presentation of sex cord ovarian tumour with rhabdomyosarcomatous component in the setting of xeroderma pigmentosum
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Background & objectives: Ovarian cancer is frequent but it pathogenesis remains unclear. The association xeroderma pigmentosum and sex cord ovarian tumour has been reported once.
We report a case of sex stromal-cord tumour with rhabdomyosarcomatous contingent in 27 year-old woman with xeroderma pigmentosum.
Methods: A 27-year-old woman presented with pelvic pain lasting for one mouth. The personal history revealed a xeroderma pigmentosum diagnosed at the age of 6 months. Physical exam found a right pelvic mass. The ultrasound exam concluded to a 20 cm, solid, ovarian tumour with ascites. The patient had laparotomy.
Results: In gross, we received 21 cm white mass with haemorrhagic and necrosis areas. The pathologic exam reported a poor differentiated sex-cord tumour with dominantly rhabdomysarcomatous component. This component was dense and arranged in diffuse sheets. There was mild atypia and few mitosis. Immunohistochemistry showed positive staining for desmin in rhabdomysarcomatous cells and for cytokeratin and inhibin-α in other tumour cell. The patient had got adjuvant chemotherapy. No recurrence was noted.
Conclusion: Xeroderma pigmentosum is a genetic disorder in which there is by a decreased ability to repair DNA damage. It is caused by mutations in nine different genes (XP). Ovarian tumours are exceptionally associated with this disorder. Some studies have explained this association to genomic instability. But this theory isn't confirmed yet. Others cases with a molecular study should be reported to better understand the physiopathology of this entity.

E-PS-17-004
Estimation of expression of KISS1 oncomarker in non-specific breast cancer
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Background & objectives: The KISS1/KISS1R signalling system is a regulator of tumour metastasis. It is also a potential prognostic marker of tumour processes. The aim of investigation is to study the features of the expression of the tumour marker KISS1 in non-specific breast carcinoma.
Methods: We explored surgical material, which was obtained from 30 women at the age of 28-63 years with a confirmed diagnosis: ductal carcinoma of the breast with distant (liver, lungs, bones) and regional (lymph nodes) metastases and without them. Metastin (Abcam) used as primary antibodies. KISS1 protein expression was detected as a homogeneous staining of tumour cell cytoplasm.
Results: The intensity of the reaction was evaluated by the semiquantitative method:(-) negative reaction, (+) - weak focal reaction, (++) – medium, (+++) - intensively with spread throughout the cytoplasm. Intense response (+++) was determined in 85% of the control tissue. In tissue samples with confirmed metastases, 9 out of 30 showed a weak (+) focal reaction. In the remaining 21 samples, expression was as follows: intense (+++) in 4.4% (1 of 21), average intensity (++) was found in 82.6% (18 of 21), weak (+) in 13, 0% (2 of 21).
Conclusion: The level of KISS1 expression can be used as a molecular marker predicting the quality of the tumour therapy response, especially in postmenopausal women.

E-PS-17-005
A new, modern, and timely way to detect NUT midline carcinomas and their differentials by a single molecular profiling method
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Background & objectives: NUT midline carcinoma (NMC) is an aggressive neoplasm, which is classically diagnosed by morphology, immunohistochemistry, and FISH-Analysis. Here, we present a new strategy to detect this rare tumour through a standard DNA methylation array analysis.
Methods: The DNA methylation profile obtained on an Infinium Human Methylation EPIC BeadChip array (Illumina, USA). The data were compared to a given dataset against more than 15'500 reference datasets mostly derived from The Cancer Genome Atlas and Gene Expression Omnibus. The analysis considers both the

DNA methylation profile and the copy number variations, extracted by conumee.
Results: Indicated a high similarity of NUT midline carcinoma to squamous carcinomas of the lung (NSCLC_SC) when compared by dimension reduction (UMAP). As opposed to NSCLC_SC, NMC has a flat genome and a circumscribed loss of heterozygosity on chromosome 15q, adjacent to the NUTM1 locus. Besides, dimension reduction discriminates the tumour from other morphological differentials.
Conclusion: In summary, we present an alternative, modern and timely way to detect a rare tumour - NUT midline carcinoma - by simultaneous methylation and CNV profiling through a single microarray. Specifically, NMC should be considered in tumours identified by methylomics to represent squamous cell carcinomas that lack significant CNV and show aberrations around the NUTM1 locus.

E-PS-17-006
A prospective study of EGFR, KRAS and ALK gene mutations in Macedonian patients with non-small-cell lung cancer
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Background & objectives: Testing gene mutations in clinical practice leads to the development of genome-based personalized medicine. Modern equipment in pathology laboratories enables benefits to patients. We aimed to analyse lung carcinoma for EGFR and KRAS gene mutations and ALK rearrangements.
Methods: We analysed 190 consecutive patients with non small cell lung cancer (NSCLC). Formalin-fixed-paraffin-embedded NSCLC tissue sections from lung biopsies were analysed using Cobas 4800 EGFRv2 IVD and KRAS IVD gene mutations kit analysed on Cobas Z480 IVD Real-Time PCR. For ALK rearrangements we used ALK IQFISH, dual colour Break-Apart Probe IVD, (Agilent Technologies).
Results: There were 33 (17.36%) female and 157 (82.63%) male patients, ranging in age from 43 to 81 years.
Forty fore (23.15%) cases were diagnosed as NSCLS and for other cases more precise diagnosis was established as follows: 4 (2.10%) Large cell lung carcinoma, 23 (12.10%) Squamous cell carcinoma, 1 (0.52%) Adenosquamous carcinoma and 118 (62.10%) Adenocarcinomas.
EGFR mutations in exon 18-22 were found in 5 (2.63%) patients with NSCLC. KRAS mutations in codons 12, 13 and 61 were found in 7 (3.68%) and ALK rearrangements were found in another 7 (3.68%) patients with NSCLC. All of them were diagnosed as well and moderately differentiated adenocarcinomas.
Conclusion: This study is the first prospective study of EGFR, KRAS and ALK gene mutations in lung neoplasms from North Macedonia population. Although in low frequency mutations of analysed genes are found, and mutation testing should be considered for all patients with NSCLC.

E-PS-17-007
A case of metastatic melanoma – BRAF molecular testing as a diagnostic tool
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Background & objectives: The objective of this case report is to highlight the importance of molecular testing in challenging cases where the histological appearances and immunohistochemistry are not sufficient to establish the correct diagnosis.
Methods: A middle aged man with a previously diagnosed glioblastoma presented with a skin lesion and enlarged axillary nodes. H&E-stained slides from each samples were reviewed, and tumour tissue was identified for analysis. Total DNA extracted from 5μm thick sections using the Cobas DNA Extraction Kit (Roche Molecular Diagnostics). V600E mutations were detected using the Cobas 4800 BRAF V600 Mutation Test.
Results: The skin excision revealed no obvious malignancy. The previous brain tumour and the axillary lymph node lesion showed a poorly differentiated tumour which was negative for S100, melan-A, and HMB45 immunostains. At molecular analysis both lesions revealed BRAF V600E mutation. The case was diagnosed as metastatic dedifferentiated melanoma.
Conclusion: In practice, the result of molecular analysis is used to direct treatment decisions, however in selected cases it can also serve as an important diagnostic tool in particular when immunohistochemical analysis is unhelpful.

E-PS-17-009
Whole exome sequencing vs. targeted panel sequencing – influence on diagnostic assessment for precision medicine in oncology
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Background & objectives: Targeted sequencing approaches by whole exome sequencing approaches are implemented in specialized diagnostics allowing a broader spectrum of therapeutic options for patient treatment. Using more focused techniques such as gene panels might have an impact on clinical decision making.
Methods: DNA/RNA pairs from 32 lung cancer patients from NCT MASTER previously undergone WES were analysed: Sequencing using the nNGM-lung cancer hotspot panel and DNAs and corresponding RNAs were sequenced using the pan cancer TSO500/TST170 panel (Illumina). We wanted to evaluate the efficiency of panel-based sequencing vs WES to detect therapy-relevant alterations and to investigate their impact on therapy decision.
Results: Sequencing of all samples applying both approaches is finished and data analysis is ongoing. 1. nNGM panel: Nine from 32 patients did not reveal any alterations. All except for four samples revealed the same relevant alterations identified by WES. Discrepancies might be due to the used hotspot gene panel design not covering the complete genes. Therapy relevant alterations in EGFR, BRAF, among others were identified. 2. TSO500/TST170: Data analysis is still ongoing, TMB assessment and MSI status is additionally collected. Finally, results will be sent blinded to NCT MASTER for clinical annotation. Recommendations based on the different sequencing approaches will be compared to the original decisions based on WES data.
Conclusion: Using different approaches for recommendations for therapy in oncology might have an impact on decision making. We therefore evaluated results from three different sequencing approaches, WES, nNGM hotspot gene panel sequencing and TSO500/TST170 hybrid-capture based sequencing and compared their putative influence on decision making. As expected, known therapy-relevant variants such as EGFR or BRAF mutations were detected applying all assays.

E-PS-17-010
Risk factors and characterisation of the mutations in exon one of vimentin gene (VIM) among Sudanese breast cancer women in Khartoum state, Sudan
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Background & objectives: Breast cancer is the most common cancer in Sudanese women. VIM gene was described as a marker for several malignant tumours. The aim of this study was to determine the mutations in exon one of VIM gene among those women.
Methods: This is a case control study involving 90 patients with breast cancer and controls. The study was conducted a cross Three hospitals in Khartoum State. The data collected through a well-structured questionnaire. DNA was extracted. PCR was conducted to amplify the exon one using specific primer. products were sent to detect the mutation in exon one of VIM gene
Results: The study showed the significant risk factors were age, family history, marriage, menopause, pregnancy, nulli-parou parous women, breast feeding, use of contraceptive drugs and grade of the disease. Samples were successfully amplified, the product size was 12 bp. DNA sequences alignment of exon one of VIM gene (Query) for two samples of exon one of VIM gene (Subject) from NCBI database, showed 100% identity. There were no mutation detected in exon one of VIM gene associated with breast cancer in Sudanese women in Khartoum State.
Conclusion: The study demonstrated family history with first degree relative, unmarried women, age at menarche, marriage, pregnancy, nulliparous women and breast feeding were significant risk factors associated with breast cancer. No mutation was detected in exon one of VIM gene in Sudanese women with breast cancer in Khartoum state.

E-PS-17-011
Establishing and validating multiple glioma markers on a single molecular platform
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Background & objectives: Molecular-based classification of brain tumours has become routine practice since the WHO classification has been updated in 2016. Biomarkers with specific clinical relevance include IDH1 and IDH2 point mutations, 1p/19q co-deletion, ATRX gene/protein expression loss and MGMT promotor methylation.
Methods: Here, we aim to integrate these four modalities in one single simultaneous analysis on the Modaplex™ platform. We have established a glioma panel for simultaneous detection of different genetic aberrations. For each marker a respective quantitative or qualitative assay was established to amplify and detect the target sequences.
Results: We demonstrate that the simple assay-development workflow of Modaplex technology enables the rapid integration of multiple genetic aberrations of different modalities onto a single platform. The IDH1 and IDH2 point mutations, 1p/19q co-deletion, reduced ATRX gene expression and MGMT promotor methylation results corresponded to the independent evaluation.
Conclusion: Currently, due to the different biological nature of these glioma-specific aberrations, several testing methods need to be applied in a stepwise procedure. The Modaplex technology enables simultaneous analysis of the molecular glioma marker and allows the molecular-based classification, further differentiation, and stratification of the therapy recommendation with temozolomide in gliomas in a time effective and tissue-sparing manner.
This study was supported by the German Federal Ministry of Education and Research - BMBF- and conducted in collaboration with Biotype, Inc.

E-PS-17-012
KRAS/NRAS mutations deserves report in non – surgical pulmonary adenocarcinomas early molecular characterisation
V. Sousa*, A.F. Ladeirinha, A. Alarcão, M. Reis Silva, T. Ferreira, A. Rodrigues, C. Vilasboas, R. Almeida, V. Almeida, A. Figueiredo, F. Barata, L. Carvalho
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Background & objectives: KRAS mutations occur in 20-40% of pulmonary adenocarcinomas (codons 12 and 13 mainly). Liquid biopsy subscripted to NGS raises the question of the print 1 first level for KRAS determination in non-surgical staged patients.
Methods: Blood of 16 patients carrying advanced adenocarcinoma recurring after targeted therapy/immunotherapy analysed by NGS after Streck tube blood collecting and DNA-extraction was done with DNA MagMAX™ Cell-Free DNA Isolation Kit. Oncomine™ Lung cfDNA Assay (11 genes) (Thermo Fisher Scientific, Waltham, MA, USA) was performed according to manufacturer's instruction by Next Generation Sequencing (NGS) in Ion S5™ System.
Results: In the 16 samples, 5 cases had KRAS/NRAS mutations where two KRAS mutations were concomitant with TP53 and EGFR or NRAS. The remaining 3 cases presented isolated KRAS or NRAS mutations. All KRAS mutations occurred in 12 or 13 codons. KRAS became a predictive biomarker of response to either target/chemotherapy and early preclinical data showed that the presence of KRAS mutation induced greater sensitivity in pemetrexed models.
Conclusion: The role of KRAS/NRAS deserves early inclusion in liquid biopsy of non-surgical adenocarcinomas to follow up therapy in advanced pulmonary carcinomas once immunotherapy seems to benefit from these molecular alterations.

E-PS-17-013
EGFR L858R and PIK3CA H1047R mutations in pulmonary adenocarcinoma – diagnosis in liquid biopsy
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Background & objectives: PI3K/Akt mutations signalling downstream EGFR pathway drive oncogenesis/progression and frequently coexist with others, relating with not yet understood resistance to EGFR TKIs in pulmonary adenocarcinoma where PIK3CA mutation ranges from 1.5% to 7.7%.
Methods: Hepatic metastasis of a 65-years-old non-smoker female stage IVb pulmonary adenocarcinoma (CK7/TTF1/vimentine positivity and CK20/mammaglobin negativity) was macrodissected for EGFR by IdyllaTM EGFR Mutation Test. Blood was collected in Streck tube. DNA-extraction performed with DNA MagMAX™ Cell-Free DNA Isolation-Kit.
Oncomine™ Lung cfDNA Assay (Thermo Fisher Scientific) panel was performed by NGS in Ion S5™ System for genomic analysis of cfDNA.
Results: EGFR presented wild-type in the hepatic metastasis cells while in liquid biopsy EGFR and PIK3CA were detected c.2573T>G;p.(Leu858Arg) and c.3140A>G;p.(His1047Arg), respectively.
The EGFR c.2573T>G;p.(Leu858Arg) mutation and PIK3CA c.3140A>G;p.(His1047Arg) mutation are associated with response to EGFR TKIs and response with PI3K/AKT/mTOR pathway inhibitors, respectively.
Conclusion: Interactions between PIK3CA/EGFR mutations are not yet clearly interpreted in pulmonary carcinomas and clinical outcome unknown, deserving more data for treatment definition.

E-PS-17-014
Pulmonary adenocarcinoma EGFR exon 20 insertion determined in liquid biopsy – case report
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Background & objectives: EGFRexon20 insertion, the most prevalent of uncommon EGFR mutations, found in 1.5–2.5% pulmonary adenocarcinomas/female gender/Asian ethnicity/never-smoking patients, has 100 cases reported in the catalog of somatic mutations in cancer-COSMIC. Given rarity, mutations and respective clinical outcomes are not fully established.
Methods: Non-smoker 61-years-old female lung biopsy correlated with clinical T2bN0M1c–IVB pulmonary adenocarcinoma (CK7/TTF1/napsin positivity and CK20/ vimentine/ CD10/ oestrogen receptors/ CCR/CD10 negativity).
FFPE macrodissected tumoral tissue was analysed for EGFR mutations IdyllaTM EGFR Mutation Test. Blood was collected in Streck tube and DNA-extraction done with DNA MagMAX™ Cell-Free DNA Isolation Kit.
Oncomine™ Lung cfDNA Assay panel was performed by Next Generation Sequencing (NGS) Ion S5™ System.
Results: In both samples, biopsy (Idylla) and liquid biopsy (NGS), EGFR exon 20 insertion c.2319_2320insCAC;p.(His773_Val774insHis) was detected with one year in between; after afatinib, osimertinib was introduced due to left kidney metastasis detection. Exon 20 insertion mutation is associated with lack of sensitivity to first-generation EGFR TKIs (erlotinib/gefitinib) and a partial response to second-generation (afatinib) and third generation (osimertinib/rociletinib); promising results for nazartinib and poziotinib are online.
Follow up has been done for 21/2 years.
Conclusion: Studies showed that different exon 20 insertions lead to different response to EGFR TKIs depending on the location in the kinase domain that they affect. Therefore, it is important to report the mutation and make the follow up.
Key words: EGFR; exon 20 insertion; liquid biopsy

E-PS-17-015
A novel SOS1-ALK fusion variant in a metastatic lung adenocarcinoma patient with remarkable response to crizotinib
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Background & objectives: Transforming ALK (anaplastic lymphoma kinase) gene rearrangements are well known as one unique subset of non-small cell lung cancer (NSCLC) other than EGFR mutations. Currently, crizotinib is the standard first-line treatment for ALK-positive NSCLC.
Methods: With the advances of detection methods, more and more uncommon ALK fusion partners are found. Herein, we presented a novel SOS1-ALK fusion and the efficacy of crizotinib to an advanced NSCLC patient who harbouring this type of fusion.
Results: A 52-year-old Chinese man with left upper lobe primary NSCLC and synchronous multiple lung metastases. The EUS-FNA of palpable left supraclavicular lymph nodes and results of immunohistochemistry staining supported lung adenocarcinoma metastasis. By using NGS assay, we found the tumour had SOS1-ALK fusion rather than other actionable mutations. In that case, the patient took the first line crizotinib and experienced a remarkable tumour response to it and tolerance well until written.
Conclusion: Considering this rare SOS1-ALK fusion and remarkable response to ALK-inhibitor, it is worthful to aware of the presence of SOS1-ALK fusion in NSCLC to guide target therapy. NGS for oncogenic alterations detection should also be encouraged in clinical practice.
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E-PS-18 Nephropathology

E-PS-18-001
C3 glomerulopathy associated monoclonal gammopathy and atypical HUS: a case report
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Background & objectives: A 68-year old man presented with haematuria, thrombocytopenia, microangiopathic haemolytic anaemia and renal dysfunction with Cr 1.3mg/dl. A diagnosis of aHUS was suspected. Result of immunofixation-electrophoresis in blood/urine showed monoclonal fraction of IgG-k, bone marrow and renal biopsies were requested.
Methods: Light and immunofluorescence microscopy along with histochemical stains were used.
Results: Thrombotic-thrombocytopenic-purpura was excluded because ADAMTS-13 activity was normal Bone marrow biopsy resulted in a diagnosis of sMM/MGRS was given with a percentage of clonal plasma cells of 12% Renal biopsy revealed findings consistent with a membranoproliferative glomerulonephritis with global mesangial matrix expansion, mesangial hypercellularity and capillary wall thickening with double contours, among others findings. Immunofluorescence microscopy revealed diffuse positive (3+) staining for C3 in the mesangium and along the capillary wall whereas IgG, IgM, IgA, C1q, C4, κ and λ light chains were all negative. A differential diagnosis between dense-deposit-disease (DDD) and C3-glomerulonephritis was given with a recommendation for further evaluation with electronic microscopy.
Conclusion: Abnormal activation of the alternative complement pathway may be associated with several conditions that result in dysregulation of the pathway such as infection and monoclonal gammopathy. It is possible that the abnormal monoclonal immunoglobulin produced acts as such a trigger factor that leads to abnormal activation of the alternative-complement pathway and contributes to the development of C3G and aHUS.

E-PS-18-002
IgA nephropathy with thrombotic microangiopathy in the context of visceral leishmaniasis with renal involvement
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Background & objectives: Renal involvement in visceral leishmaniasis is rare and is most often reported in immunocompromised patients. We present a rare case of a patient initially diagnosed as IgA nephropathy with thrombotic microangiopathy which subsequently was diagnosed with visceral leishmaniasis.
Methods: Light microscope, immunofluorescence, electron microscope and real time PCR
Results: A male patient aged 43, presented with acute renal failure, nephrotic range proteinuria and microscopic haematuria. His immunologic control demonstrated ANA1:1280, positive lupus anticoagulant and positive anti-SSA and anti-SSB. Clinically, the patient was suspected for an autoimmune disorder. The renal biopsy showed an IgA nephropathy (M0E0S1T0-C0 according to the Oxford Classification) accompanied by severe thrombotic microangiopathy, acute and chronic. The subsequent clinical and laboratory investigation revealed visceral leishmaniasis. The frozen stored

segment of the renal biopsy was then undergoing a PCR analysis that was positive for leishmania. The patient received anti-leishmania therapy which resulted in decline of his proteinuria and stabilization of his renal function. Immunologic control returned to normal.

Conclusion: The association of IgA nephropathy and thrombotic microangiopathy in the context of visceral leishmaniasis with renal involvement, is reported for the first time. Although thrombotic microangiopathy is not infrequently associated with IgA nephropathy, it is not known whether either IgA nephropathy or thrombotic microangiopathy might have any causal relation with leishmaniasis or it's just a coincidence of frequent and rare events.

E-PS-18-003

The natural history of renal pathology in LCAT deficiency through a repeated renal biopsy 10 years after the initial one

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Background & objectives: To present the evolution of the kidney lesions in a patient with LCAT deficiency undergoing a repeated renal biopsy 10 years after the initial one.

Methods: Light microscope, immunofluorescence and electron microscope. In the first biopsy the patient aged22years and presented proteinuria, microscopic haematuria and creatinine 1.2mg/dl. Light microscope showed a morphologic pattern of FSGS with some intracapillary hyaline pseudothrombi without global glomerulosclerosis, interstitial fibrosis/tubular atrophy (IFTA), inflammation or arterial intimal thickening.

Results: Ten years later, a second biopsy was performed due to appearance of nephrotic syndrome and increase of creatinine (2.2mg/dl). Apart from FSGS and intracapillary pseudothrombi, the biopsy showed global glomerulosclerosis, significant glomerular basement membrane (GBM)thickening with segmental duplications and foamy material into the duplicated GBMs, the capillary lumens and the arterial walls. IFTA progressed from absent to 50% of the cortex area. Interstitial inflammation was superimposed as well as arterial lesions. Immunofluorescence in both biopsies showed C3 deposition.

Conclusion: In the second biopsy, EM showed lipid vacuoles massively accumulated in mesangial, subendothelial, intramembranous and subepithelial locations, forming huge hump and fingerprint-like lipid accumulations. Moreover, lipid accumulation was noticed in the interstitial tissue, tubular basement membranes and arterial walls. Accumulation and expansion of lipid material, triggering IFTA and global glomerulosclerosis, seems to be the underlying cause of progressive renal damage and nephrotic proteinuria in patients with LCAT deficiency.

E-PS-18-005

Primary hyperoxaluria diagnosed on bone marrow biopsy in a renal transplant patient

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Background & objectives: Primary Hyperoxaluria is a rare autosomal recessive disorder. The most severe form is caused by deficiency of a liver-peroxisomal enzyme. Its defect leads to the conversation of glyoxylate to oxalate. Oxalate forms insoluble crystals with calcium accumulating in multiple organs.

Methods: 58-year-old woman had renal transplantation two years ago. Since infancy she had recurrent chronic pyelonephritis and nephrolithiasis resulting in end stage kidney disease. Few month after transplantation elevated paraproteins were detected. On serum electrophoresis gamma fraction showed a peak of monoclonal IgG kappa. Pathologic vertebral fracture was also revealed. Therefore, bone marrow biopsy was performed to exclude plasma cell myeloma.

Results: Bone marrow biopsy showed trilineage haematopoiesis with maturation. There were also areas rich in needle-shaped, birefringent calcium-oxalate crystals arranged in rosettes, surrounded by a foreign body giant cell reaction. Abnormal plasma cell proliferation was not detected. The diagnosis was oxalosis with secondary granulomatous reaction.

The patient received a renal transplant. Six months after renal transplantation, the renal function progressively decreased. Biopsies of the transplanted kidney showed extensive calcium-oxalate deposition in the tubules.

Secondary causes of hyperoxalosis were excluded, therefore we presume that this represents primary hyperoxaluria although genetic testing has not been performed.

In the literature we could only find three cases of primary oxalosis reported on bone marrow biopsy.

Conclusion: It is likely that changes of oxalosis are also present in native kidneys and consideration should be given to obtain a biopsy of these at the time of transplantation to screen for conditions that may affect the transplanted kidney.

E-PS-18-006

Repeat renal biopsy in a systemic lupus erythematosus patient with podocytic infolding glomerulopathy

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Background & objectives: Podocytic infolding glomerulopathy (PIG) is characterized by infolding of the podocytes into the basement membrane. The precise aetiology is not known, however, the condition is found mainly in patients with collagen diseases, such as systemic lupus erythematosus (SLE).

Methods: The 43-year-old woman first presented to us 5 years earlier with abdominal symptoms, and serum tests for ANA and anti-Sm antibody became positive. The first renal biopsy was performed when she developed haematuria and proteinuria. The second renal biopsy was performed 2 years later because of increased proteinuria despite the patient receiving treatment for SLE.

Results: The first renal biopsy revealed most glomeruli showed a bubbly appearance of the basement membrane with focal mesangial expansion histologically. IF analysis showed positivity only for IgM in the mesangial area, and there was no immune deposits by EM, but we found slight podocytic infolding into the basement membrane. The second renal biopsy showed podocytic infolding was still apparent and more evident than before by EM.

Conclusion: Most of PIG cases have underlying autoimmune disease. The condition affects women more frequently, and the average age of patients is 37.5 years. These clinical aspects seem to correspond to those of collagen diseases. It remains under debate as to whether this entity is a new disease of the podocytes of represents a non-specific reaction of the podocytes. We think that a relationship exists between PIG and autoimmune diseases or autoimmune disease-like condition.

E-PS-18-007

Light chain renal disease, in a stepwise process: a case report

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Background & objectives: Kidney is affected in multiple myeloma through deposition of abnormal light chain within various structures of the kidney.
A 43-year-old woman presented to an outside medical centre with hypertension and renal insufficiency. Initial renal biopsy diagnosed as acute tubular injury.
Methods: She was transferred to our institution for slides revision. Congo red staining and Immunohistochemistry were performed against immunoglobulins, C3, C1q, Kappa and Lambda antibodies.
Bone marrow biopsy was done then referred to the haematology department and treated for multiple myeloma. kidney functions improved. Seven months later, her creatinine raised to 7 mg/dL with proteinuria.
A renal biopsy was ordered again.
Results: First renal biopsy, tubules showed marked injury with frequent fractured PAS weakly stained hyaline casts, surrounded by cellular reaction. Congo red staining revealed no amyloid deposits. Casts were strongly positive for Kappa and weakly stained for Lambda. No glomerular or tubular basement membrane deposits. She was diagnosed as light chain cast nephropathy.
Bone marrow biopsy showed 15% monoclonal kappa plasma cells. The patient was diagnosed with multiple myeloma.
The second renal biopsy showed residual light chain casts, glomerular capillary and tubular basement membrane thickening, islands of interstitium PAS positive deposits, and granular material in arteries, with staining for only kappa (3+) in glomerular, tubular basement membrane, interstitium and arteries
Conclusion: Final pathology diagnoses included cast nephropathy and light chain deposition disease (LCDD), Kappa type. This case describes cast nephropathy and LCDD occurring in the same individual in a stepwise process.

E-PS-19 Neuropathology

E-PS-19-001
Histopathology of pilocytic astrocytoma and a rare case of haemorrhagic onset

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Background & objectives: Pilocytic Astrocytoma (PA) is a low-grade glioma which occurs predominantly in children. It usually presents signs of intracranial pressure, but haemorrhage is rare. We present this case because of its rarity and we review the relevant literature.
Methods: Here we report a case of haemorrhagic onset of cerebellar PA in a forty-year-old female who presented with a week-long history of headache and gait instability. Computed tomography and magnetic resonance imaging revealed a haemorrhagic tumour located in the right cerebellar hemisphere and total resection was performed.
Results: Histological examination revealed compact and microcystic areas. Rosenthal fibres and eosinophilic granular bodies (EGBs) were found. Haemorrhagic infiltration, hemosiderin deposition and focal inflamed aggregations of phagocytes were also observed. Microvascular proliferation and malformation was also observed, including sclerotic-thick walled and ectatic-thin walled vessels which lack elastic fibres, implying the possibility that they might be more prone to rupture under certain hemodynamic conditions.
Conclusion: Review of the literature revealed that age distribution of patients with haemorrhagic PAs tends to be older than that of patients with general PAs. These findings imply a possibility that degenerative changes in blood vessels in long-standing PAs.

E-PS-19-002
Case report: glioblastoma multiforme with metastasis in pancreas

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Background & objectives: Glioblastoma multiforme-GBM, a grade IV tumour of the central nervous system-CNS has an annual incidence of 5.26 per 100,000 population. GBM seldom metastasizes outside the CNS. The main objective of this case-report is to present a rare clinical case.
Methods: Histopathological examination was performed at brain and pancreas tissue samples.
Results: Brain tissue sample with extensive oedema, zones of cells with eosinophilic cytoplasm and thickened nucleus, some cells with degenerative corruptions, necrosis sources, saturated with blood and among them congested vessels with extravasation of red blood cells. Pancreas tissue sample with groups of irregularly big islands, fibrotic tissue, medium liparoid infiltration and vascular hyperplasia. Although GBM cure has remained elusive, progress has been made. Mouse glioma models can reveal possible molecular targets for personalized therapy. In addition, the immune system constitutes an ideal target since it penetrates the brain-blood-barrier. Therefore, immunotherapy can maximize "on-tumour" and minimize "off-tumour" effects.
Conclusion: MiRNAs' expression can help identify the cancerous stage. Finally, optune an electric device that is applied directly to the scalp and disrupts mitosis, as well as Bevacizumab, an antiangiogenesis agent, are also being tested.

E-PS-19-003
What about the adult cerebellar glioblastoma?

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Background & objectives: Adult glioblastoma of the cerebellum is a highly unusual entity. We hereby present two cases of Adult Cerebellar Glioblastoma within a period of 1-month difference each, at our institution.
Methods: The clinical data and histology reports were reviewed.
Results: Two young adults, age ≤ 45, a female and a male, with gait ataxia at presentation. The female patient had a history of Neurofibromatosis type I. On the MRI imaging, a solitary, infiltrative, cerebellar lesion, with diffuse gadolinium-enhancement after contrast, was observed.
Both tumours were right-sided, one with brainstem moulding and the other with contralateral extension. The median size was 45mm.
In both there were typical findings of a high-grade glial neoplasia. Both were p53 negative and had a low Ki-67 index (5%;10%).
Both tumours were IDH1/22 negative (wild-type), 1p/19q deletion negative and MGMT non-methylated.
The patients are alive, passed 9- and 11-months post brain surgery and radiotherapy.
Conclusion: The posterior fossa is the site of many types of tumours. Brain metastases are the most common adult malignancies of the posterior fossa and Hemangioblastoma the most common primary adult, intra-axial tumour, of this location. Glioblastomas of the cerebellum account for <1% of all intracranial Glioblastomas. In a brief period of one month we reported two cerebellar glioblastomas of the adult.

E-PS-19-004

A clinico-pathological risk score for prediction of recurrence in patients with atypical meningioma

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Background & objectives: Patients with atypical meningioma have 5-year recurrence free-survival (RFS) of 50%. For this reason, the post-surgical treatment after gross total resection is controversial.
In this study we aimed to analyse which clinical-pathological features could be helpful to predict the recurrence risk of patients with atypical meningioma and to identify high-risk ones who could benefit from adjuvant treatment.
Methods: From five different centres, we collected 200 primary atypical meningiomas treated with GTR, but with no adjuvant radiotherapy and reviewed their clinical and pathological features.
Results: Logistic multivariate regression analyses identified male sex, parasagittal site, Simpson grade 3, mitotic index ≥ 6/10 HPF and sheeting as significant and independent factors associated with recurrence risk. We formulated a risk score assigning 1 point in the presence, and 0 points in the absence, of each of those parameters. A score ≥ 2 was associated with 4.7 risk of shorter DFS (P <00001) and was the most significant predictor of recurrence.
Conclusion: The presence of at least two clinico-pathological high-risk factors, among male sex, parasagittal site, Simpson grade 3, mitotic index ≥ 6/10 HPF and sheeting, predicts recurrence of totally resected primary atypical meningiomas and could be used to identify patients who could benefit from adjuvant radiotherapy.

E-PS-19-005

Adult supratentorial extraventricular anaplastic ependymoma: a rare case

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Background & objectives: Intracranial ependymomas in adult patients are relatively rare. Most of the ependymomas develop in the ventricles however it can occur at any site in the central nervous system and extraventricular ependymomas are quite uncommon.
Methods: A 68-year-old female patient presented with having speaking problems and stutter. On physical examination there was no evidence of paresis, neural deficitis or cranial nerve abnormalities. Cranial MRI demonstrated a left temporal T1 hypointense, T2 hyperintense cystic lesion with solid components. There was contrast enhancement in solid component. In diffusion weighted imaging, there was no diffusion attenuation in cystic areas.
Results: Histologically, a cystic tumour infiltration consisting of small round cells with epithelioid arrangement which shows sharp demarcation with brain parenchyma was observed. There was also microvascular proliferation, perivascular pseudorosette formation and necrosis. GFAP, vimentin and EMA was positive and Ki67 index was high (%60-70). Olig2 and IDH-1 showed no immunreactivity and there was no loss of ATRX expression. Final diagnosis was extraventricular anaplastic ependymoma.
Conclusion: It is theorized that extraventricular ependymomas can develop from intraparenchymal or subarachnoid ependymal cysts. Although it is rare appearance, ependymomas should be considered as a differential diagnosis of a glioblastoma in adult patients presented with extraventricular intracranial mass. Considering the occurrence of EMA positive glioblastomas, this diagnosis was given with the support of radiologic characteristics of the lesion.

E-PS-19-006

Persistent and chemoresistant brain metastases of choriocarcinoma in a young female

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Background & objectives: Choriocarcinoma is a rare and invasive type of gestational trophoblastic neoplasia that rapidly metastasizes and has propensity to cause haemorrhage, making this diagnosis a medical emergency. It can develop from any gestational trophoblastic tissue.
Methods: A 22-year-old Venezuelan female visiting her auntie in Spain, presented to the Emergency Department with an epileptic seizure in 2017. TC showed an hyperdense mass of 26 mm with frontoparietal location in the left brain and a pulmonary mass in the left inferior lobe. They suspected glioma and practised a surgical excision of the brain mass.
Results: The diagnosis was choriocarcinoma metastasis with necro-haemorrhagic changes. When they asked her she told that she had a delivery in 2014 and a molar pregnancy treated with curettage in 2015. The gynaecological exam revealed nothing abnormal. She underwent long-term follow-up by oncologists evaluating her chorionic gonadotropin levels and treating her with chemotherapy. Nonetheless, a new parietal right mass appeared in 2018, undergoing radiosurgery. They finally had to remove it surgically in March 2019 but in October TC showed a lesion in the same location that was surgically treated in 2020 and diagnosed as a choriocarcinoma recidive.
Conclusion: Most women who are found to have choriocarcinoma can be cured but delayed diagnosis may increase the risk of metastasis and chemotherapy resistance, affecting its prognosis. Following molar pregnancy, women should be followed-up and our patient wasn´t followed-up for various reasons so brain metastases were already present at time of diagnosis. We reiterate the importance of early diagnosis and treatment resulting in improved prognosis and outcome for patients.

E-PS-19-008

Capillary hemangioblastoma presenting as cerebellopontine angle tumour: a case report

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Background & objectives: In the Philippines, primary adult brain tumours are predominantly meningiomas and glial tumours. Metastatic tumours (3.2%) and hemangioblastomas (2.2%) comprise the minority of adult brain tumours. There is no reported incidence of brain tumours in the cerebellopontine angle (CPA) in the Philippines but one local study showed incidence of 10.7% in the cerebellum or brain stem.
Given the predominance of slow-growing tumours in the Philippines, surgery alone is commonly favoured. In this study, capillary hemangioblastoma occurring in the CPA is presented.
Methods: A 41-year-old, Filipino female presented with diffuse headache gradually progressing for 1 month. MRI showed an enhancing mass lesion measuring 3.8 x 3.0 x 2.6 cm located at the left CPA with significant oedema and mass effect with compression of the left ventricle. She underwent suboccipital craniectomy. Intraoperative findings showed a very vascular tumour, which profusely bled upon biopsy.
Results: Submitted were multiple light brown to dark brown soft to friable tissue fragments aggregately measuring 0.4 x 0.3 x 0.2 cm. This was composed of spindle cells forming anastomosing vascular channels with slightly foamy stromal cells with plump, hyperchromatic nuclei. Immunohistochemical studies showed reactivity for Vimentin and Inhibin and negative staining for S-100. The immunohistophenotypic profile supported the diagnosis of hemangioblastoma.
Conclusion: Vascular brain tumours may pose a problem in surgical therapy alone because profuse bleeding may hinder the procedure.

Identifying uncommon tumours in certain brain areas should be considered as this may help in the management of such cases.

E-PS-19-009

A retrospective study of neuropathological features and clinical correlations in high-grade gliomas

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Background & objectives: High-grade gliomas are the most aggressive primary malignant brain tumours of controversial origin, occurring at all ages, with low survival rates and increasing incidence. Our study aimed to examine the epidemiological and pathological characteristics of high-grade-gliomas from a clinical perspective.
Methods: We performed a retrospective research at Colentina University Clinical Hospital over a period of 5 years (2015-2019) and selected the cases morphologically diagnosed as high-grade gliomas, including the ones diagnosed after a former WHO Classification of Tumours. Data collected included sex, age, morphology, location, tumour recurrence and main presenting symptoms.
Results: Our study included 143 patients, age between 8y and 86y, 84 men and 59 women. Glioblastoma NOS was the most frequent tumour type diagnosed (78%), followed by anaplastic astrocytoma (4.8%), anaplastic mixed glioma (4.8%), giant cell glioblastoma (4.1%), anaplastic oligodendroglioma (2.7%), glioblastoma with oligodendroglial component (2.7%) and glioblastoma with primitive neuronal component (2%). Most common tumour locations were in frontal lobe (35%), temporal lobe (25%), parietal lobe (13%), whilst uncommon sites were thalamus (3.6%), cerebellum (1.8%). There were 25 cases of recurrences (24 GBM and one anaplastic oligodendroglioma), earliest recurrence-4 months and the latest one-4 years. The main onset symptoms: seizures, followed by speech difficulties, motor changes and visual disturbances.
Conclusion: The most frequent high-grade gliomas diagnosed in the last five years in our department were NOS glioblastomas, with a sex ratio M/F – 1.42/1 and median age 54y, predominantly located in frontal lobe, associated with maximum recurrence rate. Directions for future research are to investigate the molecular features and their correlation with neuropathological features, while the last one are essential, especially when molecular studies are not within reach.

E-PS-19-010

Morphological and genetic studies of gliomas to develop new approaches to targeted therapy

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Background & objectives: The objective is to study the expression and variants of coexpression of transcription factors NeuroD1, Prox1, FoxM1, somatostatin receptors of the 2nd and 5th type, CD38 and CXCR4 receptors in glioblastoma.
Methods: The methods included an immunohistochemical study with antibodies to NeuroD1, Prox1, FoxM1, somatostatin receptors of the 2nd and 5th type, CD38 and CXCR4 receptors and moAn analysis of the protein coexpression in various glioblastomasrphometric analysis of glioblastoma fragments from 21 patients (surgical material).
Results: Results: glioblastoma cells expressed NeuroD1 in 100%, FoxM1 in 86%, CXCR4 in 76%, Prox1 in 57%, CD38 in 10%, SSTR2 and STR5 in 100% cases. The average number of cells with expression of NeuroD1, FoxM1, CXCR4, Prox1, CD38, SSTR2 and SSTR5 was 95 ±1%, 83±6%, 76±6%, 58±7%, 11±3%, 2±1%, 7±%1 respectively. Six variants of the protein coexpression were revealed. The FoxM1+/NeuroD1+/Prox1-/CXCR4+/CD38- immunophenotype was found most frequently (in 38% of cases).
Conclusion: Conclusion: the expression of CD38 was detected in glioblastoma cells. According to the data obtained, a new personalized approach to treatment is required with definition of targets for exposure and the corresponding spectrum of drugs in each individual case.

E-PS-19-011

Morphological and molecular spectrum of glioma according to WHO classification

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Background & objectives: Updated WHO classification for glioma includes histopathological & molecular patterns of glial tumours for grading. The aim of the study was to determine the frequency of Glial tumours & to perform its grading according to modified WHO classification 2016.
Methods: This retrospective study was conducted in the Oncology department, Jinnah Post Graduate Medical centre (JPMC), Karachi, Pakistan. Diagnosed cases of Glioma registered between January 2017 to December 2019 in the oncology ward were included in the study. Grading was performed according to WHO classification 2016. Data analysis was carried out by SPSS version 25.0.
Results: Among 115 patients male to female ratio was 2.1:1. Mean age was 38.41. Oligodendroglioma was the most common morphological type (53.5%). High-grade tumours including Grade 3 and 4 constituted 54.2% of cases, followed by grade 2 (40.2%). The most common presenting complaint was headache (42.2%). GFAP expression was positive in 80.5% of cases, followed by 6.1% cases of 1P\19q codeletion, triple positive and Ki67 positivity in 1.2% each.
Conclusion: Oligodendroglioma (grade 2) was the most common individual histological type, however, grade 3 and 4 tumours together constituted majority of cases. Temporoparietal lobe was the most common site of the tumour followed by the frontal lobe. Headache was the most frequent presenting complaint. Most tumours expressed GFAP, followed by 1p/19q codeletion, Triple positive and ki67 expression, respectively.

E-PS-19-012

Uncommon finding in a common tumour - a medulloblastoma with loss of mismatch repair protein expression in a young child

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Background & objectives: Microsatellite instability is an uncommon event in brain tumours. We describe a medulloblastoma with loss of mismatch repair protein expression by immunohistochemistry in a 31-month-old girl.
Methods: The young girl with mild developmental delay, multiple café au lait spots and suspected hearing impairment since birth, was worked up for possible Neurofibromatosis 1. Brain imaging revealed a cerebellar tumour. Resection was performed.
Results: The tumour was histologically a medulloblastoma of classic morphology and molecularly subgroup 3 without MYC amplification. Further mismatch repair protein immunohistochemistry was performed. Results showed loss of MSH6 staining while staining of MLH1, PMS2 and MSH2 was preserved.
Conclusion: Microsatellite instability (MSI) is an uncommon event in brain tumour. MSI testing is not reflex testing nor recommendation under the current WHO classification. However, detection of MSI is important in clinical management and prognosis of the tumour. Detection requires high index of suspicion and a multidisciplinary approach.

E-PS-19-013

The effect of destruction of the mucous membrane of the olfactory zone of the nasal septum on the cytoarchitectonics of the pyramidal layer of the hippocampus

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Background & objectives: Injury of smell in rats provokes changes in the hippocampus and complex behavioural responses in response to odor irritation. Objective. to study the effect of destruction of nasal septum olfactory zone mucous on hippocampal pyramidal layer cytoarchitectonics
Methods: Injury to the nasal septum mucosa in the olfactory zone was performed under anaesthesia with tiletamine hydrochloride and zolazepam hydrochloride. 10 rats were control group (CG). The experimental group included 30 rats. The serial sections of the brain were stained with toluidine blue. Dark nerons (DN) were studied in the subfields of the hippocampus 2, 4&6 days after surgery.
Results: In the subfields CA1,CA2,CA3&DG on 2nd day after the operation, the number of DN was greater than in CG($p<0.001$). On 4th day, the amount of DN increased in CA1&CA2 zones, compared with 2nd day&CG($p<0.01$). On 4th day in CA3&DG, there were no differences with CG. On 6th day, in CA1, the amount of DN decreased, compared with 2nd day($p<0.001$),but was greater than in CG ($p<0.01$). In CA2,CA3&DG there were no differences with CG.
Conclusion: The dysfunction of the peripheral part of the analytic analyser leads to the appearance of dark nerons in various subfields of the hippocampus. It may also indicate impaired behaviour and memory with this injury.
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E-PS-19-014

Evaluation of squash smear technique in rapid diagnosis of neoplastic and non-neoplastic lesions of the central nervous system & spinal cord

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Background & objectives: Intraoperative consultation of CNS lesions is considered to be an important preliminary diagnostic tool to distinguish neoplastic lesions from non-neoplastic conditions at surgery. In intraoperative setting goal is not to diagnose and grade every case definitively, rather to provide sufficient preliminary information to optimize the surgery. The aim of this study was to assess the utility of intraoperative squash smear cytology of lesions of Central Nervous System (CNS) & spinal cord and correlate with the final histopathological diagnosis.
Methods: A total of 109 cases of CNS & spinal cord lesions were included in the prospective study from January 2011 to March 2012 at Institute of Medical Sciences, Banaras Hindu University, Varanasi. Intraoperative specimens were used for crush/squash smears and correlated with the final histopathological diagnosis.
Results: The patients presented in the age range of 2.5–70 years with the median age of 31.5 years. Of 106 patients, 66 patients were males & 40 patents were females with male predominance. The diagnostic accuracy was found to be 88.67% (including partially correlated cases) whereas it was calculated as 85.90% excluding partial correlated cases. The sensitivity and specificity were 99.09% and 87.5% respectively.
Conclusion: In conclusion, squash preparations provide fairly accurate diagnoses on cytological evaluation of CNS & spinal cord lesions.

E-PS-19-015

Meningeal perineurioma – a case report

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Background & objectives: Perineurioma is an uncommon, usually benign, spindle cell tumour of peripheral nerve sheath origin with a predilection for the soft tissues. Only one intracerebral example has been described.
Methods: A 56 years-old woman with an epileptic status, has been incidentally discovered with a parietal (right) tumour of 3 cm diameter while undergoing computer tomography, on the assumption of it being a meningioma. Total surgical resection was performed.
Results: The surgical specimen was white to tan measuring 2x2x1,5 cm. Histologically, the tumour composed of anastomosing cords of fusiform cells. Nuclear atypia was mild and mitotic activity undetectable. Tumour cells coexpressed EMA (focally) and Vimentin. No staining for S100, GFAP, HHF-35, Desmin, SMA, CD34, CD57, Ker AE1/AE3 was detected. The MIB-1 labelling index averaged 1,5%.
Conclusion: A diagnosis of perineurioma was performed, in the differential diagnostic context of which it is apt to being misconstrued as either meningioma, solitary fibrous tumour, or neurofibroma.

E-PS-19-016

The relationship between clinical factors with meningioma histopathologic grade in Siloam Hospital Lippo Village 2014-2018

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Background & objectives: Meningioma are the most common intracranial tumour of central nervous system tumours. Although the prevalence is lower, the WHO grade II and III meningioma are more aggressive, with higher rates of mitosis, are more likely to recur after surgery and have lower survival rates. The ability to differentiate between WHO I and WHO II/III meningioma before surgery can contribute to a large clinical benefit in helping the neurosurgeon making the best management planning.
Methods: This is an observational analytic study using cross-sectional design. Sample will be recruited using consecutive sampling. A retrospective chart review of meningioma patients in Siloam Hospital Lippo Village, Tangerang, Indonesia between 2014 - 2018 will be performed. Relationship between analysed variables and meningioma grade investigated using Chi-square and Fisher-exact.
Results: Total 98 (69%) people suffered meningioma from low grade and 44 (31%) people suffered from high grade. Clinical factors (tumour location, tumour size, oedema, necrosis, age, gender) had significant results $p \leq 0.05$ with Chi Square and Fisher-exact statistical tests. Multivariate results also show that all 6 variables have a close relationship between each other.
Conclusion: There is a relationship between clinical factors with histopathological meningioma grade in patients at Siloam Hospital Lippo Village, Tangerang in 2014-2018.

E-PS-19-017

Papillary tumour of the pineal region – a case report of a rare entity and review of the literature

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Background & objectives: The papillary tumour of the pineal region (PTPR) is an extremely rare neuroepithelial tumour occurring in the pineal region and is characterized by a combination of papillary and solid areas, with epithelial-like cells. It occurs both in children and adults.
Methods: We report the case of a 55-year-old male with headache and ataxia lasting for a few months. The brain MRI showed an ill-defined pineal region space occupying lesion, with solid and cystic components, associated with hydrocephalus. The patient underwent surgery to remove the tumour.
Results: The neuropathological analysis showed a neoplasia of epithelial morphology, with both papillary areas and areas of high cellular density where rosettes and pseudo-rosettes could be observed. In the papillary areas, some blood vessels were lined by tall columnar cells with pale cytoplasm. There were no mitoses or necrotic areas. The immunohistochemistry study using antibodies against the cytokeratin AE1/AE3 (CKAE1/AE3), epithelial membrane antigen (EMA), glial fibrillary acidic protein (GFAP), neuron specific enolase (NSE), synaptophysin and neurofilament proteins was only positive for CKAE1/AE3 and NSE. The proliferative index (% Ki-67) was low.
Conclusion: This case illustrates the main features of this rare pineal tumour, whose precise histological grading criteria remains to be defined, although its biological behaviour might correspond to WHO grade II or III. The overall 10-year survival is around 70%.

E-PS-19-019
Diffuse midline glioma with histone H3 K27M mutation: a report of 3 cases in adults
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Background & objectives: Diffuse midline glioma, H3 K27M-mutant, recently codified in the 2016 World Health Organisation classification of central nervous system tumours, is an infiltrative high grade predominantly astrocytic glioma, usually occurring in children. In IDH-wildtype diffusely infiltrative gliomas centred in midline structures, a H3 K27M mutation confers a worse prognosis; the biologic behaviour corresponds to WHO grade IV, regardless of the histologic grade. We describe 3 cases from our adult neuropathology practice, encountered over 18 months.
Methods: A 55-year-old male, on follow-up after radiotherapy for nasopharyngeal carcinoma, presented with hoarseness. Magnetic resonance imaging (MRI) showed a right cerebellomedullary angle cistern tumour.
A 48-year-old male presented with right-sided facial numbness. MRI showed a heterogeneously enhancing tumour in the right hemipons and middle cerebellar peduncle.
A 25-year-old male presented with blurred vision. MRI showed a suprasellar / hypothalamic-optic chiasmatic tumour.
Results: Biopsy in each case showed a diffuse astrocytic tumour. Histological high-grade features were identified in Cases 2 and 3. On immunohistochemistry, the tumour cells showed strong nuclear staining for K27M-mutant H3, and no staining for the IDH1 R132H mutant protein. The first patient is on follow-up 4 months post-diagnosis. The second and third patients died of disease 5 months and 2 months post-biopsy, respectively.
Conclusion: Although less common in adults, the diagnosis of diffuse midline glioma, H3 K27M-mutant is readily made with the antibody to K27M-mutant H3 and enables better prognostication in adult patients.

E-PS-19-024
Uncommon case of synchronic tumours, a case review
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Background & objectives: Multiple primary malignant tumours are a relevant issue because of the importance of their prompt diagnosis for adequate management. We aim to describe the case of a 53-year-old male who was found unconscious and his histological findings.
Methods: Upon arrival, a CT scan was performed, suggesting the possibility of a primary brain tumour in the right temporal space. He was urgently operated, and an intraoperative biopsy was obtained, informed as high-grade tumour. The tumour was excised.
One month after the brain surgery, during follow-up, his general practitioner identified some lumps in the neck, which were biopsied.
Results: The histological analysis of the brain tumour revealed the presence of a rhabdoid meningioma. Histologically it presents abundant eosinophilic cytoplasm, cytoplasmic inclusion with eccentrically placed vesicular nuclei and prominent nucleoli.
The study of the biopsy of the lumps identified in the neck, revealed a follicular lymphoma grade 3B, indicating that the patient presented two synchronous tumours of different lineages, one meningothelial and the other lymphoid.
Conclusion: As the prevalence of synchronic multiple primary malignant tumours is growing-up, it is essential to establish robust protocols for the best follow-up of the patients, so we can improve their prognosis and quality of life. Fortunately, the standardized, rapid performance and the targeted management of the present case allow our patient to stay alive, even though the poor outcome that this tumour normally presents.

E-PS-19-025
Diffuse midline glioma in a 4-year-old girl: a case report
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Background & objectives: We report the case of a very young girl with a glial tumour. Diffuse midline gliomas a rare subtype of glial tumours characterized by infiltrative midline high-grade tumours with astrocytic differentiation diagnosed at an average age of 7 years.
Methods: Due to right facial paralysis which did not respond to corticosteroid therapy, a magnetic resonance was carried out, and the diagnosis of a low-grade glioma was suggested. Therefore, the patient was operated in the Donostia University Hospital and biopsy was handed to the Pathology Service. The patient died 21 months after the surgery and an autopsy was performed.
Results: Histological studies of the biopsy revealed glial proliferation with low-moderate cellularity, without mitotic figures, microvascular proliferation or necrosis, however, Ki67 >10% and H3-K27M mutation were detected at 12 de Octubre Hospital, suggestive of diffuse midline glioma of the pons.
The autopsy performed at Araba University Hospital revealed a distortion of the brain stem, by a white, jelly-like lesion that totally involved the brain stem.
Conclusion: We report the histological and autopsy findings in a girl without any remarkable personal history, diagnosed of a diffuse midline glioma of the pons 55 months earlier than the average expected age. Even if the prognosis is poor, it is even worst in the presence of the H3-K27M mutation which leads to more than 90% of patients deceasing before 2 years after diagnosis, as the present case.

E-PS-19-026
Schwannoma with neuroblastoma-like rosettes
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Background & objectives: Schwannoma is typically benign nerve sheath tumour arising from differentiated Schwann cells. This tumour is encapsulated with solitary growth in 90% of all cases, however some morphologically diverse variants have been reported, which may cause diagnostic confusion.
Methods: A 41-year-old male presented with a history of chronic pain in the cervical region, lasting from 2011. MRI revealed an extensive extraaxial tumour of the craniocervical junction. The intradural extramedullary tumour was well encapsulated, measured 25x25mm and was dislocating the spinal cord to the left. The patient was admitted to the neurosurgery department, where the tumour was subtotally resected.
Results: Macroscopically the tumour was fragmented, pale and solid, with hard consistency. Microscopically we found irregular bone trabeculae admixed with tumorous proliferation with large rosette-like structures with homogeneous material in the centre and small, round to oval palisading cells at the periphery with scarce cytoplasm, without any atypia or increased mitotic activity. Beside rosettes, the tumour consisted of bland looking, spindle-shaped cells with corrugated nuclei. The density of this population was variable, with signs of degenerative atypia in the more cellular areas. Immunohistochemistry demonstrated expression of S100, CD99, D2-40, negativity for MUC4, GFAP, PR, CD56, synaptophysin, chromogranine, bcl-2 and AE1/3, with low level of Ki-67 (< 1%) proliferative index.
Conclusion: The diagnosis according to clinical, histopathological and immunohistochemical results was schwannoma with neuroblastoma-like rosettes. Low-grade fibromyxoid sarcoma (hyalinizing spindle cell tumour with giant rosettes) was considered in the differential diagnosis, but MUC4 negativity excluded this diagnosis.

E-PS-19-027
Progressive multifocal leukoencephalopathy associated with Ibrutinib treatment
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Background & objectives: Progressive multifocal leukoencephalopathy (PML) is rare, but highly fatal demyelinating disorder of the central nervous system, caused by reactivation of John Cunningham poliomavirus (JCV), affecting almost exclusively patients with compromised immune system. Hereby we present a drug-associated case of PML.
Methods: 62-year old female patient was diagnosed with a small cell variant of mantle cell lymphoma of the conjunctiva treated with rituximab-based chemotherapy, leading to complete remission. Disease relapsed 7 years later, followed by Ibrutinib treatment. Three weeks after treatment initiation patient started to develop neurological symptoms, and MRI showed newly developed multiple hyperintense lesions in white matter on FLAIR sequence.
Results: In spite of discontinuation of Ibrutinib treatment patient died due to neurologic deterioration and subsequent bronchopneumonia. Autopsy did not reveal any visible changes of brain tissue, however, histological examination of brain showed subcortical areas of demyelination. Oligodendrocytes and astrocytes around the lesions showed discrete cytological and nuclear atypia, with sparse large hyperchromatic nuclear inclusions in astrocytes. Surrounding brain parenchyma displayed signs of microglial activation and small amount of T cells (CD3+, CD8+). Real-time PCR test performed on formalin-fixed paraffin-embedded brain tissue from areas of evident demyelination detected DNA of JCV. Clinical symptomatology, with MRI and histological changes followed by detection of JCV DNA has led to final diagnosis of PML.
Conclusion: PML development has been initially associated with intrinsic disorders of the immune system; however, with the implementation of new immunomodulatory medications, the drug associated PML has become more frequent. This case report presents a possible severe adverse effect of the immunomodulatory drug Ibrutinib, and the importance of multidisciplinary approach in the diagnosis of PML.

E-PS-19-028
Embryonal tumour with multilayered rosettes (ETMR)
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Background & objectives: The 2016 update of the WHO Classification of Tumours of the CNS has redefined a number of tumours. Embryonal Tumour With Multilayered Rosettes is a recently described pathological entity. They are rare tumour affecting young children. Prognosis is extremely poor.
Methods: We retrieved and reviewed H&E stained microscopy glass slides of 13 ETMR cases with history of headache, vomiting and pain. These cases were treated at different institutes and diagnosed at our institute between March 2008 and July 2019. Morphologic features such as presence of papillary/tubular-trabecular architecture, surface blebs, external blebs, primitive cell component, neuronal, glial and mesenchymal differentiation were assessed.
Results: Patients' age ranged from 8 months to 10 years with median of 3.63 years. Female to Male ratio was 3:2. Brain was the most commonly involved site.
Most of the tumours were received in multiple pieces. All the cases showed features of malignancy. Follow-up of 6 patients could be attained and 3 were found to have expired due to some undiagnosed disease rest were all healthy with a 2 weeks follow up history. Treatment of all patients was excision alone with few patients who received radiotherapy.
Microscopically, as presence of papillary/tubular-trabecular architecture, surface blebs, external blebs, primitive cell component, neuronal, glial and mesenchymal differentiation was observed in all cases.
Conclusion: ETMR are a distinct entity with majority of them behaving aggressively even after being treated by local excision. Although the WHO currently recognizes 3 distinct histopathological entities-embryonal tumour with abundant neuropil and true rosettes, ependymoblastoma and medulloepithelioma. Recent studies indicate that these tumours have a common molecular profile and clinical course and that they are now classified as a single entity.

E-PS-19-029
Immunohistochemical characterisation and histopathology of astrocytic neoplasms at a tertiary Nigerian hospital
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Background & objectives: To describe the histologic features and pattern of expression of selected molecular markers of tumour biology including epithelial growth factor receptor (EGFR), mutant p53 and mutant isocitrate dehydrogenase-1 (IDH-1R132H) among astrocytic neoplasms at the University College Hospital, Ibadan, Nigeria.
Methods: Retrospective study involving 81 histologically diagnosed CNS neoplasms between January 2004 and December 2015. Ethical clearance was obtained. Immunohistochemistry was done using IDH-1 R132H, p53 and EGFR monoclonal antibodies. Cases were reviewed using the WHO Classification (2016). Membranous and cytoplasmic staining of EGFR and IDH-1R132H monoclonal antibodies respectively were regarded positive, nuclear staining of p53 mouse antibody was regarded positive.
Results: Males constituted a majority of cases, 50 (61.7%). Male - Female ratio was 1.6:1. Mean age was 30.6 years. There was a tendency for tumours to be of higher WHO grades with increasing age, albeit glioblastoma cases tended to present at younger ages. The higher WHO grades were more likely to be located supratentorially. Glioblastomas accounted for most of the diagnosis 39 (48.1%), followed by pilocytic astrocytomas at 23 (28.4%). There was a low positive cytoplasmic expression of IDH-1 with only 3 (3.7%) being positive, 8 (9.9%) showed a positive nuclear expression for mutant

p53 while 17 (21%) showed membranous positivity for EGFR expression.
Conclusion: Glioblastomas in this study presented in younger patients. Optimal stratification for astrocytomas can be achieved using a combination of IDH-1/EGFR immunohistochemistry.

E-PS-19-031
Glioblastoma with epithelial metaplasia: diagnostic pitfalls and the importance of adequate sampling
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Background & objectives: Glioblastoma is one of the most common brain tumours. However, few other neoplasms match its heterogeneity. While the name "glioblastoma multiforme" is no longer in use, it perfectly encompasses the variable histology of this tumour.
Methods: The glial nature of most glioblastomas becomes apparent during microscopic evaluation but, with the increase of stereotaxic needle biopsies, new difficulties arise.
We present the case of a 65 years old man, admitted to our hospital with seizures and left crural paresis. Neuroimaging revealed a small parasagittal, cortical-subcortical mass in the right parietal lobe, with important peritumoral oedema.
Results: A needle biopsy was performed.
Microscopic examination of the resulted tissue revealed a poorly differentiated epithelial proliferation with focal gland formation. Our diagnosis was of metastatic adenocarcinoma.
Immunohistochemical positivity for CK7 and TTF1, suggested a pulmonary origin. However, detailed lung scans and subsequent clinical investigations failed to find the primary tumour. Complete ablation of the brain lesion was decided, providing a 20/15/6 mm sample.
New microscopic features became apparent.
Conclusion: The epithelial aspects, consisting of both poorly differentiated gland structures and squamous morules, were surrounded by a fibrillary glial stroma with an important gemistocytic component and frequent mitoses.
While both a tumour association as well as reactive gliosis were taken into consideration, these are less likely than glioblastoma with epithelial metaplasia, especially in the current clinical setting. Ancillary tests are of limited use since such glioblastomas can express a variety of epithelial markers and often don't stain for glial ones.

E-PS-19-032
Calcifying pseudoneoplasm of the neuraxis: a rare but reassuring cause of generalised tonic clonic seizures
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Background & objectives: Calcifying pseudoneoplasm of the neuraxis is a rare benign lesion with around 60 reported cases. It is predominantly found in young adults without gender predilection. It carries good prognosis unlike the other common calcifying lesions of the brain.
Methods: A 30-year-old male with no known co-morbidities was brought by ambulance, reported to be convulsing for a few minutes by his roommate after which he became sleepy but was fully conscious when the paramedics arrived. An MRI head with contrast showed a well-defined lesion in left parietal lobe with areas of curvilinear enhancement along with calcification.
Results: Possibility of a long-standing vascular malformation with calcification was raised. Craniotomy with complete resection of the lesion was done. Histopathological analysis showed a calcified lesion composed of chondromyxoid matrix in a nodular pattern exhibiting radial fibrillarity at the periphery focally covered by palisading spindled to epithelioid cells with little fibrous stroma, calcification and osseous metaplasia. Adjacent brain parenchyma showed Rosenthal fibres.
Upon immunohistochemistry, the spindle cells stained positive for Epithelial membrane antigen (EMA), Vimentin and Progesterone receptor (PR). It stained negative for Glial Fibrillary protein (GFAP). Diagnosis of Calcifying pseudoneoplasm of neuroxis (CAPNON) was rendered.
Conclusion: Calcifying pseudoneoplasm of the neuraxis (CAPNON) are rare benign brain lesions that present incidentally or with neurological symptoms like seizures. Since many CNS lesions are associated with calcifications, both metastatic, neoplastic and non-neoplastic, it is important to recognize this lesion as it carries good prognosis.

E-PS-19-033
A rare ossified retroperitoneal schwannoma associated with clear cell renal cell carcinoma: a case report
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Background & objectives: An “ancient” schwannoma is characterized by various degenerative changes, but ossification is uncommon and only a few descriptions can be found in the world literature. We report a case of ossified retroperitoneal schwannoma which was detected simultaneously with kidney cancer.
Methods: A 52-year-old man was admitted to the hospital with a tumour of the left kidney 3.7 cm in diameter. The examination revealed an additional tumour of the retroperitoneal space 12.0 cm in diameter. The kidney tumour was resected, and the retroperitoneal tumour was removed. The connection between them was not revealed. Histological and immunohistochemical studies of these tumours were performed.
Results: Microscopically the kidney tumour was a clear cell renal cell carcinoma, G1. The second tumour had a different structure. It was composed of closely packed, hyperchromatic spindle-shaped cells, in some places mitotically active with Ki-67 up to 20%. There were areas of sclerosis, hyalinization, xanthomatous and inflammatory cell infiltration, irregularly spaced vessels, and foci of ossification of various sizes. Immunohistochemically, cellular cites arranged in bundles or interlacing fascicles were S-100, SOX10 and NSE strongly positive. This tumour was diagnosed as a benign schwannoma with severe degenerative changes including ossification (“ancient” schwannoma) and cellular areas (Antoni A).
Conclusion: Ossification in schwannomas is a very rare process and may complicate the diagnosis. Correct assessment of the whole tumour structure and the use of immunohistochemical markers help to avoid diagnostical mistakes. Connection of this unusual schwannoma ossification with kidney cancer remained unclear.

E-PS-19-034
Single neuroimagistically described brain lesion resulted in two different primary brain tumours
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Background & objectives: Glioblastomas are the most frequent malignant brain tumours in adults, accounting for 45-50% of all primary malignant brain neoplasms. Schwannomas are benign, representing 8% of all intracranial tumours, but the coexistence of these lesions is extremely rare.
Methods: We report the case of a 59 years old female who was admitted to the ‘Bagdasar-Arseni Clinical Emergency Hospital’ accusing neurocognitive changes and receptive aphasia which progressively developed within the last two months. She had left hypoacusis for 10 years. Neuroimaging described an irregular, heterogeneously contrast-

enhancing mass with surrounding oedema and hemosiderin deposits in the temporal-cerebellar region.
Results: The intraoperative consultation surprisingly revealed two different lesions. The temporoparietal mass showed typical features of glioblastoma while the one in the cerebellopontine angle revealed a schwannoma with a predominant Antoni A pattern. Total ablation of the temporoparietal tumour and subtotal ablation of the one in the cerebellopontine angle were performed. The follow-up of the patient revealed recurrence of the temporoparietal glioblastoma after two months.
Conclusion: Multiple primary brain tumours with different histology occurring in the same patient is a very rare finding and the pathogenesis of this condition is still unclear. When a high-grade glioma is associated the prognosis is very poor. While the neuroimaging suggested a single lesion, the intraoperative consultation revealed two different tumours. When the lesions develop adjacent to each other, the case can represent a diagnostic challenge for the pathologist.

E-PS-19-035
Ganglioglioma with atypical localisation in a toddler
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Background & objectives: Ganglioglioma is a rare slowly growing primary benign tumour of the central nervous system (CNS), that preferentially presents in the temporal lobe of children and young adults. It is a well-differentiated neuroepithelial tumour, but some of them may be aggressive.
Methods: We present the case of a 3-year-old male child, with a medical history of a brain stem tumour, which was discovered during an imagistic investigation and diagnosed as a glioma. The tissue samples were processed and examined with standard H&E technique, special stains for nervous tissue such as Nissl and Bielschowsky silver stain and immunohistochemistry.
Results: Grossly, the brain stem tumour was nodular, quite well-circumscribed, partially encapsulated, with firm consistency, measuring approx. 2 cm in maximum diameter. Microscopically, the tumour showed a biphasic proliferation consisting of moderate differentiated ganglion cells, evidenced by Nissl and Bielschowsky silver stains and neoplastic astrocytic type glial cells arranged in a fascicular and solid pattern with areas of moderate anaplastic features and abundant intermixed glial fibres with focal microcystic degeneration. The histological aspects correlated with IHC tests were suggestive of ganglioglioma. The aforementioned immunohistochemical markers GFAP, S-100, NFT were positive, PCNA expressed in 1-2% tumour cells and IDH1 was negative.
Conclusion: The histopathological investigation and immunohistochemical tests confirmed the diagnosis of ganglioglioma, a rare primary benign tumour of the CNS, with atypical localization.

E-PS-19-036
The wide spectrum of brain secondary tumours – a retrospective study of pathological findings
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Background & objectives: Metastases are the most common brain tumours in adults. Cancer databases, often incomplete, lead to underestimation of their incidence, which appears to be increasing. This study evaluates the origin, histological types of brain metastasis, illustrating the challenging diagnostic algorithm implied.
Methods: We reviewed 107 consecutive cases of cerebral secondary tumours recorded between 2015-2019 in our department, including 60% men and 40% women, aged 29-79 (median age 58 years), most of them diagnosed between 50-69 years, both intraparenchymal and meningeal.
Usual and special stains and immunohistochemical assays were performed for an accurate diagnosis, correlated with clinical and neuroimaging data.
Results: Primaries were mainly represented by lung carcinomas-43%, melanoma-19% and breast cancers-16%, while digestive tract-6%, kidney-3% and salivary glands-3% cancers were less frequent origins.
Some were unusual primary neoplasms (one carcinosarcoma of salivary glands, one basaloid pulmonary squamous-cell carcinoma). 10% of the tumours had rare primary locations: pancreas, uterus, ovary, soft tissue, testis, thyroid, urothelium. In few cases-2%, origin remained undetermined despite extensive immunohistochemical workout.
Most carcinomas were poorly differentiated (62%), only one well differentiated thyroid tumour. 60% of the pulmonary tumours were adenocarcinomas (63% moderately differentiated). All the breast tumours were poorly differentiated invasive carcinomas of no-special-type.
The number of brain metastases increased over five years from 9 to 47.
Conclusion: The features of brain metastases are those of high-grade, aggressive tumours, mostly pulmonary adenocarcinoma, melanoma, and breast invasive carcinoma. Although exceptional, other primaries should be considered, and sometimes, even the differential diagnosis with a primary tumour can be a difficult task for the pathologist.
Of all the cases, adenocarcinoma, melanoma, squamous-cell carcinoma are the predominant histological types.
Incidence of secondary brain tumours has constantly increased in recent years.

E-PS-20 Ophthalmic Pathology

E-PS-20-002
Endocrine mucin-producing sweat gland carcinoma of the eyelid and its progression to mucinous carcinoma – two case reports
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Background & objectives: Endocrine mucin-producing sweat gland carcinoma (EMPSGC) is a rare neuroendocrine appendageal skin tumour that may be a precursor of mucinous carcinoma. This study aims to establish the diagnostic challenges and to emphasize the possibility of coexistence of both entities.
Methods: We present two separate cases of a 54- and a 74- years-old females with excisional biopsies of small cystic lesions of the lower eyelids. After routine tissue processing and microscopic analysis, further examination was performed, including histochemistry (PAS staining) and immunohistochemistry (CK7, neuroendocrine, myoepithelial markers, Ki 67 and others). Comparison of both cases led to our conclusions.
Results: In both cases, the examination revealed a similar mucin-secreting neuroendocrine neoplasm with morphological and immunohistochemical features corresponding to EMPSGC. Elaboration of a myoepithelial layer by immunohistochemistry confirms primary cutaneous origin and excludes metastatic adenocarcinoma. By contrast, in the case of the 74- years-old female, the focal presence of larger extracellular pools of stromal mucin, containing floating nests of tumour cells, indicates the progression to mucinous adenocarcinoma.
Conclusion: Endocrine mucin producing sweat gland carcinoma (EMPSGC) and cutaneous mucinous adenocarcinoma are two separate entities with primary origin and similar histopathological characteristics. Hybrid lesions containing components of both entities exist and such cases should be diagnosed as cutaneous mucinous adenocarcinoma (WHO classification of tumours, 4th edition).

E-PS-20-003

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) of the conjunctiva: a case report and review of the literature

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Background & objectives: Conjunctival lymphoma accounts for nearly 25% cases of ocular adnexal lymphomas, and normally occurs unilaterally in middle-aged and elderly individuals. The most frequent are extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) and follicular lymphoma, both generally low-grade.
Methods: We report the case of a 54-year-old male with a one-year history of a salmon patch lesion in the right eye. The lesion was biopsied and submitted to both flow cytometry and histopathological analysis. The left eye was unremarkable.
Results: We received three 2mm-6mm biopsy fragments, whose histological analysis showed connective tissue extensively occupied by monotonous sheets of small lymphocytes. The immunohistochemical study carried out showed universal and intense immunoreactivity in the described cells for CD20, as well as BCL2 and CD43 expression in more than 30% of those cells. CD3 and CD5 marked reactive T lymphocytes present in the background. Cyclin D1, CD10, BCL6 and CD23 were all negative in the neoplastic lymphocytes. A diagnosis of extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) was made, which was corroborated by the flow cytometry results. The ensuing bone marrow and CT scan studies were negative for systemic disease involvement.
Conclusion: This case illustrates the main immunophenotypical features of MALT conjunctival lymphoma, which was confined to the right eye. After a dismal response to aggressive chemotherapy, radiation therapy yielded positive results and the patient is currently disease-free under continuous follow-up.

E-PS-20-004

A case of hybrid neurofibroma/schwannoma of the orbit

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Background & objectives: Hybrid Neurofibroma/Schwannoma is a rare tumour that was first described in 1998 by Feany et al. It is part of Hybrid peripheral nerve sheath tumours (HPNSTs) which involve combined morphologies of neurofibroma, schwannoma and perineuroma.
Methods: We report a 78-year-old male, who had exophthalmos of the left eye. He had a past ocular history of post-surgical left facial paralysis after preauricular parotid tumour exeresis and left ocular hypertension. At the exploration, he had left eye ptosis. An orbital computed tomography scan showed a 20x18mm left intra-conal orbital expansive process.
Results: The clinic-radiologic diagnosis was a left intraconal cavernous angioma. After that, a left orbitotomy was performed. The gross examination showed an 18 x 16 x 11 mm whitish and solid mass. Microscopically, it revealed two different types of morphologies consistent with hybrid neurofibroma/schwannoma tumour. Immunohistochemistry demonstrated positivity for S100 protein in Schwann cells and CD34 in the neurofibromatous component.
Neurogenic lesions of the orbit, specifically, peripheral nerve tumours are uncommon. Furthermore, HPNSTs are even less frequent. All the four cases reported in the orbit, included our case, concur with the same type of HPNST. Nevertheless, it is not known what the triggers to develop it are.
Conclusion: In other body locations, Neurofibroma/Schwannoma has been described in association with neurofibromatosis or schwannomatosis and local recurrence has been reported. Since that, it is important to take into consideration as a differential diagnosis of orbital peripheral nerve sheath tumours.

E-PS-20-005

A case of eosinophilic angiocentric fibrosis with concurrent granuloma faciale

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Background & objectives: Eosinophilic angiocentric fibrosis (EAF) is an uncommon, chronic, idiopathic disorder mostly occurs in sinonasal cavity. There are isolated reports of orbital lesions. Granuloma faciale (GF) which is considered as a cutaneous variant of EAF, coexist in a quarter of patients.
Methods: Here we present clinical, histopathological and immunohistochemical findings of a patient with orbital EAF and GF.
Results: A 62-year-old male presented with right retro-orbital pain. Histopathologic examination of the mass which was hard in consistency revealed an inflammatory infiltrate in a background of sclerosis with conspicuous concentric pattern around small-calibre arterioles. Inflammatory infiltrate was rich in eosinophils, accompanied by lymphocytes and plasma cells. Immunohistochemistry was performed to rule out IgG4-related disease. Staining for CD34 was present on endothelial cells in sclerotic nodules. The history of bilateral telangiectatic, erythematous, slightly depressed forehead lesion and histopathologic diagnosis of GF was obtained from the patient through personal communication. The clinical history and distinctive morphology were the key features for diagnosis of EAF.
Conclusion: EAF should be kept in mind in orbital biopsies with idiopathic orbital inflammation which was formerly known as orbital pseudotumor. It has been proposed that EAF and GF are a part of IgG4 spectrum of disease. Further investigations are needed in order to clarify the relationship between these two entities and IgG4-related disease. Eosinophil-rich inflammation and perivascular concentric fibrosis in histopathologic examination and accompanying skin lesions are clues for diagnosis.

E-PS-21 Other Topics

E-PS-21-001

Ultrastructural changes of the liver parenchyma in the experiment

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Background & objectives: The increased intake of copper has an adverse effect on organism, lead to parenchymal organs damage, including liver tissue.
To study the ultrastructural changes in the liver parenchyma after the exposure by copper-containing (Cu-10%) polymetallic dust.
Methods: The experiment included outbred white male rats weighing 120-170 g for 30 days. The dust was injected intratracheally simultaneously (50 mg/1.0 ml of physiological saline). Ultrastructural changes were evaluated using electron microscopy. The material was rats liver tissue. Manipulations were fulfilled according to «Rules for biomedical experiments conducting» of MH RK (12.11. 2009 №697). General morphological research methods were used.
Results: Ultrastructural study of liver hepatocytes revealed cell signs oedema. The GER tubules and Golgi complex were expanded and fragmented. Hepatocyte nuclei had scalloped outlines. Tightly packed

ribonucleotides granules were unevenly arranged near nuclear membrane. Fine-grained osmiophil material was located in nuclear membrane zone. Mitochondria were polymorphic, partially destroyed, swollen, with increased sizes and small cristae amount. Glycogen granules had reduced osmiophilism, blurred contours; membrane osmiophil formations were located near plasmalemma.
Conclusion: The initial mechanism of liver damage development is the expressed toxic effect of polymetallic copper-containing (Cu-10%) dust on the hepatocytes ultrastructure. Mitochondrial dysfunction, destruction of the GER tubules, the Golgi complex and blurring of the contours of the glycogen granule were observed.

E-PS-21-002
Gingival oxalosis a very rare location of hyperoxaluria
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Background & objectives: Hyperoxaluria is a metabolic disease with excessive urinary calcium oxalate excretion which can be primary or secondary. Inability to excrete oxalate through the kidneys leads to its deposition in various organs. Oral manifestations of hyperoxaluria are very rare.
Methods: The aim of this study is to report a rare case of gingival oxalosis in a 35-year old male patient with a history of chronic renal and hepatic failure, diagnosed in the department of pathology of Monastir of Tunisia with a review of the literature.
Results: This patient presented with a dental mobility. Panoramic dental radiography showed a generalized bone lysis and root resorption. Langerhans Cell Histiocytosis was suspected. A gingival biopsy was performed. It revealed a huge granulomatous inflammation with foreign body reaction surrounding many crystalline deposits. In polarized light, these deposits were green and presented a birefringent aspect. These deposits were interpreted as calcium oxalate crystals. The patient was diagnosed with gingival oxalosis.
Conclusion: Oral manifestations of hyperoxaluria are of particular interest because of the unusual location of the oxalate crystal deposition, resulting in aggressive tooth resorption and alveolar bone loss, which may be misdiagnosed.

E-PS-21-003
Case report of familial chylomicronemia syndrome, the most rare type of dyslipidemia (type I)
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Background & objectives: Familial chylomicronemia is a rare primary dyslipidaemia(1/1.000.000 in the general population)with excessively high triglycerides(TG)>2000mg/dl. We present a case with familial chylomicronemia, who reported abdominal pain and discuss its diagnosis and treatment.
Methods: Our patient is a 50 year old female with known history of diabetes mellitus T2(DM)and chronic recurrent abdominal pain, smoker, with a BMI of 31.2kg/m2,social drinker. No family history of DM, with family history of premature death. Macroscopically showed xanthelasmas in right eyelid. Abdominal ultrasound showed hepatomegaly(22cm)with diffuse hepatic steatosis. The patient's serum was severely lipemic(emulsified),in such a level that it was impossible to calculate biochemical parameters.
Results: After 24-hour fasting: Triglycerides(TGs):11.389mg/dl,(LDL):88mg/dl,(HDL):63mg/dl,pseudoponatriemia(Na):120mmol/L,ApoA1:129(normal values:115-220), ApoB:130(n.v.: 60-160),VLDL: 311.0mg/dl(n.v.:0-30).During her hospitalization, she refused plasmapheresis and was given instructions for fasting, intravenous hydration and antilipidemic treatment with atorvastatin, fenofibrate, and niacin. Gradually there was a decrease in triglycerides. The patient was given instructions for strict diet and drug treatment. A re-audit was sheduled after two weeks, two months and one year. Specifically, after one year we had the following results: triglycerides:1128mg/dl, (LDL):60mg/dl,(HDL):16mg/ldl, cholesterol:279mg/dl,Na131mg/dl. Furthermore, carotid ultrasound, as well as ultrasonography of the lower extremity veins and arteries showed not significant stenosis. and depth of eye in nature. Fundoscopy showed no abnormal findings. Genetic testing and checking of the lipidemic profile of the offspring of the patient was recommended.
Conclusion: Dyslipidemia, both familial and acquired, is a silent risk for the patient's health. The diagnosis in this case was based on an excessive increase in triglycerides >2000mg/dl,in lipemic serum, in pseudoponatriemia (2-4mEq/L for every1000TG),in chronic recurrent abdominal pain and hepatomegaly (due to mucosal deposition).Other complications include acute pancreatitis(the most common)without elevated serum amylase(!), due to inflammation of the pancreatic tissue, splenomegaly and lipaemia retinalis. There is no cure and a strict diet for lifetime is required.

E-PS-21-004
Endobronchial paraganglioma: a rare paraganglioma location
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Background & objectives: Paragangliomas are tumours arising from the extra-adrenal paraganglion system. The first case of endobronchial paraganglioma, corroborated by immunohistochemistry, was reported in 2001, followed by four other well documented cases. We present a specific one in a 27-year-old woman.
Methods: The morphologic characteristics associated with immunohistochemical study were evaluated according to scientific literature.
Results: The microscopic examination revealed that the tumour consisted of cells organized in clusters with organoid pattern, showing round to oval nuclei, conspicuous nucleoli and slightly granular cytoplasm, beside hyalinized beams, calcification foci, and vascular invasion. It was found metastatic involvement of one local lymph node. Immunohistochemical staining for chromogranin, synaptophysin and CD56 were positive, and negative for pankeratin AE1/AE3 and TTF-1. In addition, S-100 protein was positive in sustentacular cells.
Conclusion: The immunohistochemical study is an important enlightenment to microscopic features. In this circumstance, it corroborated to the diagnosis of this rare case of endobronchial paraganglioma, a differential diagnosis to carcinoid tumours in pulmonary area.

E-PS-21-005
Russell-body-containing lymphoid cells as one of the indications of transplantation immunity
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Background & objectives: Lymphoid cells that contain aggregated immunoglobulins (Russel bodies) are found in tissues of patients with various diseases. The aim of the current research is to add data on participation of the Russel body-containing cells in transplantation immunity.
Methods: The current study is the result of histopathological changes' evaluation in an experiment on 30 WISTAR rats with auto-, iso- and allotransplantation of skin flaps.
Results: During the study, on the third day of the experiment, in the group of animals with allotransplantation, a significant number of cells with Russel

bodies (including Mott cells) in the form of a "demarcation shaft" was detected between the skin flap and the surrounding graft bed. The intensity of this cellular reaction persisted until the twelfth day of the experiment.
Conclusion: The research data expands the current knowledge on cells with Russell bodies in transplantation immunity of the human body to represent them as one of the key factors contributing to the foreign tissue rejection.

E-PS-21-006
Three-in-one: an unusual case report of triple primary malignant neoplasms
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Background & objectives: Multiple primary malignant neoplasms (MPMN) are rare. In this case report, we present a case with three primary, metachronous malignant tumours which developed over a period of four years involving the breast, bladder, and the gynaecological tract.
Methods: A 48 year old woman with no prior medical conditions presented with a right breast mass with axillary lymphadenopathy diagnosed as triple negative, invasive breast carcinoma. A year later she was diagnosed with endocervical adenocarcinoma. After treatment, 8 months later she developed, bladder and retroperitoneal masses with pelvic lymphadenopathy with histology distinct from the breast and genital tract tumours.
Results: The breast malignancy was diagnosed as triple negative invasive ductal carcinoma with nodal metastasis. She was treated with surgery and chemotherapy and subsequently developed per vaginal bleeding. Pap smear revealed an adenocarcinoma. A Wertheims' hysterectomy was performed and revealed a submucosal uterine tumour with histology and immunoprofile of endocervical adenocarcinoma. She completed her chemotherapy, and 8 months later presented with symptoms of acute renal failure and deep vein thrombosis. Imaging revealed a retroperitoneal and bladder base tumour with pelvic and paraaortic lymphadenopathy with lung metastases. The liver, bones and adrenal were not involved. Histology of the bladder base tumour revealed a hepatoid adenocarcinoma, distinct from the breast and uterine tumours.
Conclusion: Multiple primary malignancies in a single patient are rare. This case exhibited three different primary malignancies over a course of four years. Judicious application of antibodies is critical to diagnose and exclude recurrent/ metastatic tumours for appropriate chemotherapy.

E-PS-21-007
Aspects of mutul relations: clinic and prosecture
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Background & objectives: Historically, due to the development of specialization in medicine, the competencies of clinicians and autopsy doctors have been fragmented and at different poles relative to one formally common goal - to protect the patient's health.To establish the existence of facts confirming the objective existence of social groups of pathologists and doctors of clinical specialties, to identify the prerequisites for the occurrence of intergroup conflicts between them. Significant differences, both practical and psychological, arose in the organization and conditions of their work
Methods: Anonymous questionnaire, including closed questions. For each of the questions in the questionnaire, an analysis was made of the frequency and structure of responses; identification and analysis of correlations between specific answers to various questions in groups of subjects was carried out, comparison and analysis of the answers of pathologists and clinicians to general questions of the questionnaire.
Results: the study showed the reasonable existence of social groups of pathologists, and clinicians confirmed the presence of some prerequisites for the occurrence of intergroup conflict; Clinicians showed a tendency to underestimate the role of the pathoanatomical service in clinical work and to misunderstand the problems arising from its interaction. In addition, areas for further research were identified.
Conclusion: The interaction of the pathologist and clinician in identifying and discussing medical errors is binary: it is both professional (medical) and social.
Today, the creative potential of collaboration between clinicians and pathologists is weakening.

E-PS-21-008
Occupational hazards among pathologists: results from a nationwide online questionnaire in Morocco
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Background & objectives: The profession of pathologist exposes to various occupational risks at each stage of the sample processing. This study aimed to provide the first comprehensive assessment of the health situation of pathologists using a questionnaire sent to all pathologists in our country.
Methods: A questionnaire, to be completed online and anonymously, was developed, and sent by email to all Moroccan pathologists. It included 52 questions with single or multiple-choice answers, related to the epidemiological characteristics of pathologists, seniority in the profession, modes of exercise, working conditions, pathologies that they presented, and feelings towards their profession. Free comments were possible.
Results: 102 pathologists responded to the survey.
72% worked full time, with 28% of liberal practitioners.
86% reported musculoskeletal disorders (MSDs), predominantly in the neck (64%).
Visual disturbances affected 72,5% of the respondents, mainly of myopia type (67% of them).
62% of pathologists had injured themselves or had splashes in the mucous membranes during gross sections.
33% suffers from psychological disorders such as burnout (24%).
Despite the described health risks, Moroccan pathologists seemed happy at work for more than 50% of them. They had a good lifestyle with only 35% of respondents who were overweight, 8% of smokers and 36% who did sports at least once a week.
Conclusion: This online questionnaire study is the first comprehensive occupational health assessment of a nationwide cohort of pathologists in Morocco.
Emphasis should be placed on primary prevention, focusing on ergonomic workplace optimisation and reduction of work overload.

E-PS-21-009
The role of the surgical incision method for injury regeneration
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Background & objectives: Modern methods of electrosurgery are necessary for conducting surgeries, especially in emergency conditions, such as when tracheostomy is performed in patients with tumour laryngeal stenosis. Aim: to compare the effects of radio-wave(RW)& molecular resonance (MR) surgery on rat neck skin regeneration.
Methods: Cuts were made with a microsurgical RW-generator(1group)&MR-generator(2group) on neck skin of 10rat's.Cytological study of preparations obtained using the superficial biopsy method(May-Grünwald stain). Cytograms were determined for 5 types. After surgery at 1,2,4,6,8,10&12days rats were scored 2 from each group and a histological study of postoperative wounds (H&E, toluidine

blue stain).In assessing morphological changes we evaluated necrosis, the severity of inflammatory changes, oedema, proliferative changes, epithelization.
Results: Cytological examination showed that from day 2 the number of neutrophils decreased in gr.1 ($p<0.01$), and from day 5 the number of fibroblasts increased, compared with gr.2 ($p<0.005$). In gr.1, the thickness of the necrosis is less than in gr.2 (87.5+8.1vs 112±6.5), from 3day, oedema $p<0.005$), the mast cells number ($p<0.005$) and neutrophilic infiltration of the wound edges were more in gr.2($p<0.005$), proliferative changes and epithelialization were better in gr.1($p<0.001$).
Conclusion: RW exposure is a more effective way of transforming electric energy in the vibration of tissue molecules, which allows to achieve the dissection at lower power output, as compared to the MR method. These studies have revealed that the inflammatory response and the healing time for wounds are significantly less after RW exposure compared to MR method

E-PS-21-010
Carcinogenesis after a nuclear power plant accident in Fukushima
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Background & objectives: An earthquake in Japan occurred in March 2011 was causing melting down of nuclear power plant in Fukushima. For 6 years there had no people, in 2017 people came back and lived for 3 years up to 825 populations.
Methods: 20,298 people lived before the earthquake, and 4% of them were returned. The spatial radiation dose of Namie in January 2020 is 0.3 micro Sievert, which is one tenth of the radiation dose 10 years ago. Among them the frequency of malignancies was investigated.
Results: Occurrence of thyroid cancer isn't admitted in 22 children who returned. The malignant tumours of 22 examples among 825 repatriates appeared after an earthquake disaster. It is higher frequency compared with the number of malignant tumours of Japan ($P<0.01$). The kinds of cancer are 4 gastric cancers, 4 prostate, 4 colon, 3 lung, 2 oesophagus, 2 liver, a duodenal papilla Vater cancer, a urinary bladder, and a pancreas cancer.
Conclusion: Even in low dose radiation exposure, carcinogenesis will be main factor to threaten the elderly person. We need not disaster like Fukushima. No more Fukushima.

E-PS-21-011
The effect of the naphthalan oil emulsion on skin regeneration by the example of a rat dermatitis model
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Background & objectives: Optimization of the healing of injuries remains an urgent scientific and practical task. The aim was to study the effect of an emulsion of naphthalan oil on the skin of rats in which a dermatitis model was previously reproduced.
Methods: A model of dermatitis was reproduced on the skin of the back of 30sexually female Wistar rats, which were bathed in a bathtub with a 0.0003% Naftalan oil emulsion for 10min.(1 roup,10rats), 15 min.(2group,10rats)&20min.(3group,10rats) for 5days. 8days after the start of bathing, the rats were sacrificed, and the damaged areas of the skin were stained with H&E and the intensity of inflammation.
Results: In 1 group of 5rats, intraepidermal infiltration, hyperaemia & leukocyte infiltrates in the dermis were observed, in 2 rats-acantholysis. In 2group in 8rats, there were no signs of dermatitis, and in 2 rats there were manifestations of polymorphic cell infiltrates in the papillary dermis. In 3 group 6 rats also had intraepidermal infiltration, oedema, hyperaemia in the dermis, and the remaining rats of this group showed less signs of dermatitis.
Conclusion: Naftalan oil can reduce the signs of skin inflammation in rats in a dermatitis model with a 15 minute exposure for 5 days. Naftalan oil has a sebostatic, anti-inflammatory, antipruritic effect. We have developed a treatment regimen for dermatitis in a previously recreated model that showed a good therapeutic effect.

E-PS-21-012
Unexpected adulthood mesenteric cystic lymphangioma
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Background & objectives: Lymphangiomas are rare benign tumours. Lymphangiomas in the peritoneal cavity are extremely rare, particularly in adults, representing less than 1% of all lymphangiomas. We report a case of mesenteric cystic lymphangioma to show its epidemiologic, clinical, and pathological features.
Methods: A single 37-year-old woman, with no history, presented an abdominal pain that had lasted for 3 months. Abdominal examination revealed distension and tenderness during palpation of the central quadrant. Abdominal and pelvis scan revealed a giant uterine mass. Laparotomy was performed.
Results: During the operation, numerous mesenteric cysts were found. They had a varying size. The cystic walls were generally thin, but some walls were relatively thick. Microscopic examination revealed that the cystic walls comprised of smooth muscle were lined with flat endothelial cells. The stroma showed various sizes of small lymphatic spaces lined by a flat endothelium and containing small lymphoid cells. The stroma also contained smooth-muscle bands and scattered lymphoid infiltrates. Few subendothelial lymphoid follicles were observed. A mesenteric cystic lymphangioma was finally retained. The main differential diagnosis is benign multicystic mesothelioma. The uterine mass was a leiomyoma.
Conclusion: Lymphangioma of the mesentery is rare. Preoperative diagnosis is often difficult due to the frequent silent clinical course. the definitive diagnosis is confirmed by histopathology after a complete surgical resection.

E-PS-21-013
Memory game: the use of a playful approach for learning pathology
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Background & objectives: Medical Education is moving towards a more innovative path in order to facilitate learning. The use of games is characterized as a playful practice increasingly used. The aim is evaluating the applicability of memory games in the teaching-learning process of Pathology.
Methods: A memory game was created using both radiographic and pathologic images of glomerulopathies and chronic obstructive pulmonary disease. The game was applied through PowerPoint after two weeks of practical classes on these subjects. The students of the sixth semester were divided into groups and after the game, they answered an opinion survey on the Google Forms platform.
Results: Of the 50 students who participated, most 36 (72%) were between 18 and 22 years old and 34 (68%) were female and 16 (32%), male. 49 (98%) students considered that the memory game helped to memorize the content given in class and considers the use of playful approaches a good option to review the content. Finally, 47 (94%) students would like the memory game to be applied again
Conclusion: In conclusion, playful activities stimulate and facilitate the students' learning about the pathology slides and content, since it makes the learning environment more interactive and dynamic.

E-PS-21-014

3D digital copies of macroscopic pieces: an innovative methodology in the pathology teaching

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Background & objectives: The use of macroscopic pieces in the teaching of pathology is essential for learning and accurate diagnosis. The integration of 3D copies as a study tool is an innovative approach that should benefit the assessed learning process.
Methods: A total of 3 models of anatomical structures were generated using the Qlone app on a cell phone. The models were a heart with cardiomegaly, a pregnant uterus and a liver with steatosis. After being shown to third semester medicine students, they answered an opinion survey on the Google Forms platform.
Results: Of the 51 students who participated, 50 (98%) students confirmed that the use of the images helped in the learning process and 50 (98%) that the images were useful for the study at home. The quality of the images was good to 50 (98%) of them and 42 (82,4%) said that they were able to have clinical reasoning and complete diagnosis through them. It is possible to consider the decrease in positive responses to this last question, the fact that these students are starting the pathology course.
Conclusion: The scores demonstrated a better understanding of study content and the possibility of implementing a new approach in pathology teaching.

E-PS-21-015

Commonest cancers in Karachi, Pakistan: second report (2016-2019) from the largest public sector pathology-based cancer registry of Karachi

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Background & objectives: Nationally representative cancer data have never been published from Pakistan since independence (1947). It is therefore highly relevant to report high quality regional data. This report details 2016-2019 cancer data representing all districts of Karachi, Pakistan.
Methods: A Pathology-based-cancer-registry was established at the largest government-run diagnostic and reference-centre of Karachi (Ref no. IRB-459/DUHS/-14) in 2014. First report detailing 2010-2015 cancer data from the registry was published in 2016. This is the second report from the registry reporting a total of 9350 cancers diagnosed during 2016-2019. Our data are high-quality regional data representing all districts of Karachi, Pakistan.
Results: During 2016-2019, a total of 9,350 cancers (including 392 non-melanoma-skin-cancers) were diagnosed. Of these, 3447 (36.8%) were in males while 5,903 (63.1%) were in females. Incidence rates for all cancers (excluding NMSC) were 37.01-per-100,000 for males and 73.2-per-100,000 for females. In males, cancer of lip-and-oral-cavity was the most common (36.03%, ASR13.3), followed by oesophagus (6.7%, ASR2.5) and colorectum (6.6%, ASR2.4). In females, breast cancer was most frequent(56%, ASR41.1), followed by cancers of lip-and-oral-cavity (9.1%, ASR6.6) and oesophagus (4.7%, ASR3.4). Alarmingly, incidence of tumours associated with tobacco usage is very high in Karachi, demanding for urgent measures by relevant authorities to cease the use of tobacco in the city.
Conclusion: We report high quality regional cancer data representing all districts of Karachi, Pakistan. Being the largest public sector stake holder in cancer diagnostics, our data strengthen regional, national, and international cancer statistics from Pakistan.

E-PS-21-016

Congo red negative amyloid-like deposits: diagnostic challenge and logical approach

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Background & objectives: Amyloid is an extracellular fibrillar deposit with β-pleated sheet conformation with a typical H&E and Congo red appearance. We present a series of Congo red negative amyloid-like deposits (CRNALD), highlighting its diagnostic challenge and need of awareness for the entity.
Methods: Three cases of rare CRNALD are described, drawing attention to the need of clinical correlation and/or further testing to reach a correct diagnosis. The literature was reviewed, emphasizing in the logical approach to the differential diagnosis and importance of correctly assessing these deposits due to the specific clinical and therapeutic implications.
Results: Patient #1 presented with skin, pharynx, and oral cavity CRNALD. It was later recognised as with an history of lipoid proteinosis. Patient #2 presented with renal CRNALD that immunofluorescence and electron microscopy identified as a light-chain deposition disease in the context of multiple myeloma. Patient #3 presented with respiratory tract and skin CRNALD, later confirmed PAS-positive, of probable IgM nature in context of a lymphoplasmacytic lymphoma.
Conclusion: CRNALD must be identified and separated from amyloid. Its rare occurrence limits the awareness of the entity. Congo red stain has limitations in sensitivity and specificity further increasing the diagnostic difficulties. Complementing traditional histological findings with clinical history and use of other methods, such as electron microscopy or immunofluorescence, is essential to avoid delays in diagnosis and treatment. Proper specimen collection and preservation for these latter techniques should be guaranteed.

E-PS-21-017

Well differentiated papillary mesothelioma: an unusual entity to must keep in mind with literature review

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Background & objectives: Well Differentiated Papillary Mesothelioma (WDPM) is a rare neoplasm of mesothelial origin which occurs in women of reproductive age, and occasionally in adult, predominantly in the abdominal cavity. The clinical course is indolent, and the diagnosis is incidental.
Methods: We present three cases of WDPM in our centre: Two men and one woman, all middle-aged, with an excresent pelvic peritoneal lesion found during surgery for other causes. None have suffered exposure to asbestos or have other at-risk personal history, and the lesions had not been observed in previous imaging studies.
Results: A histological study reveals surface papillary structures with fibrovascular axes coated by a monolayer epithelium of cuboidal cells, without cytological atypia or mitosis. No stromal or adjacent organ invasion was identified. The epithelial component tested positive for Calretinin, WT1 and CK 5-6 and negative for MOC 31. The cell proliferation rate (Ki-67) was 5 – 10 %. More specific WDPM markers such as BAP1 and L1CAM have recently been described, which are negative in Malignant Mesothelioma (MM). Mutations in the TRAF7 and CDC42 genes, which are not found in MM, have also been identified, confirming their specific molecular origin.
Conclusion: The differential diagnoses include MM, carcinomas of gynaecological or peritoneal origin and reactive mesothelial hyperplasia. WDPM tend to have a favourable clinical course but some cases can recur and have malignant potential by the presence of microinvasion.

E-PS-22 Paediatric and Perinatal Pathology

E-PS-22-001
Alveolar soft part sarcoma: a misleading benign neoplasm

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Background & objectives: Alveolar soft tissue sarcoma (ASPS) is a rare malignant neoplasm, more common in children and young adults, predominantly in females. Typically appears on the head, neck and limbs. Clinically, it seems an indolent intramuscular lesion.
Methods: A 14-year-old female, with a tumefaction in her left forearm, accompanied by pain and impotence. Ultrasound revealed a 24mm hypoechogenic nodular lesion, suggestive of a vascular malformation in ultrasound doppler. After clinical discussion, vigilance was decided. Two-years later, imaging control revealed lesion growth, reaching 35mm. Surgical excision was performed.
Results: Through gross examination, a 35mm well circumscribed nodular lesion was observed, whitish, lobulated and of elastic consistency. Microscopically, it was of expansive growth, with nested and pseudoalveolar pattern. Cells were polygonal, with abundant eosinophilic cytoplasm, and mildly pleomorphic nucleus. PAS-D technique revealed the presence of intracytoplasmic crystals. Immunohistochemistry was negative for vimentin, S100 protein, AE1/AE3, α-actin, desmin, neuroendocrine markers and HMB-45; positivity for MyoD1 and TFE3. ASPL-TFE3 fusion gene was identified.
Conclusion: ASPS is an aggressive malignancy, with 50% of patients presenting metastasis at the time of diagnosis. It has unknown histogenesis, possibly with striated muscle origin. Radiologic features may be misleading, frequently suggesting a vascular malformation, leading to diagnosis delay, and even prevent a potentially curative intervention.
Doctors should be aware of this entity, particularly in young females, since early core biopsy may be lifesaving.

E-PS-22-002
Plexiform fibrohistiocytic tumour: reporting a challenging diagnosis

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Background & objectives: Plexiform fibrohistiocytic tumour (PFHT) is a rare mesenchymal neoplasia typically affecting children and young adults. It is a subcutaneous lesion, mostly in limbs and trunk. The histologic features may be doubtful, and differential diagnosis is particularly difficult with inflammatory processes.
Methods: Report of case of a 6-year-old female child with no relevant medical history, presenting with a single infiltrative cutaneous lesion located in the left arm, with 1.5cm, rounded and reddish.
The diagnosis was rendered in a biopsy sample.
Results: Microscopic examination showed an infiltrative lesion at the interface of deep dermis to subcutaneous tissue. It was composed by bundles of monotonous spindle cells, and nodular aggregates of histiocytic cells, with rare multinucleated giant cells. There was a background of diffuse or nodular lymphplasmocytic infiltrate. Immunohistochemistry showed α-actin expression in the fusiform component and CD68 in histiocytic aggregates, with negativity for: S100, EMA, desmin, CD34, MITF and NSE.
Patient underwent surgical excision.
Conclusion: PFHT is a neoplasia of intermediate malignancy, rarely metastasizing, locally aggressive with highly infiltrative borders.
Morphology may be variable, and three distinct growth patterns are considered, depending on the predominant cell, fibrohistiocytic, fibroblastic and mixed.
Since cellular atypia is usually absent, and mitosis are scarce, the diagnosis can be quite challenging.
Complete surgical excision is crucial, since local recurrence is common, occuring in around 40% of the cases.

E-PS-22-003
The histopathological landscape in placenta accreta spectrum – a case report series

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Background & objectives: Placenta accreta spectrum (PAS) includes clinicomorphological conditions, often requiring emergency hysterectomy. Usually, the histopathology parallels the etiopathogeny and risk factors of this condition. Our short case series present the morphological aspects of PAS, correlated with pathophysiological and clinical background.
Methods: We present five cases with different degrees of PAS, diagnosed between 2009-2019, at the "Elena Doamna" Obstetrics and Gynaecology University Hospital of Iasi. The postpartum hysterectomy specimens have been histologically assessed by routine, trichrome, and CD146 immunohistochemical techniques. Maternal age, gestational age, degree of adherence/invasion, implantation site intermediate trophoblast, villous trophoblast, decidua, basal plate myometrial fibres have been evaluated.
Results: Three cases presented direct adherence of chorionic villi to the myometrium (placenta accreta), one case presented implantation site intermediate trophoblast (ISIT) between myometrium and villous tissue (placenta accreta), and one case presented the penetration of placental villi through the uterine wall (placenta percreta), all cases with partial (one case) and complete (four cases) absence of the decidua basalis. Two cases of placenta accreta presented myometrial fibres in the basal plate. The characteristic excessive ISIT invasion as well as maternal vascular changes were highlighted through immunostaining with CD146. The most unexpected case was of the patient of 17 years, in which the degree of myometrial invasion was the most advanced.
Conclusion: Immunohistochemistry represents a useful tool for avoiding diagnosis pitfalls in placenta accreta. The presented cases support the pathogenesis involved in PAS disorders, the extension of the study being able to shed new light on other possible theories of the disease.

E-PS-22-004
The extreme case of lethal multiple pterygium syndrome

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Background & objectives: Multiple pterygium syndrome is an uncommon disorder encompassing skin webbing, cystic hygroma, and joint contractures. We present the case of lethal multiple pterygium syndrome with extreme morphological changes, clinically manifested as intrauterine foetal death at 25th gestational week.
Methods: Conventional foetal autopsy, placenta histomorphology, postmortem foetal radiography, array-based comparative genome hybridization as well as whole-exome sequencing of foetus and parents (Agilent SureSelect Human All Exon) followed by bioinformatical gene filtration analysis were employed.
Results: Postmortal foetal radiography was unremarkable. We found a male foetus with a dorsal multilocular cyst contacting 300 ml of serous liquid, muscular atrophy and pronounced skin webbing around neck and all peripheral joints with very limited passive flexion and extension. The face was deformed with open and luxated mandibula and open eyes. There was no sign of lip cleft. The internal examination demonstrated partial diaphragm agenesis with intrathoracic herniation of spleen and

colon, cardiac dislocation, and pulmonary hypoplasia. Foetal histology revealed calcified thrombus in renal vessels. The placenta was macrosomic with the histopathological findings of foetal vascular malperfusion. Surprisingly, no mutations usually associated with the condition were detected.
Conclusion: This case of multiple pterygium syndrome is featured by the prominent neck and joint webbing, muscular atrophy, cystic hygroma as well as some secondary changes. The normal cervical vertebra and male sex exclude Turner, Noonan, and Klippel-Feil syndromes. Whole-exome sequencing was unexpectedly negative for the known associated mutations. The condition is usually linked to gene mutations in embryonic acetylcholine receptors, actin-binding receptor, and skeletal muscle calcium release channel.

E-PS-22-005
Nasal glial heterotopia: a case report
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Background & objectives: The nasal glial heterotopia is a rare and benign disease. Nose and nasopharynx are the most common sites involved. Histopathological examination with immunochemistry is the diagnosis key.
The aim of the study is to discuss clinicopathological features of this disease.
Methods: A one year-old female child was presented with a 2 cm, rapidly growing, nasal, painless mass. There is no familiar or personal history. An excision of the mass was practiced.
Results: We received three, white, solid fragments measuring between 1 and 2,5 cm.
The histological examination revealed mature astrocytes with fibrillary glial processes and connective tissue. There are no neural cells. The immunoreactivity for glial fibrillary acidic protein (GFAP) confirmed the diagnosis.
Conclusion: The rarity of nasal glial heterotopy makes clinical diagnosis very difficult. It occurs commonly in female under 2 year-old.
Histological examination with immunohistochemistry ensures correct diagnosis. The mean differential diagnosis is encephalocele. Biopsy or fine needle aspiration is contraindicated because of the increased risk of meningitis or perhaps the removal of functional brain material from an encephalocele. The treatment of choice is complete surgical excision. The recurrence is rare.

E-PS-22-006
The role of placental examination in reducing the incidence of intrauterine and neonatal deaths: a retrospective analysis
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Background & objectives: Post-mortem examination of the foetus along with microscopic evaluation of the placenta is performed in order to elucidate the causes of death. Our objective was to analyse how many of the perinatal deaths find their morphological changes in the placenta.
Methods: The post-mortem examination of 39 consecutive perinatal deaths that occurred during December 2018 to June 2019 performed in our Maternity Unit, plus the histopathological analysis of the corresponding placentas were re-analysed. We compared the proportion of cases in which the diagnosis was established following the autopsy results with the proportion of cases elucidated after the additional examination of the placenta.
Results: From the 39 autopsies, we excluded 17 cases that had no placenta available. 10 (45.45%) of them were intrauterine deaths and 12 (54.54%) were neonatal deaths. After the autopsy, the causes of death could be determined in 10 of 22 cases (45.45%); placentas showed modifications that could explain foetal death in 19 out of 22 cases (86.36%). Most common changes were: infections (63.63%), placental abruption (40.9%) and placental abnormalities (59.09%).
Conclusion: Our study highlights the importance of further histopathological examination of the placenta in all cases of perinatal death.

E-PS-22-008
Oncocytic adrenocortical tumours in paediatric age: what score system for malignancy?
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Background & objectives: The aim is to report the pathological features of two rare cases of oncocytic adrenocortical tumours (ACTs) classified as “malignant adrenocortical carcinomas” in paediatric age and to establish the correlation between pathological features and clinical behaviour
Methods: We herein report on two rare cases of oncocytic ACTs, respectively in a 7-year-old boy and in a 4-month-old girl. The Lin–Weiss–Bisceglia scoring system, used for the adult counterpart tumours, was applied: if an oncocytic tumour shows at least one or more major criterions, it is classified as “malignant”.
Results: A 7-year-old boy and a 6-months-old girl presented a mass, respectively, weighed g 80 and g 65, and measuring cm 6x5x3.5 and cm 5x4x2.5. Both tumours were composed almost entirely of cells exhibiting oncocytic morphology. In the first case a unique atypical mitosis, >5 mitoses per 50 high-power fields, as well as a focal sinusoidal invasion of tumour capsule were identified. In the second case a high mitotic index, rare, atypical mitoses, foci of necrosis and sinusoidal invasion were seen. Both tumours were classified as “oncocytic adrenocortical carcinomas”. The patients are well after a follow-up period of 69 and 21 months, respectively.
Conclusion: The rarity of paediatric oncocytic ACTs makes difficult the identification of pathological criteria useful for prognostic purposes. We report on two cases of oncocytic adrenocortical carcinomas without evidence of adverse events after a follow-up period of 69 and 21 months, respectively. Although we admit that follow-up is relatively short, our results raise the question of the reliability of the Lin-Weiss-Bisceglia score system in predicting clinical behaviour in paediatric patients.

E-PS-22-009
A rare cause of precocious puberty in male children
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Background & objectives: Male precocious puberty (MPP) is rare, may be central related to brain/spinal cord anomalies (tumours, radiation, injury, hydrocephalus), congenital adrenal hyperplasia, hypothyroidism. Peripheral MPP may result from adrenal and testicular tumours, McCune-Albright and Peutz Jegerhs syndromes, testosterone exposure, genetic disorders.
Methods: Two 7 and 9 year-old boys presented isolated precocious puberty characterized by growth acceleration and secondary sex characteristics. Ultrasounds showed left 0.8 cm testicular nodule of the upper pole in one case and a central right 0,5cm testicular nodule in the second case.

Hormonal testing showed increased testosterone levels. Partial orchiectomy under ultrasound removing 1/3 of testicular volume was performed.
Results: Grossly, specimens weighted 1g each and consisted in 1cm testicular parenchyma containing respectively 0,5 and 0.6 cm tan-brown, unencapsulated, completely resected nodules. They were composed of thin vascularized septa containing polyhedral eosinophilic Leydig cells with excentred regular nuclei containing a small central nucleoli. Seminiferous tubes with active spermatogenesis were entrapped within the nodules.
Tumour cells expressed calretinin, inhibin, MelanA. We concluded to benign sex cord tumours corresponding to prepubertal Leydig cell tumours. No LH receptor activating mutation was identified on genetic testing.
Conclusion: Leydig cell tumours are rare in male children and usually benign. Despite their very small size, they locally induce spermatogenesis and peripheral precocious puberty.

E-PS-22-010
Metachronous occurrence of neuroblastic tumour and pancreatic exocrine adenocarcinoma
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Background & objectives: Paediatric pancreatic carcinomas are exceedingly rare. Syndromic association of neuroblastomas with other embryonal tumours is already known, but association of neuroblastomas with pancreatic carcinomas has not yet been reported.
Methods: This 17 year-old girl presented at the age of 2, stage 4 thoracoabdominal neuroblastic tumour. She received chemotherapy and MIBG targeted radiotherapy. At the age of 14, she underwent debulking surgery for compressive exudative enteropathy. Pathological examination showed incompletely resected intermixed ganglioneuroblastoma with lymph node metastasis. She underwent complementary surgery consisting in partial pancreatectomy.
Results: Tumorectomy measuring 11x10x4.5cm and weighting 177g had 2 components: multinodular myxoid and necrotic. Interestingly, myxoid component corresponding to ganglioneuroblastoma was admixed with sheets of cohesive epithelial atypical cells exhibiting glandular differentiation with comedo-necrosis and perineural invasions. Residual pancreatic ducts and Langerhans islets were entrapped. Neoplastic cells expressed strongly pankeratins, focally CK7 and weakly P53. Neuroendocrine markers, BCL10, PHOX2B, WT1, ALK and betacatenin were negative. MMR protein expression was retained. In summary, this tumour exhibited features of pancreatic exocrine adenocarcinoma adjacent to ganglioneuroblastoma. KRAS activating mutation was further identified on FFPE tumoral tissue. The patient has progressive liver metastasis, under genticitabin and MEK inhibitors, waiting for KRAS targeted therapy.
Conclusion: This is the first report of pancreatic exocrine adenocarcinoma associated with neuroblastic tumour suggesting a second cancer related to MIBG targeted radiotherapy.

E-PS-22-016
Renal mesenchymal tumours of childhood: a 40 year experience in a tertiary hospital
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Background & objectives: The majority of renal tumours in children are Wilms tumours. All other paediatric tumours are less than 15% and are considered rare malignancies of childhood. These include Clear Cell Sarcoma (CCSK), rhabdoid tumour (RT) and congenital mesoblastic nephroma (CMN).
Methods: Approximately 1000 nephrectomies were performed in children (0-18 years old) between 1980-2020. We reviewed the histological diagnoses in our database. 18% of the cases were tumoral. The majority of them were nephroblastomas, 6 cases carcinomas and 20 cases mesenchymal tumours (35% sarcomas, 50% CMN, and 15% RT).
Results: We reviewed the histology, immunohistochemistry, and molecular findings in the 20 cases. Eleven were in boys and 9 in girls, ages between 8 months and 18 years. Most of the cases were CMN (10 cases), 3 rhabdoid tumours were diagnosed in small patients (8 months-2 years) and 7 cases were sarcomas (CCSK and synovial sarcoma). In the sarcoma group, the age gap was between 2 and12 years. The CCSK had all been treated with chemotherapy before surgery and had low tumoral necrosis. Synovial sarcoma had monophasic pattern and molecular confirmation (X;18 traslocation). All the cases were graded according to the SIOP protocol.
Conclusion: According to our review, renal mesenchymal tumours were 13% of the tumoral cases. CMN being the most common, and CCSK second. The clinical presentation, and evolution followed what is described in the literature. The most difficult diagnosis was in the sarcoma group, were ancillary molecular studies were performed.

E-PS-22-017
Uncommon kidney tumour association in children – case report
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Background & objectives: Coexistence of nephroblastoma and papillary renal cell carcinoma is an extremely rare paediatric renal malignancy with only few cases described in the literature. Clinico-pathological features and prognosis related to this association are uncertain, and no standard treatment is available.
Methods: We present a case of a 6-year old girl admitted in 2019 for a kidney mass at the Children's Emergency Hospital "St. Mary" Iasi, Romania. A surgical intervention was performed. The excised specimen was specifically processed through paraffin embedding technique for standard histological and immunohistochemical exams.
Results: The microscopic assessment revealed two different tumour aspects: a three-phase proliferation represented by small, mitotic active, undifferentiated cells associated with epithelial and stromal components, and a papillary proliferation with connective-vascular axes lined by single layers of large, eosinophilic cells, with hyperchromatic nuclei. Immunohistochemistry revealed caldesmon positive in stromal component, CD56 focally positive in blastemal cells, WT1 positive in blastemal cells and negative in papillary component, EMA positive in papillary component.
Conclusion: The histopathological aspects correlated to the immunohistochemical profile led to the diagnosis of nephroblastoma associated with papillary renal cell carcinoma, type 1. The key element of this case consists in the rarity of this diagnostic entity, in children. Therefore, each reported case can contribute to a better understanding of the pathogenesis and a more accurate clinico-pathological characterization.

E-PS-22-018
A case of inguinal nephrogenic rests in an 11-month-old boy
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Background & objectives: Ectopic nephrogenic rests(ENRs) are very rare lesions that may be located in several different sites including the inguinal canal. They are mostly found incidentally and should be differentiated with extrarenal Wilms tumour which is also a very rare entity.

Methods: This study reports a case of an ENR located in the inguinal canal in 11-month-old male patient. The clinical diagnosis was right cryptorchidism and the boy was admitted at the hospital for the surgical removal of the inguinal mass.
Results: During the surgery a tissue mass was excised and the histopathological diagnosis confirmed the ENR.
Conclusion: Nephrogenic rests should be properly diagnose even in very unusual sites.

E-PS-22-019
Congenital cystic adenomatoid malformation – presentation of 11 cases
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Background & objectives: The purpose of this study was to present cases of CCAM in terms of pathohistological features, gender and site distribution as well as to compare the results with Stocker's classification.
Methods: A retrospective review was performed on eleven cases of CCAM obtained in four years period (2015-2019) in University Children's Hospital in Cracow, Poland.
Results: The cases for this study were 7 boys and 4 girls (64% vs 36%), patients age at operation ranged from 4 days to 10 months. 6 cases involved the left lung (55%) whereas the right lung was involved in 5 cases (45%). Histopathological examination showed congenital cystic adenomatoid malformation type I in 7 cases (64%), type II in 3 cases (27%) and type III in 1 case (9%). No congenital cystic adenomatoid malformation type 0 and IV was diagnosed.
Conclusion: Data obtained from this study fell into Stocker's classification proving its usefulness.

E-PS-22-021
Parvovirus B19 as a foetal pathogen: correlation with apoptosis and inflammation mechanisms
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Background & objectives: This specific research paper aimed to correlate the presence of B19 virus with inflammation and apoptosis levels in placentas as well as with spontaneous abortions.
Methods: We used 152 placental samples from spontaneous abortions and 42 samples from women who choose to terminate their pregnancy as controls. We performed immunohistochemistry to evaluate IL-6, IL-1a, TNF-a, M30, TUNEL, B19 and NF-κB expression and also H&E staining to look for characteristic morphological changes in the tissue due to viral presence. The statistical analysis was performed using SPSS.
Results: Higher expression of all inflammation and apoptosis markers was found in the study group with statistical significance (p<0,001). Then, higher expression of IL-6, IL-1a, M30, TUNEL and NF-κB was correlated with higher age of the mother while higher expression levels of IL-6, TNF-a και NF-κB was correlated with higher trimester of the pregnancy (p<0,001). Moreover, B19 presence was correlated with higher levels of all apoptosis and inflammation markers with statistical significance (p<0,001). Last but not least, when multivariate logistic regression was performed the presence of B19 remained an independent risk factor for high expression of all markers (p<0,001).
Conclusion: This research seems to consolidate a relationship of cause and effect between B19 presence and higher inflammation and apoptosis levels, which have been known to be able to cause spontaneous abortions. However, more studies are needed in order to be able to confirm these results.

E-PS-22-022
Investigation of the involvement of inflammation and apoptosis in foetal pathogenesis due to EBV infection
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Background & objectives: This research paper aimed to evaluate the expression of apoptotic, and inflammatory markers in relation to EBV presence in spontaneous abortions in Thrace population.
Methods: We used 152 placental samples from spontaneous abortions and 42 from normal pregnancies as controls. We studied the expression levels of TNF-a, IL-6, IL-1a NF-κB, M30 and TUNEL and EBV presence via immunohistochemistry. The biomarkers' expression was evaluated using a semi-quantitative system while viral presence was evaluated with a binary system and then statistical analysis was performed using SPSS.
Results: Higher expression of all the biomarkers was found in the study group (p<0,001), as well as all positive EBV cases. We also found that higher age of the mother correlated with higher expression of IL-6, IL-1a, TUNEL, M30 and NF-kB with statistical significance, while higher pregnancy stage was correlated also with higher expression levels of NF-kB (p=0,011), TNF-a (p=0,016) and IL-6 (p=0,003). Moreover, viral presence was found in correlation with higher expression of all markers (p<0,001). Moreover, multiple logistic regression showed that EBV remained an independent risk factor for high expression of all markers.
Conclusion: In conclusion, this research seems to establish a causative relationship between the presence of EBV virus and higher levels of apoptosis and inflammation. Moreover, we know from the literature that higher levels of these processes have been correlated with spontaneous abortions. However, more research is needed to establish these results.

E-PS-22-023
Audit of clinical indications for the histopathological assessment of placentas in a single tertiary referral centre
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Background & objectives: There is a considerable delay of reporting placenta specimens which calls for an urgent review of current practice. The aim is to assess which indications are associated with normal morphology and to evaluate areas to focus on for workload savings.
Methods: Data on clinical indications (D code) and morphology information (M code) for all placentas received between 31/8/17 and 2/5/18 were collected and examined. Likelihood of each indication to result in a normal or abnormal outcome was determined using odds ratios.
Results: 86 placentas (7.34%) out of a total of 1172 placentas received were reported as normal. Prematurity was the most frequently cited indication for submission in histologically normal placentas (39.5% of all normal placentas). The majority of preterm placentas reported as normal were from >32 weeks gestation. <32 weeks gestation was twice more likely to be associated with abnormal report than >32 weeks gestation. On further analysis of preterm cases, an indication of admission to the Neonatal Unit (NNU) was 16.87 and an indication of maternal diabetes was 6.77 times more likely to result in a diagnosis of a normal placenta compared to a histological abnormality.
Conclusion: These data taken together would suggest that examination of the following subgroups to gather more evidence could result in additional workload savings: indication cited as (i) either admission to NNU or maternal diabetes and (ii) gestation <32 weeks.

E-PS-22-025

Congenital disorder of glycosylation type IIL of a child 7 months old

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Background & objectives: CDG2L is a rare multisystem genetic disorder with autosomal recessive inheritance. The disease is clinically manifested by gastrointestinal, liver, hematologic abnormalities, impaired psychomotor development. The goal is to show the importance of genetic expertise for successful final diagnosis of CDG2L
Methods: The research oversaw a premature child, who died at the age of 7 months. Intravital molecular-genetic examination has revealed a mutation in the COG 6 gene (606977), which describes patients with congenital disorders of glycosylation type IIL (OMIM 614576). The autopsy material research has used basic histological methods with Masson's trichrome stain and immunohistochemically reactions (CK7, CK19 and CD 31).
Results: A premature boy was from the fifth pregnancy, the third premature surgical birth at 33 weeks of gestation. Since birth the child is in a hard condition. He repeatedly had a surgical intervention for ulcerative-necrotic enterocolitis, perforation of the small intestine and development of adhesive disease. The clinical symptoms of the disease: toxicity, jaundice, liver failure, coagulopathy, anaemia, and metabolic encephalopathy. Death was caused by addition of a bacterial infection.
Conclusion: The autopsy examination has revealed characteristic changes for CDG2: microcephaly with internal hydrocephalus; common haemorrhages in the lungs, stomach and intestines; necrosis in the spleen; hepatic degeneration and fibrosis, proliferation of bile ductus, cholestasis; cortical dysplasia of the kidneys. Diagnosis of congenital disorders of glycosylation (CDG2L) is based on typical clinical and morphological picture of the disease. Molecular-genetic examination has revealed a mutation in the gene COG6; it was crucial to the successful final diagnosis of the CDG2L.

E-PS-22-026

Clinical and morphological diagnosis of secondary haematophagocytic lymphohistiocytosis associated with Epstein-Barr viral infection of a child 14 years old

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Background & objectives: Secondary postinfectious haematophagocytic lymphohistiocytosis (HLH) is a rare clinical syndrome, caused most often by viral infection. HLH is characterized by excessive immune activation of cytotoxic T-lymphocytes, organ infiltration by activated macrophages; manifested by cytopenia, hyperferritinemia, hepatosplenomegaly, SIRS, sepsis, multiorgan failure.
Methods: Clinical, laboratory, morphological diagnosis of HLH was performed of a child 14 years old, who had an EBV-infection and died as a result of multiorgan failure. EBV intravital diagnosis is based on PCR tests. The autopsy material research has used basic histological methods with Masson's trichrome, PAS-reaction, Perl's method, immunohistochemically reactions (CD 68, EBV), detection of EBV encoded RNA (EBER).
Results: A 14 year old girl has experienced jaundice in two weeks after suffering from infectious mononucleosis. She has hepatosplenomegaly, lymphadenopathy, ascites, hydrothorax, cholecystitis, haemorrhagic rash on body and limbs, common haemorrhages in the stomach, small and large intestine, haemolytic anaemia. Lately generalized bacterial and fungal infections were developed. Death occurred in one and half months after the onset of the disease due to bacterial infection, severe pneumonia, SIRS, multiorgan failure.
Conclusion: The autopsy research has revealed characteristic HLH associated with EBV-infection: lymphohistiocytosis infiltration with hemophagocytosis in the bone marrow, lymph nodes, liver, spleen, pancreas and kidneys with development of active interstitial hepatitis, pancreatitis, nephritis, severe bacterial-fungal pneumonia. Clinical and morphological diagnosis of secondary HLH after infectious mononucleosis is based on a typical clinical, laboratory (thrombocytopenia, anaemia, hyperferritinemia) and morphological picture of the disease using modern research methods: PCR tests, immunohistochemically methods and detection of EBV encoded RNA (EBER).

E-PS-22-027

Post-mortem MRI and CT at autopsy of new-born with intrapericardial teratoma: a case report

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Background & objectives: We present the case of new-born boy who was born by caesarean section due to foetal heart failure at the gestational age of 32 weeks to evaluate the effectiveness of post-mortem MRI and CT for the new-born with intrapericardial teratoma.
Methods: CT and 3TMRI of the deceased new-born body were performed 13 hours after death before the autopsy. The analysis of tomograms and 3D-reconstructions were performed. Virtopsy data were compared with the results of conventional autopsy. With Virtopsy of the body, signs of non-immune hydrops fetalis as anasarca, bilateral hydrothorax, ascites, hydropericardium, as well as lung hypoplasia were detected.
Results: An inhomogeneous soft tissue tumour of irregular round shape, which is closely adjacent to the wall of the right heart atrium and pulmonary trunk, volume of 29 cm^3, was detected in the pericardial cavity. Multiple cysts, 1-6 mm in diameter, filled with liquid contents, were determined in the tumour structure. The pronounced vascularization of the tumour tissue due to vessels emanating from the heart wall in the area was detected.
Conclusion: Microscopic examination revealed a picture of mature teratoma with elements of dense and loose fibrous connective, adipose and muscle tissue; cartilage, salivary glands, neuroglia, as well as cysts lined with intestinal, bronchial, single-layer cubic and multi-row epithelium. Post-mortem CT and MRI allowed to identify the growth source and structural features of the tumour, and severity of non-immune hydrops fetalis and lung hypoplasia. Virtopsy increases the efficiency of pathological study, which demonstrates the feasibility of post-mortem CT and MRI dead new-borns.

E-PS-22-028

Presentation of a primarily genetically diagnosed Fuhrmann syndrome

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Background & objectives: Fuhrmann syndrome (fibular a-/hypoplasia, femoral bowing, poly-, syn-/oligodactyly) and Al-Awadi/Raas-Rothschild (AARR) syndrome (phocomelia syndrome with limb/pelvic hypoplasia/aplasia, renal anomalies, cleft palate, hypertelorism and micro-retrognatia) are both caused by mutation of WNT7A- gene at locus 3p25.1.
Methods: A Fetus of gestational week 15 of consanguine parents (mother: G5/P1) was examined macroscopically, radiologically and histologically. Of interest: after a live born child that died 2 days post-partum in the 2 following pregnancies Fuhrman syndrome was genetically diagnosed and pregnancies terminated without autopsy. The foetus examinated now was again prenatally genetically diagnosis as Fuhrmann syndrome.
Results: Phokomelia of the lower limbs was the dominant feature, furthermore signs were micro-retrognatia and hypertelorism. Radiology confirmed missing ulnae, oligo- and syndactyly, highly hypoplastic pelvis and aplasia resp. shortening of the lower limbs. Internal autopsy revealed as additional

malformations a split uvula, left sided diaphragmal defect, consecutive herniation of the left liver lobe, the spleen and stomach into the thorax, a two-part pancreas and a lung sequester on the left side. Histology, though slightly hampered by autolysis, displayed organs' development according to gestational age. Likewise, brain was developed according to gestational age.
Conclusion: Our case presents malformations typical for AARR syndrome. As mutation of WNT7A- gene at locus 3p25.1 is responsible both for AARR and Fuhrmann syndrome. Hence, the exact diagnosis might be missed when based only on genetics and autopsy is omitted.

E-PS-22-029
Holoprosencephaly: case report
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Background & objectives: Holoprosencephaly (HPE) is a structural anomaly that compromises the development of the anterior brain. Such changes cause several neurological impacts and dysmorphisms on the brain and face, which can be incompatible with life.
Methods: L.R.G., 21 years old, female. The patient underwent routine ultrasonography (US) in Brazil, in which a single, longitudinal and cephalic foetus, placenta with anterior insertion, heterogeneous texture with multiple cystic areas, the largest with 3.9 cm of diameter absence of cardiofoetal beats (BFC), foetal movements and muscle tone was noted.
Results: The macroscopic anatomopathological report indicates a foetus weighing 140g, measuring 13cm in head-buttock length, 2.5cm in foot length and undetermined sex. The material also presents cyanosis in extremities and head, elongation of the skullcap, oedema, detachment of the skin, proboscis, cyclopia and low implantation of the ears. At the opening, organs with signs of diffuse maceration were noted. The microscopic report indicates a gestational age of approximately 4 to 5 lunar months, organs in universal autolysis - a fact that prevented the classification of the HPE type of the conceptus - and evident signs of holoprosencephaly.
Conclusion: Therefore, new research must be carried out to find out if there are changes in the epidemiological data and to further develop ways of preventing the disease.

E-PS-22-031
Long segment jejuno-ileal duplication with extensive gastric heterotopia: a rare case report
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Background & objectives: Duplications of the gastrointestinal tract are rare congenital anomalies that generally occur in the small intestine. Enteric duplications produce complications such as intestinal obstruction or haemorrhage.
Methods: A 20 months old girl patient presented with anaemia and recurrent episodes of bleeding from rectum since 4 months old. Clinical examination, endoscopy and colonoscopy revealed no abnormality. Suspecting a Meckel's diverticulum, a dynamic abdominal scintigraphy was performed. The ultrasonographic and MRI feature suggestive of duplication cyst.
Results: Accompanied by intraoperative consultation with frozen sections, exploratory laparotomy was performed and a 75 cm long tubular jejuno-ileal duplication cyst communicating with the ileal lumen was excised. Macroscopic examination of the surgical specimen showed double lumen with the septum containing the muscularis propria. On microscopic examination duplication segment was revealed entirely with heterotrophic gastric mucosa. There was 1 cm diameter of ulcer found in the normal portion of the small intestine.
Conclusion: The diagnosis of an enteric duplication is difficult to make clinically because the wide spectrum of symptoms and unspecific signs frequently simulate other diseases.

E-PS-22-032
An oxymoron: a desmoplastic small round cell tumour with spindle cells and without desmoplastic stroma
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Background & objectives: We report a rare variant of intra-abdominal desmoplastic small round cell tumour (DSRCT) with unusual spindle cell morphology and without desmoplastic stromal reaction. Diagnostic clues and differential diagnosis are emphasized.
Methods: A 12-year-old boy with autoimmune lymphoproliferative syndrome (ALPS) suffered of vague abdominal pain. TC examination revealed an abdominal mass, as well as multiple nodules. Patient underwent laparotomy showing multiple omental nodules. Partial omentectomy with numerous nodules, ranging from 4 to 40 mm, was performed for histological examination.
Results: Histologically, nodules were composed of relatively bland-looking spindle cells arranged in a fascicular growth pattern with focal whorling. Mitoses were rare (2mitoses/10HPF) and focal areas of necrosis was seen. Desmoplastic stromal reaction was absent. Tumour was reminiscent of an infantile fibrosarsoma. Immunohostochemically neoplastic cells were positive for vimentin, desmin, WT-1 (nuclear staining-C-terminus) and EMA. The clinical presentation and the polyphenotypic immunoprofile suggested the diagnosis of DSRCT with unusual morphology, which was supported by the detection of EWSR1-WT1 fusion gene (PCR). The patient was treated according to the protocol EpSSG-2005 with reduction of the masses, but he died after ten months for disease progression.
Conclusion: The present case widens the morphological spectrum of DSRCT. Only rare cases of DSRCT with spindle cell morphology and without desmoplastic stromal reaction are reported in the literature so far. Molecular studies are mandatory in confirming the diagnosis.

E-PS-22-033
Bardet Biedl syndrome in a foetus
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Background & objectives: Bardet Biedl Syndrome is reported at post-mortem of a 23 week foetus. In older children phenotypic traits include renal anomalies, obesity, dysmorphic extremities, retinitis pigmentosa, hypogonadism and intellectual disabilities. In our case we observed post-axial polydactyly and renal cysts.
Methods: A 23 week foetus was referred for post mortem following a finding of enlarged cystic kidneys and subsequent management.
Post-mortem examination was performed according to Royal College guidelines including histology of the kidneys.
Genetic analysis included microarray of amniotic fluid and exome sequence.
Results: Examination showed a 591 g male baby of foot length 38 mm. There was post-axial polydactyly of both feet and left hand, talipes of the left foot, enlarged cystic kidneys (Right kidney 13.9 g and Left kidney 13.4 g) and a small urinary bladder. No encephalocoele was seen.
Histology of kidneys revealed incomplete nephrogenic zones. Glomeruli and tubules were seen. There were cystic spaces lined by epithelial cells; larger centrally than peripherally. Some cystic glomeruli were seen. Features of a ductal plate malformation were not seen in the liver.
Microarray was reported as arr(1-22)x2,(X,Y)x1
Exome sequence revealed compound heterozygous mutations in MKKS consistent with Bardet Biedl syndrome type 6.

Conclusion: Bardet Biedl Syndrome is an autosomal recessive ciliopathy with broad clinical manifestations. More than 20 genes have been implicated to date, relating to the development and function of cilia. There is heterogeneity but severe renal disease has been described with dysfunction of BBS6 more so than in other genes.
In a foetus with polydactyly and renal cysts Bardet Biedl Syndrome should be considered in the differential diagnosis.

E-PS-22-034
Hydrocephalus in foetuses revealing a spectrum of Walker-Warburg syndrome (type II lissencephaly): a foetal neuropathological study of 5 cases
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Background & objectives: Walker Warburg Syndrome (WWS) is a lethal, genetically heterogeneous autosomal recessive disorder characterized by a spectrum of lesions including, a type II lissencephaly (Cobblestone lissencephaly), retinal malformation, cerebellar malformation, and congenital muscular dystrophy.
Methods: We report the autopsy findings of 5 cases, two of them are a siblings with hydrocephalus on ultrasound between 20 and 22 gestational weeks in 3 cases and at 37 Weeks for two others. Hydrocephalus was associated with occipital encephalocele in one case and 4th ventricle cyst suggesting a Dandy-Walker malformation in the other case.
Results: Pathology findings in all cases showed lissencephaly, hydrocephalus, diffuse and severe cerebral and cerebellar cortical dysplasia with glial and neuronal displacement into the leptomeninges, consistent with diagnosis of Walker Warburg syndrome.
Conclusion: Foetal hydrocephalus was the major manifestation leading to the prenatal detection of this syndrome. Our cases are highlighting the necessity to look for associated anomalies in foetuses or new-born infants with hydrocephalus in order to establish a better prenatal diagnosis and an effective family genetic counselling

E-PS-23 Pathology in Favour of Developing Countries

E-PS-23-001
Analysis of turnaround time of surgical pathology specimens at a tertiary care hospital, Lahore
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Background & objectives: Turnaround time is an important parameter of customer satisfaction. The laboratories located in our tertiary care hospitals face many challenges including equipment breakdown, power failure, unavailability of reagents and absence of adequate information system which hinder the routine processing and require analysis.
Methods: A cross-sectional descriptive study was conducted at the Department of Pathology, King Edward Medical University, Lahore from September,2016 to January,2017 in which turnaround time of 241 surgical pathology specimens were included. Turnaround time was analysed by using a pre designed time log sheet covering all the steps during slide preparation.
Results: Major causes of delay in turnaround time included re-cuts, intra and extra departmental consultation and re-gross of the surgical specimens after initial grossing. Maximum number of delays were observed in benign neoplasms (87) and inflammatory lesions; mainly because of intradepartmental consultations to determine the exact category of the lesion.
Conclusion: Using turnaround time to benchmark specimen workflow in anatomical pathology is an important quality tool that helps in identifying potential areas resulting in delayed reporting of laboratory tests.

E-PS-23-002
Cystic fibrosis of the lung: diagnostic challenges in a resource limited setting - a case report
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Background & objectives: Cystic Fibrosis is an autosomal recessive disorder due to mutation in cystic fibrosis transmembrane regulator, characterized by viscid mucous secretions in all exocrine glands.
Objective: Reporting a suspected case of Cystic Fibrosis and its diagnostic challenges in resource limited setting.
Methods: A retrospective review of the patient following clinical and radiological diagnosis. The case was sent for histological evaluation at Muhimbili National Hospital-Tanzania. Histopathological diagnosis was reached after gross examination and evaluation of hematoxylin and eosin stained sections which revealed characteristics pointing out to the differential diagnosis of cystic Fibrosis
Results: A 21 years old African male with history of several admissions at Muhimbili National Hospital complaining of Productive Cough for more than 17 years, Difficult in breathing and fever. He had no history of Tuberculosis infection. He never smoked cigarette or drank alcohol. No familial history of similar disease. Radiological review revealed fibrocavitatory disease. He underwent left Lobectomy and specimen was sent for histopathology. Grossly, the tissue appeared grey in colour, measured 10*6.5*7.5cm. On its cut section-multiple cavities lined by thick grey bands. Microscopically, Distorted lung architecture replaced by Glandular hyperplasia and cysts which are filled by mucin and separated by thick fibrous septa, Bronchoectasia and inflammation were noted.
Conclusion: Literature demonstrates low incidence of Cystic Fibrosis in African population which leads to physician not to consider it as possible diagnosis. However, absence of genetic screening programs for Cystic Fibrosis in low resource settings which may result in missed or under diagnosis. Other diagnostic tests like sweat chloride test has also been a challenge. Limited facility and expertise coupled to delayed reporting limits treatment options which could be possible elsewhere.

E-PS-23-003
Implementation of the Paris system for reporting urinary cytology on voided urine samples in a resource-limited setting
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Background & objectives: Urine cytology has wide variability in reporting terminologies and rates resulting in apathy among clinicians towards it. This study was undertaken to restore the significance of urine cytology by applying recently introduced 'Paris System' and to evaluate its diagnostic yield.
Methods: A descriptive study was conducted over one and a half year (January 2016 to June 2017). A total of 100 single voided urine specimens from 100 patients were processed using cytocentrifuge. Conventional smears were studied and reported according to 'The Paris System.' Results were correlated with histopathology where available considering it as gold standard to evaluate the diagnostic yield.
Results: The cytologic diagnoses were Negative for High-Grade Urothelial Carcinoma in 60%, Unsatisfactory/Non-diagnostic in 29%, High-Grade Urothelial Carcinoma in 6%, Atypical Urothelial Cells in 3%, and Suspicious for High-Grade Urothelial Carcinoma in 2% cases. Follow up histopathology results were retrieved from 25 cases. A sensitivity of 71.42%, specificity of 88.88%, positive predictive value of 83.33%, negative predictive value of 80% and accuracy of 81.25% was calculated.
Conclusion: The main objective of this study was diagnostic categorization of urine cytology. Statistical analysis shows that urine cytology is a useful test for diagnosing urothelial carcinoma. Adoption of universal reporting system, understanding of diagnostic categories and their clinical implications, accepting the limitations of cytology, minimizing sampling and interpretation errors, and judicious clinical use are all necessary to

extract maximum benefit of urinary cytology. 'The Paris System' as such provides a common groundwork for effective use of urine cytology.

E-PS-24 Pulmonary Pathology

E-PS-24-001

Integrated radio-pathological diagnosis of pulmonary MALT lymphomas, a series of 14 cases

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Background & objectives: Pulmonary MALT lymphomas (pMALTomas) are rare and there are limited studies on imaging features. Given the current trend in clinical practice to increase diagnostic efficacy through joint radio-pathological assessment, we evaluate possible correlations between CT manifestations and histological characteristics.

Methods: We reviewed clinicoradiological information from the medical records of 14 patients aged from 50 to 84 years with pathologic diagnosis of pMALTomas between 2001 and 2019. Lesion characteristics, distribution and laterality within the lungs were analysed on CT. Treatment and follow up were also assessed.

Results: Lesions manifested as consolidation (n5), nodule (n5) or mass (n4). 5 cases were bilateral; 8 out of 9 unilateral cases were identified as solitary lesions. Most cases had random lung distribution. 7/14 cases radiologists considered the possibility of neoplasm.

Histologic findings were common in all cases, a dense heterogeneous lymphoid population that distorted the architecture of the bronchi and pulmonary parenchyma. Thirteen received chemotherapy and there have been no recurrences.

Conclusion: It is difficult to establish a correlation between the radiological pattern and the pathological diagnosis of pMALTomas. Although it can present various patterns on CT, it is an entity that must be taken into account when making a differential diagnosis of a pulmonary process.

Histologically, it shares features with other MALT lymphomas arising in different sites.

Pulmonary MALT lymphomas are low grade tumours with a low recurrence rate after surgical and chemotherapeutic treatment.

E-PS-24-002

The expression of p40 in lung carcinomas

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Background & objectives: Specific subclassification of lung carcinomas is necessary for the therapeutic management. P40 is very promising marker in cancer research. The purpose of this study was to determine the significance of P40 expression in various types of lung carcinomas.

Methods: We examined 54 cases, including 28 adenocarcinomas, 14 squamous cell carcinomas (SCC) and 12 small cell carcinomas. P40 positive staining (+) was based on nuclear staining of the tumour cells. Attention was given to the approximate percentage of tumour cells stained and the intensity of staining (weak, moderate, strong).

Results: Extensive P40(+) was noted in 13/54 (24,07%) of the lung carcinomas: 3/28 (10,71%) adenocarcinomas and 10/14 (71,42%) SCC but was negative in 12/12 small cell carcinomas. The mean percentage of SCC P40(+) was 73,6%, 7 with strong, 2 with moderate and 1 with weak intensity. The 3 cases of adenocarcinomas that reacted with P40 stained 1 moderately and 2 weakly with the mean percentage of the positive cells 27,4%.

Conclusion: P40, that is a useful immunohistochemical marker of subclassification of lung cancer, could provide guidance for personalized therapy.

E-PS-24-004

Pulmonary aspergilloma due to aspergillus flavus associated with oxalosis

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Background & objectives: Oxalosis (calcium oxalate deposition) is associated with several conditions, including aspergillosis. Some Aspergillus species produce oxalic acid, which reacts with tissue calcium or blood to precipitate calcium oxalate.

Methods: A 47-year-old man with no particular past medical history, presented with a one-month history of haemoptysis. Chest computed tomography showed a cavity in the right upper lobe measuring 46x73 mm, with surrounding infiltration, and an intracavitary nodular lesion. Bronchoscopy revealed an inflammatory mucosa in the right upper lobe bronchus with white lesions that were biopsied.

Results: Histological examination of the biopsy specimen highlighted the birefringent calcium oxalate crystals by polarization associated with branching septate hyphae and severe erosions in the bronchial epithelium. The culture of bronchoalveolar lavage specimens yielded Aspergillus flavus. These findings have confirmed the diagnosis of pulmonary aspergilloma due to Aspergillus flavus associated with oxalosis. After an initial treatment with Voriconazole, the patient was planned for right upper lobectomy.

Conclusion: The presence of associated oxalosis in a given Aspergillus infection should be stated in the pathology report not only for its potential clinical significance but also for its diagnostic value.

E-PS-24-005

Primary pulmonary synovial sarcoma: a very rare presentation

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Background & objectives: Synovial sarcoma of lung is a very rare aggressive tumour accounting for 0.5% of all primary lung malignancy. Only a few cases of synovial sarcoma involving the thoracic region have been reported in the literature.

Methods: we report a case of 32-year old male, who presented with chest pain, dry cough and shortness of breath for one month. The computer tomography scan showed well defined mass measuring 6x6x4.8 cm in right infra hilar region along with pleural effusion. The thoracotomic biopsy was performed.

Results: Histologically, tumour cells were round to spindle shaped arranged in sheets and fascicles having moderate amount of cytoplasm with indistinct cell border. The nuclei are round to oval having irregular nuclear membrane with hyperchromatism and inconspicuous nucleoli. Myxoid changes along with pericytoma like branching blood vessels were also noted. Necrosis and mitotic figures(6/10HPF) were also seen. Immunohistochemically, neoplastic cells were positive for EMA, CD99 and TLE-1 and negative for CK, CD 34 and STAT 6. So, the final pathological diagnosis was primary pulmonary biphasic synovial sarcoma.

Conclusion: In conclusion, we demonstrate a rare case of primary pulmonary synovial sarcoma. It is a rare tumour so histopathology is required to establish the diagnosis and immunohistochemistry is preferable for detection of the tumour subtype of this rare tumour entity.

Abbreviation: CD99- Cluster of differentiation, CK- Cytokeratin, EMA- Epithelial Membrane Antigen, STAT 6- Signal transducer and activator of transcription 6,TLE 1- Transduction like enhancer of split 1.

E-PS-24-006

Diagnostic concordance in pulmonary tumours

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Background & objectives: International diagnostic guidelines recommend immunohistochemical staining with p40 and TTF-1 (the more specific clone 8G7G3/1, not the commonly used more sensitive SPT24) in non-small cell carcinoma without clear morphological features. Neuroendocrine markers are recommended only in cases with neuroendocrine morphology.
Methods: In total, 52 unselective real-world bronchial and transthoracic lung biopsies from suspected pulmonary tumours were included in the study. For all cases, sections stained with hematoxylin-eosin, p40 and TTF-1 (clone SPT24) were scanned at x40.
Results: Almost 30 pathology consultants that sign out at least one lung cancer case per year have received the digitalized cases in February 2020 and will individually diagnose them as primarily lung cancer (specified as adenocarcinoma, squamous cell carcinoma, small cell carcinoma, non-small cell carcinoma not otherwise specified etc.), metastasis to the lung, suspicion of malignant tumour, atypia of unclear significance, benign/non-neoplastic lesion. Also, for each case, the pathologist shall state if further diagnostic immunohistochemical markers are needed. The diagnostic concordance, any misclassifications relating to TTF-1 clone SPT24, and recognition of neuroendocrine morphology will be evaluated. Data will be presented at the ECP.
Conclusion: The study may provide insight into how current diagnostic guidelines work in practice, if there may be need for revision of guidelines, and/or need for e.g. education or quality assurance in diagnostics of pulmonary tumours.

E-PS-24-007
FISH and protein expression of ALK rearrangement in cell-block may be different – case report
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Background & objectives: Mutations in EGFR, HER2 and BRAF, translocations of ALK, ROS1 and RET became determinant targets. FISH keeps being the leading test to identify ALK gene rearrangement. We report a case of ALK-rearrangement where tumoral cells were ALK IHC negative.
Methods: A 58-year-old woman presented a RUL adenocarcinoma diagnosed after a FNA-cell block CK7/VIM/TTF1 positive, classified as stage IIIb. Mutational status was asked to the Molecular Pathology Lab.
Results: Close association between a positive FISH test and modestly elevated ALK protein in tumour cells allows ALK IHC to be used, either to select cases for confirmatory FISH testing and as the primary therapy-determining test. EGFR and ROS1 were wild type and ALK IHC analysis (clone 5A4; 1:25; Leica) was negative. FISH was prepared manually as recommended by ZytoVision, probe used was ZytoLight ® SPEC ALK Dual Colour Break Apart Probe. This case presented single 3´signals in 76% tumour cells. This case was ALK rearranged FISH positive and negative for ALK IHC.
Conclusion: This case highlighted the belief that both IHC and FISH analyses should be carried out together to avoid ALK misdiagnosis, allowing either knowledge and technology attention in cell-block. Being aware of these particular cases, avoids missing patients in IHC-based screening.

E-PS-24-008
Comparison of different HNF4α clones for invasive mucinous adenocarcinoma of the lung
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Background & objectives: Hepatocyte nuclear factor 4α (HNF4α) is a marker for invasive mucinous adenocarcinoma (IMA). However, studies using different HNF4α clones showed variable results. We aim to investigate the expression of HNF4α in IMA and non-mucinous adenocarcinoma (NMA) using different HNF4α clones.
Methods: Two commercially available HNF4α antibodies (clones H9 and H1415) were used to examine HNF4α expression in 30 IMA and 40 NMA cases. The intensity and proportion were separately evaluated by three pathologists, and an average Histoscore (range, 0-300) was calculated. Receiver operating characteristic (ROC) curve was used to determine the optimal cut-off value, sensitivity and specificity of each clone.
Results: The IMA group showed a significantly higher mean Histoscore than the NMA group for both H1415 (136.1 vs. 6.3) and H9 (60.3 vs. 2.7) ($p<0.001$ for both comparisons). Using ROC curve to determine the Histoscore cut-off value at 27.65 (clone H1415) and 14.85 (clone H9), H1415 showed a higher sensitivity (83.3% vs. 70.0%) with similar specificity (95.0% vs 95.0%) compared to H9.
Conclusion: Our results demonstrates that HNF4α expression is significantly higher in IMA compared to NMA and is a reliable marker for distinguishing IMA from NMA. Although both clones show high specificity for IMA, clone H1415 is more sensitive compared to H9, and the stronger staining intensity of clone H1415 also makes it more suitable for usage in clinical practice.

E-PS-24-011
Alveolar adenoma of the lung
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Background & objectives: Alveolar adenoma of the lung is a rare benign tumour. About 40 cases were reported in English medical literature. Histogenesis weren't confirmed. Alveolar adenoma often resembles normal lung parenchyma. We present a clinical case of alveolar adenoma of the lung.
Methods: A 38 years old female patient was examined with chest x-ray which showed a small 2 cm in diameter nodule in the lower lobe of the left lung. This lesion was surgically removed then histological and immunohistochemical analyses were provided.
Results: Histological re-examination showed that tumour consisted of alveolar-like network spaced lined by cuboidal cells with hyperchromic nuclei. Thin stroma contains spindle-like cells, matrix and lymphocytes. Immunohistochemistry analysis showed that epithelial cells were diffusely positive for TTF-1, CD34 was expressed only by endothelial cells of blood vessels. Stromal cells were positive for vimentin. Ki-67 had very low expression both in the epithelium and stroma. Alveolar adenoma was diagnosed based on these findings. After 19 month in March 2018 on the computed tomography a new 13 mm tumour was noted near surgical suture. Morphological verification wasn't made due to patient's health status.
Conclusion: This patient had alveolar adenoma of the lung but radical surgical treatment was not performed. Key moment of this case is a potential relapse of this rare tumour.

E-PS-24-012
New clinical context in lung adenocarcinoma
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Background & objectives: To establish the prevalence of KRAS G12C mutation in lung adenocarcinoma as well as its possible coexistence or not with mutations in EGFR, ALK and BRAF.
Also studying a possible morphological correlation with mutations in KRAS.
Methods: Retrospective study of codons 12 and 13 of KRAS by pyrosequencing (Pyromark Q24 Advanced) in 301 patients with pulmonary

adenocarcinoma and conventional molecular panel (EGFR, ALK, BRAF, ROS1) diagnosed at University Hospital of the Canary Islands between November 2017 and January 2020.
Correlation of molecular findings with morphological characteristics in paraffin sections stained with HE.
Results: KRAS was mutated in 34,88% of cases, being KRAS G12C the most frequent mutation (15,95%).
Eight KRAS mutated adenocarcinomas (7,76%) coexist with EGFR mutations, and two others (1,94%) coexist with BRAF V600. Therefore, the coexistence of this alterations is possible (p=0,025). None was associated to ALK.
There is no statistically significant association between morphology and mutations in KRAS, even after studied the mucinous phenotype which seemed to be associated (p=0,57).
Conclusion: KRAS activating mutations are the most frequent drivers in human cancer, among these mutations, KRAS G12C is the most prevalent in lung adenocarcinoma.
The published series that address the prevalence of KRAS G12C in lung adenocarcinoma are few and controversial, further in our knowledge, ours is the first studied by pyrosequencing.
Due to development of KRAS inhibitors during last year, it seems necessary to prepare for the new clinical context.

E-PS-24-015
A tricky lesion for the untrained eye: pulmonary hydatid disease
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Background & objectives: Hydatid disease, caused by the larvae of Echinococcus granulosus can mimic lung tumour clinically. Identification of typical scolex provides the histological diagnosis, but it is not observed in most cases. In this study, we re-evaluated clinico-pathological features of this disease.
Methods: Records/slides of 184 pulmonary cases, diagnosed between 2005-2020 were reviewed, and clinico-pathological features (age, gender, clinical diagnosis, surgical procedure, and microscopic features) were re-evaluated.
Results: Median age was 46 years (6-89), and female/male ratio was 103/81. Clinical diagnosis was straightforward in most cases, only 5 cases had clinical/radiological suspicion of malignancy. Cystectomy was performed in the majority (89.5%); wedge resections (7%), lobectomies (3%) and chest wall resections (0.5%) requiring loss of pulmonary parenchyma were relatively rare. Microscopically, laminated basophilic cuticle, was the most consistent finding, and germinal layer and/or scolex were visible in a minority of cases.
Conclusion: Echinococcosis, is a common zoonotic disease in some parts of the world and diagnosis is usually easy for experienced clinician/pathologist. However, in the present era due to increased travel and immigration, the disease may be seen practically all over the world and can be tricky for the untrained eye. Variable microscopic features should be kept in mind, when evaluating an unusual pulmonary mass.

E-PS-24-016
Late metastases from endometrial carcinoma – a potential mimic for primary lung adenocarcinoma
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Background & objectives: The lungs are a common site for solid organ tumour metastases. However, metastases from endometrial carcinoma to the lung are uncommon. Late metastases, particularly from endometrioid endometrial adenocarcinoma, therefore, have the potential to mimic primary lung adenocarcinoma. We describe four cases of late metastases from endometrioid endometrial carcinoma to the lung.
Methods: Following an index case, cases of late (>5 years) metastatic endometrioid endometrial adenocarcinoma to lung were identified from the pathology database. The original hysterectomy slides as well as the pulmonary metastases slides were reviewed. A unified panel of immunohistochemistry was performed on representative uterine and pulmonary tumour blocks consisting of: Oestrogen receptor (ER), Progesterone receptor, PAX8, p16, p53 and CDX2.
Results: Four cases of late metastases from endometrioid endometrial adenocarcinoma to the lung were identified, of which two were isolated. The recurrence interval ranged from 7.3 years to 14.5 years with a mean time to recurrence of 9 years. All cases involved low grade (grade 1 or 2) endometrioid endometrial primaries. The metastases all had similar morphological appearances to their respective primary tumours. All primary and metastatic tumours showed ER positivity.
Conclusion: Whilst rare, metastases from endometrial carcinomas to the lung should be considered in patients with a relevant history, regardless of timeframe. If morphological appearances are not typical of lung adenocarcinoma, additional history should be sought. ER immunohistochemistry can be helpful.

E-PS-24-017
Primary pulmonary enteric adenocarcinoma: a study of six cases
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Background & objectives: Primary Pulmonary Enteric Adenocarcinoma (PEAC) is an extremely rare type of pulmonary adenocarcinoma divided into adenocarcinomas with enteric morphology and with enteric differentiation. We present six cases of PEACs with their histological, immunohistochemical and genetic features.
Methods: Clinical examination, routine pathohistological examination with hematoxylin/eosin staining accompanied by immunohistochemical examination and genetic testing.
Results: Histologically, out of the six cases reported only 2 were pure enteric type. The rest of them were colloid with enteric component and one was enteric with papillary and mucinous sections. Immunohistochemical examination showed 5/6 tumours to be cytokeratin (CK)7 positive. CK20 was positive in 2/6 of the cases and all were CDX2 negative. Napsin A was diffusely positive in all of the cases. Thyroid transcription factor-1 (TTF-1) was positive in five out of the six cases. EGFR and ALK testing showed all of the tumours to be negative. A colonoscopy was performed on all of the patients and proved no tumour formation in the colon.
Conclusion: PEACs are predominantly ones with enteric morphology and in fewer cases with enteric differentiation. Both of these are suggested to be a coherent group of tumours defined by the lack of EGFR and ALK mutations, typical histological and immunohistochemical patterns.

E-PS-24-018
Squamous cell carcinoma developing from solitary bronchial papilloma
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Background & objectives: Bronchial papillomas accompany upper respiratory papillomatosis. Tumour development from these lesions is rare and appears in long-term lesions. We present a case of squamous cell carcinoma developing on the background of solitary papilloma, which is human papilloma virus PCR positive.

Methods: A 65-year-old male patient has respiratory distress with effort, and in the examinations a mass lesion obstructing atelectasis and lumen in the right upper lobe is detected. The patient is diagnosed non-small cell lung carcinoma by intraoperative consultation and the right lower lobectomy is performed.
Results: In macroscopic examination of lobectomy material; A lesion filling the right main bronchus which size 2.9x2 cm and infiltrating the bronchus in a focal area was observed. The microscopic sections of the lesion ,tumour cells are eosinophilic cytoplasm with nucleolar prominence, mitotic activities are frequent. The lesion had a squamous papilloma feature in large areas and the fibrovascular core and squamoid morules are seen in these areas. In a focal area, squamous cell carcinoma infiltrating the bronchial wall and cartilage was observed. Immunohistochemically pansitokeratin, p63 and p16 applied and all were positive. Human papilloma virus positivity was determined by PCR. Laryngeal papillomas were not observed in the patient's subsequent controls.
Conclusion: Although bronchial papilomas are benign lesions, these patients are known in the literature of tumoral development in the long term. Careful examination is important as these cases can cause diagnostic problems during intraoperative consultation.

E-PS-24-019
Intra-bronchial mucoepidermoid carcinoma in a 9-years-old girl: a case report and literature review
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Background & objectives: Bronchial tumours are very rare in paediatric age group. Mucoepidermoid carcinoma is a rare tumour of the lung comprising <1% of all lung tumours. We report a case of Mucoepidermoid carcinoma in a 9-year-old girl who presented with chronic cough.
Methods: A nine -year-old girl presented with one year history of chronic cough diagnosed initially as tuberculosis. Her CT chest showed left lung collapse, clear right lung with compensatory emphysema. Microscopic of bronchoscopic biopsy revealed a low-grade mucoepidermoid carcinoma. She underwent total left lung pneumoectomy.
Results: MEC is the commonest salivary gland malignancy in childhood. Bronchial Mucoepidermoid carcinoma presents primarily with symptoms bronchial irritation and obstruction. They are classified as high or low grade mucoepidermoid based on their histologic appearance. Radical surgery is the treatment of choice, patients with low-grade Mucoepidermoid carcinomas have a generally good prognosis.
Conclusion: Bronchial tumours are rare in childhood and are often overlooked owing to its nonspecific presentation Patients with low-grade Mucoepidermoid carcinoma s generally have a good prognosis after primary surgical resection. When a child presents with persistent respiratory symptoms needs further workup to rule out an obstructive process.

E-PS-24-020
Diffuse idiopathic neuroendocrine cell hyperplasia, tumourlets and multifocal typical carcinoid tumours of the lung: present of a case
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Background & objectives: Diffuse intrapulmonary neuroendocrine cell hyperplasia (DIPNECH) is a rare condition, presented as a generalised proliferation of neuroendocrine cells of the lung, considered by the WHO a potential preinvasive lesion of typical pulmonary carcinoid tumours.
Methods: We present a case of a 62 years old, asthmatic female patient, admitted to the Thoracic Surgery Department with dry cough and dyspnoea. On thoracic CT scan a 13x16 mm dominant nodule was described in the left lower lobe, associated with numerous disseminated nodules in both pulmonary fields. Multiple tumour nodules from left inferior lobe were resected by axillary thoracotomy.
Results: The histopathological examination revealed multiple nodules in the lung parenchyma, the largest one with 7 mm diameter, with organoid architecture, consisting of polygonal, medium sized, monomorphic neuroendocrine type cells with eosinophilic cytoplasm, finely granular nuclear chromatin, some of them with conspicuous nucleoli and 1 mitotic figure/2 mm2. Tumour emboli and intratumoral necrosis was not observed. The background stroma was hyalinised and highly vascularised. The tumour cells expressed TTF-1, Chromogranin, Synaptophysin and CD56. The Ki-67 proliferation index was <2%. In the bronchial walls multiple foci of neuroendocrine cell hyperplasia was noted.
Conclusion: A final diagnosis of diffuse idiopathic neuroendocrine cell hyperplasia (DIPNECH) associated with multifocal typical peripheric carcinoid tumour of the lung was made. In the setting of DIPNECH multiple carcinoid tumours can develop and according to the new AJCC staging this should not be regarded as intrapulmonary metastases, but as separate primaries.

E-PS-24-021
Neuroendocrine tumour of the breast with pulmonary metastasis 30 years after mastectomy
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Background & objectives: We describe an uncommon case with a mammary neuroendocrine tumour (NET) showing metastasis to the lung 30 years after mastectomy with axillary lymph node dissection.
Methods: A 77-year-old postmenopausal Japanese woman diagnosed with urothelial carcinoma of the urinary bladder, and a past history of Stage I right breast cancer at the age of 43, underwent transurethral resection of the bladder tumour. During examination and follow-up for this urothelial tumour, CT revealed a left pulmonary nodule in the upper lobe that showed a tendency to grow.
Results: The cut surface of the partially resected lung specimen contained a relatively well-circumscribed, grey-whitish, solid tumour, measuring 17.5x17x11 mm in size. This lesion was histopathologically composed of solid growth of invasive polygonal cells with finely granular, slightly eosinophilic cytoplasm and a highly vascular stroma. Their nuclei had ovoid or irregular shapes, a finely granular chromatin pattern, and small nucleoli. Twenty-seven mitotic figures were observed per 10 HPFs. Vascular involvement was occasionally detected. Immunohistochemically, the neoplastic cells were positive for synaptophysin, mammaglobin and GATA3, and negative for TTF-1. Cell reactive rates for the oestrogen receptor and the progesterone receptor were 90% and 5%. The HER2 score was estimated to be 1+.
Conclusion: It has recently been demonstrated that neuroendocrine mammary neoplasms follow a more aggressive clinical course, even though most immuno-express ER and/or PgR with negativity for HER2, than invasive carcinomas of no special type, with poorer local and distant recurrence-free survivals as well as overall survival. Intriguingly, the present breast NET of histological and nuclear grade 3 with a high MIB-1 index (71.2%) showed rather indolent biological behaviour without adjuvant therapy.
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E-PS-24-022

Value of immunohistochemistry for detection of BRAF V600E mutation

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Background & objectives: BRAF-V600E mutation is identified in many malignancies. Detection is usually performed by PCR or NGS, with longer turnaround times (TAT) and higher costs than immunohistochemistry (IHC). Our goal was to compare detection of BRAF-V600E mutation by PCR and IHC.
Methods: We tested 46 archival cases for BRAF-V600E mutation. We performed parallel PCR and IHC testing on 5 melanomas (MM), 5 papillary thyroid carcinomas (PTC), 5 colorectal adenocarcinomas (CRC), 12 cases of pulmonary Langerhans cell histocytosis (PLCH), one Erdheim-Chester disease. Additionally, we performed IHC on 8 BRAF-V600E mutated lung adenocarcinomas (LADC) and 10 BRAF-V600E wild type lung adenocarcinomas (PCR).
Results: All 8 cases of PCR-detected BRAF-V600E mutated lung adenocarcinomas showed a positive staining by IHC. The 10 BRAF-V600E wild type lung adenocarcinomas did not stain. One case of CRC, one PLCH, 3 MM, and 2 PTC were positive both by PCR and IHC, while all cases that were negative by PCR were also negative by IHC, which indicates a 100% concordance rate between the two methods.
Conclusion: Comparison of PCR detected BRAF-V600E mutation with ICH showed a 100% concordance in the results, which indicates that IHC can be used with confidence instead of PCR to detect BRAF-V600E mutation in a variety of malignancies and other disease which can harbour this mutation, thus shortening TAT and costs.

E-PS-24-024

A significant discordance between PANAMutyper™ and targeted deep sequencing for detecting EGFR mutation in non-small cell lung cancer

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Background & objectives: *EGFR* mutations are predictive biomarkers for targeted therapy in lung cancer. This study aimed to screen *EGFR* mutations by PNA clamping-assisted fluorescence melting curve analysis, and to evaluate the feasibility of targeted deep sequencing for detecting the mutations.
Methods: We examined *EGFR* mutations in exons 18, 19, 20, and 21 using PNA clamping-assisted fluorescence melting curve analysis (PANAMutyper™) for consecutive 2,135 non-small cell lung cancer (NSCLC) tissues from August 2017 to September 2019. Of these, targeted deep sequencing was performed in 82 patients.
Results: *EGFR* mutations were identified in 46.0% of the tumours (933/2030); 442(47.4%) had mutations at exon 19, 404(43.3%) at exon 21, 156(16.7%) at exon 20 (including 90 cases with T790M), and 38(4.1%) at exon 18. 11.1% (10/90) of T790M mutations was identified in TKI-naïve patients. Interestingly, 30.0% (3/10) of the primary T790M existed alone without L858R or exon 19 deletions. We observed a significant discordance (24.4%: 20/82) of the *EGFR* mutation between PANAMutyper™ and targeted deep sequencing. Targeted deep sequencing revealed eleven nonsynonymous single-nucleotide variations, eleven insertion-deletion variations and two amplifications in *EGFR*, which were not detectable by the PANAMutyper™. In two cases, *EGFR* mutations were detected only in PANAMutyper™.
Conclusion: Taken together, our study demonstrates that primary *EGFR* T790M alone exists and there is a significant discordance between PANAMutyper™ and targeted deep sequencing. The significance of these discrepancies should be carefully interpreted for the patient's treatment and clinical outcome.

E-PS-24-025

The diagnosis of pleural tumour other than mesothelioma in a woman in the second decade of life - a case report

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Background & objectives: Epithelioid haemangioendothelioma (EH) is a low-grade vascular tumour in multiple locations, but as a primary neoplasm in the pleura it is extremely rare. Pleural EH is a sporadic tumour whose etiopathogenesis is not well defined.
Methods: We present the case of a patient in the second decade of life who debuted with a left pleural effusion, bilateral pleural and pulmonary nodules in the context of a left lower lobar pulmonary mass confirmed by thoracic CT and body PET. Cultures and PCR for negative mycobacteria.
Results: Under the optical microscope, nests of abnormal endothelial cells, consisting of epithelioid or histiocytoid cells, were seen. The nuclei of the cells are eccentric, vacuolated and similar to the cells in the signet ring. The cytoplasm is eosinophilic, with vacuoles of different sizes in the cytoplasm of some tumour cells. Immunohistochemistry was positive for CD31, D2-40 and focally for calretinin, HMB-45 and CEA, being negative for CD-34, CK7, napsin A, TTF-1, pancytokeratin, common leukocyte antigen, WT-1 and e-cadherin. The proliferation index was less than 10%. Based on the exceptional clinical and radiological and histopathologic findings, it was concluded an HEP.
Conclusion: HEP is an infrequent tumour, derived from vascular endothelial cells with unclear pathogenesis and a variety of clinical manifestations, with similarities to other thoracic diseases and a complex differential diagnosis. The diagnosis depends mainly on the histopathological examination and additional immunohistochemistry to confirm that the tumour originated in the endothelium. The improvement in the knowledge of HEP histopathology is important to increase the rate of early diagnosis and improve prognosis.

E-PS-24-026

Primary pulmonary high-grade mucoepidermoid carcinoma in 31-year-old pregnant woman

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Background & objectives: Primary pulmonary mucoepidermoid carcinoma (MEC) is a rare entity (0.1-0.2% of all lung cancers). MECs are characterized by mucus secreting, squamous and intermediate-type cells, subclassified as low or high-grade tumours. More than 50% of MECs affect population under 30 years.
Methods: A 31-year-old woman in 36th week of gestation was admitted due to haemoptysis. Bronchoscopy revealed bronchial intraluminal mass, obstructing the orifice of the right lower lobe. Transbronchial needle aspiration and biopsy were performed. Prior to surgical treatment, caesarean section was carried out with good neonatal outcome. Afterwards, video-assisted thoracoscopic right lower lobectomy with mediastinal lymph node dissection was done.
Results: On transbronchial biopsy the diagnosis of MEC was obtained. Immunohistochemistry showed p40 positivity, TTF-1 negativity and Ki67 up to 15% in hot spots. On surgical specimen the diagnosis of high-grade MEC was confirmed with single peribronchial lymph node involvement. Despite recommendation, patient refused adjuvant treatment. During the follow up period of 7 months there is no evidence of disease progression.
Conclusion: It is important to distinguish MECs from MEC-like pulmonary, usually adenosquamous, cancers. And it is important to distinguish low-grade MECs from high-grade MECs. Low-grade MECs are usually considered being cured by optimal surgical treatment, having excellent 5-year survival rate. In contrast, high-grade counterparts are more aggressive and harbour prognosis similar to other non small cell lung cancers.

E-PS-24-027

PD-L1 expression by immunohistochemistry (IHC) in non-small cell lung carcinoma (NSCLC): experience of two lung cancer referral centres in Dublin

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Background & objectives: Assessment of PDL1 expression in NSCLC is essential when anti-PD-L1 immunotherapy is considered. This study aimed to evaluate sample quantity, referral source, specimen site, specimen type, NSCLC subtype, insufficient samples and rate of positive, low positive and negative PD-L1 expression.
Methods: Information on PD-L1 IHC tests was obtained from the Laboratory Information System in two university Hospitals lung cancer centres., from January 2018 – August 2019. PD-L1 IHC was performed using the SP263 antibody kit on the Ventana Benchmark Ultra on cases from 18 different institutions (of which 46% were referred cases).
Results: 583 tests performed on samples from were identified (male 53%). Sites known for 92%; lung (66%), lymph node (16%), bone/soft tissue (7%), pleural fluid (3.5%), others (<3%); Biopsies 72%, resections 10%, cytology 18%, adenocarcinoma (58%), squamous cell carcinoma (32%), NOS (9%), others (<1%).
95% adequate samples:

	<1%	1-49%	>50%
Overall	52%	16%	32%
Adenocarcinoma	50%	18%	32%
Squamous cell carcinoma	59%	20%	21%

Insufficient samples were 5% of the cohort.
Conclusion: Testing for PD-L1 by IHC in both referral centres has been successful, benefitting 18 institutions nationwide. The rates of positive, low positive and negative results in this cohort is in line with international published data. The results were similar in both referral centres.

E-PS-24-029

Neuroendocrine marker expression in malignant pleural solitary fibrous tumours: a case report

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Background & objectives: Neuroendocrine(NE) markers have been exceptionally reported in malignant pleural solitary fibrous tumours (PSFTs).These markers are often used in cytological samples in presence of small/medium size cells with high mitotic rate. This could lead to pitfalls especially if clinical information is lacking/incomplete
Methods: We describe the case of a middle age woman that was admitted to our hospital for a paratracheal mass for a 4R lymph-node enlargement, with a pathologic uptake at 68Ga-DOTATOC. Transbronchial needle aspiration was performed.
Results: The microscopic examination of the cytological specimen showed solid nests, weakly positive for cytokeratines, synaptophysin and high proliferative index (Ki67) thus a metastasis of a NE tumour was suspected. During multidisciplinary discussion physicians reported a previous large thoracic mass, surgically resected two years before, diagnosed as malignant PSFT. Based on this information, STAT6 was additionally performed in cytological sample, revealing a diffuse and strong expression, thus leading to a more appropriate diagnosis of PSFT metastasis.
Conclusion: Reporting this unusual case, we would like to point out the rare occurrence of NE markers in malignant PSFTs in order to avoid potential diagnostic pitfalls, especially in small biopsy/cytological samples.

E-PS-24-031

Endobronchial lipoma: an extremely rare benign mesenchymal lung neoplasm

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Background & objectives: Endothoracic lipomas are categorized into 5 groups: endobronchial, parenchymatous, pleural, mediastinal, and cardiac. Benign neoplasms of the tracheobronchial tree are rare, and lipomas are one of the most uncommon. Endobronchial lipomas (EL) represent 0.1–0.5% of all lung neoplasms.
Methods: We present the case of a 73-year-old man with a clinical history of lung adenocarcinoma with a contralateral pedunculated, white, "polyplike" lesion founded during a follow-up flexible bronchoscopy. The mass was endoscopically resected and the histology revealed a well circumscribed mass composed of a collection of mature fat cells without atypia and an intact overlying squamous epithelium.
Results: EL affect adults in their 5th-6th decade of life with a size range from 1-5 cm, they are more common in men, obesity and smoking are considered risk factors although there are no conclusive studies. Patients could be asymptomatic or present with cough, haemoptysis, recurrent pneumonia, wheeze, or dyspnoea that may have been present for years. EL could be also found incidentally on a radiograph or during bronchoscopy performed for a different indication, as in our case. The radiographic suggestion of endobronchial lipomas is usually made by CT scan showing an intrabronchial lesion of fat attenuation with no enhancing contrast. The lesion is characterized by mature adipose tissue without atypia.
Conclusion: Most published cases are located in the first 3 subdivisions of the tracheobronchial tree. EL is more common on the right side as in our case. Early surgical excision is essential to avoid permanent pulmonary damage due to obstruction.

E-PS-24-032

Ectopic intra-pulmonary thyroid tissue: a case report

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Background & objectives: The presence of ectopic intrapulmonary thyroid is extremely rare, with few cases reported in the literature. We report a case of ectopic intrapulmonary thyroid presented as a pulmonary nodule in a patient with history of thyroidectomy for a benign condition.
Methods: A 75-years-old woman presented with chronic cough with dyspnoea and wheezes for last one year. There is a history of hemithyroidectomy for a benign condition for more than 20 years with thyroxine replacement. Examination showed a prolonged expiration and few crackles in posterior chest. Laboratory results show normal inflammatory markers with normal thyroid functions.
Results: Chest computed tomography (CT) showed a right rounded lung nodule. The initial diagnosis was considering carcinoid tumour and a frozen section was arranged. On surgery, the nodule was found to be located in the fissure between upper and lower lung lobes and was enclosed in a thin fibrous capsule. The nodule measured 2.5 X 2.0 X 1.5 cm with a tan brown cut surface. Frozen section showed a capsulated mass formed of thyroid follicles without evidence or malignancy or teratomatous elements and was reported as ectopic thyroid tissue. The subsequent histopathology report confirmed the diagnosis.

Conclusion: Ectopic intrapulmonary thyroid is extremely rare but can be confused with primary or metastatic pulmonary tumours from other sites. This case report denotes the importance of considering intrapulmonary heterotrophic thyroid tissue in the differential diagnoses of a pulmonary nodule.

E-PS-24-033

CD68 as a marker of pulmonary sarcoidosis in differential diagnosis

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Background & objectives: A great number of clinical manifestations of pulmonary sarcoidosis determines diagnostic difficulties.
Objective: to study the diagnostic significance of the method of CD68 immunophenotyping of biopsy material in the differential diagnosis of sarcoidosis with the other disseminated lung diseases (DLD).
Methods: 153 medical records of patients with X-ray morphological indices of disseminated lung affection (44 cases of which were with sarcoidosis).
Results: The clinical diagnosis in patients with DLD from the disease onset until the time of adequate therapy appointment ranges from 3-4 weeks to several years. After a histological examination, pulmonary sarcoidosis was morphologically verified in 42% cases, while in the initial clinical diagnosis it was detected in 9%. A comparative immunohistochemical study of lung tissue in heterogeneous groups by histological phenotype was carried out. It was established that the expression of CD68 in the alveolar lumen was not statistically significant in the studied groups, whereas in stroma of lung tissue in patients, in groups with lung sarcoidosis, the expression of CD68 was high 10.5±1.1.
Conclusion: High expression of CD68 in the stroma of the lung tissue can be used as a diagnostic marker of pulmonary sarcoidosis in thoracobiopsy materials and to be the differential diagnosis criterion for morphological verification of clinical diagnosis.

E-PS-24-034

The role of mitochondrial reactive oxygen species in reprogramming of mesothelioma cell line

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Background & objectives: We investigated whether human malignant mesothelioma cell line Mero-14 expresses pluripotency genes (such as OCT4, NANOG and SOX2) and whether their expression is affected by reactive oxygen species (ROS) produced by mitochondria.
Methods: Expression of OCT4, NANOG and SOX2, and control genes found in mesothelial cells, vimentin and cytokeratin 7 was analysed by DAB immunohistochemistry. ROS generation was identified using CM-H2DCFDA fluorescence indicator and quantified using the EVOS imaging system. Complex III inhibitor antimycin A was used to stimulate mitochondrial ROS generation, while mitoTEMPO was used to scavenge ROS generated by mitochondria.
Results: Mero-14 cells exhibited NANOG and SOX2 expression and no expression of OCT4. Complex III inhibitor antimycin A dose-dependently increased mitochondrial ROS generation. At lower, but not higher concentrations antimycin A enhanced NANOG expression. Although SOX2, vimentin and cytokeratin 7 were expressed in Mero-14 cells the use of antimycin A did not affect their expression levels. mitoTEMPO abrogated antimycin A-induced increase in NANOG expression.
Conclusion: Mero-14 cells express pluripotency genes NANOG and SOX2. ROS generated by mitochondria induce NANOG expression and may trigger reprogramming of mesothelioma cells toward more malignant phenotypes.
This research is supported by the Croatian Science Foundation.

E-PS-24-035

Lung carcinoma with synchronous gastric metastasis at presentation–a case report

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Background & objectives: Gastrointestinal metastasis from primary lung cancer are rare (incidence of 0.5-10%-the latter in autopsy evaluations) and their presence indicates advanced stage and poor prognosis. Small intestine is the most frequent location and the estimated incidence in the stomach is 0.2-0.5%.
Methods: A 58-year-old woman, heavy smoker, with haemoptysis underwent a CT-scan. A 75x35mm superior right lung lobe nodule was detected with chest wall extension and supraclavicular, axillary, mediastinal and ipsilateral hilar lymphadenopathies. Due to a gastric PET-scan hypermetabolism focus she was submitted to an upper endoscopy that revealed two polypoid lesions in the gastric body. Lung and gastric biopsies were performed.
Results: Lung biopsy: high grade solid malignant neoplasm with marked pleomorphism and numerous mitosis. Immunohistochemistry showed multifocal positivity for Cam5.2 and focal for CK7; CK20, TTF-1, napsinA, p63, calretinin, neuroendocrine markers and CDX2 were negative.
Gastric biopsies: normal epithelium with infiltration of the lamina propria by a malignant neoplasm with similar characteristics.
A poorly differentiated lung carcinoma with synchronous gastric metastasis at presentation was favoured. No molecular alteration was found.
Conclusion: Gastric metastasis from lung cancer are exceptional but possible events, usually associated with late-stage disease. Therefore, pathologists must be aware of this rare occurrence, even with an unusual immunoprofile. Their presence should be considered in these patients' work-up.

E-PS-24-036

YAP1 and RB loss of expression in TTF-1 negative small cell lung carcinoma (SCLC)

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Background & objectives: 25% of SCLC are Thyroid Transcription Factor-1 (TTF-1) negative and challenging to diagnose if neuroendocrine markers are absent. Inactivation of retinoblastoma protein (RB) drives SCLC therefore we assessed RB and its downstream target Yes-associated protein-1 (YAP1) expression in these tumours.
Methods: Our cohort included from 10 patients (9 men, 1woman aged 58-78). Tissue samples were obtained from transbronchial biopsies (6/10), lymph nodes (3/10) and pericardium (1/10). Diagnosis of SCLC was established based on morphological and immunophenotypical (routine stains for CK8/18, TTF-1, chromogranin, synaptophysin, CD56 and Ki-67). Additional, immunohistochemistry was performed on formalin-fixed paraffin embedded sections with antibodies against YAP1 and RB.
Results: All the cases were TTF-1 negative. 9/10 were CK8/18 positive (1 focally) with a dot-like pattern, 5/10 were chromogranin A positive (all focally), 7/10 were synaptophysin positive (3 focally) and 7/10 were CD56 positive (1 focally). Proliferation marker Ki-67 was above 90% in all cases. One case was neuroendocrine marker negative, one showed only focal positivity for chromogranin and synaptophysin whereas two cases showed positivity only for CD56. YAP1 expression was abolished

in all cases (0/10) and RB expression was lost in 9/10 cases. The only specimen with intact RB expression was the neuroendocrine-negative.
Conclusion: YAP1 loss is a robust marker of SCLC, even in TTF-1 negative and neuroendocrine negative cases. RB expression is also abolished except from the neuroendocrine negative case. YAP1 and RB immunohistochemistry helps to establish diagnosis of SCLC in challenging cases.

E-PS-24-038
A rare and benign tumour of lung which acts as a malignant tumour
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Background & objectives: Sclerosing haemangioma is a rare and generally benign lung tumour. Yet, difficulties of discriminating the characteristic features of the tumour, either benign or malignant, increases the clinical importance of this tumour. Therefore, immunohistochemical staining is significant for a definitive diagnosis.
Methods: We would like to discuss our case of a 66 year-old woman who presented with complaints of cough, pain in left side of her chest and weight loss for the last six months.
Results: A surgical operation was performed due to existing of a 3 cm mass in the left hilus area. According to the frozen examination and tru-cut biopsy results, the mass was seemed as a benign tumour. However, they had not been sufficient to rule out malignancy, then the patient was diagnosed with sclerosing haemangioma accompanied by high Ki-67 rate (%6-7) based on the staining results. After a successful operation and a postoperative care, the patient was discharged to continue follow-up at outpatient clinic. On her follow-ups, any pathology has not been reported yet.
Conclusion: Although sclerosing haemangioma is known as benign, the tumour had some malignancy features such as high Ki-67 rate (Ki-67: %6-7) and high SUVmax (SUVmax: 5) value in our case.

E-PS-24-039
PD-L1 status in patients of the Moscow region with non-small cell lung cancer
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Background & objectives: Today to determine the treatment tactics for non-small cell lung cancer (NSCLC), the doctor needs to know, in addition to histology and the presence of activating mutations in the tumour, the level of PD-L1 expression.
Methods: In 2018, as part of the program of RUSSCO, 125 patients of the Moscow Region with NSCLC were examined to determine the status of PD-L1. The average age was 60.7 years. The expression of PD-L1 was determined by the immunohistochemical method (IHC) using the kit - PD-L1 IHC 22C3 pharmDx (DAKO). Patients with more than 1% stained cells were positive.
Results: In the studied group, men predominated (107/125 people). The majority of patients smoked - 56 people, 33 people did not smoke, and 36 people were with unknown smoking status. 46 patients had a histological diagnosis lung adenocarcinoma (AC) with absence of driver mutations, 75 people - squamous cell carcinoma (SCC) and 4 people - undifferentiated lung cancer (UDLC). The total number of patients with NSCLC with a positive status of PD-L1 was 46.8% (59 people). Patients with SCC prevailed in positive group (42 patients), in negative group number of patients with AC and SCC was approximately equal (30 people and 28 people, respectively).
Conclusion: Thus, in the cohort of patients with NSCLC in the Moscow region, prevailed men who smoke, and the number of positive cases was 46.8%.

E-PS-25 Soft Tissue and Bone Pathology

E-PS-25-002
Neonatal osteofibrous dysplasia with novel genetic mutation by next generation sequencing: case report and literature review
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Background & objectives: Osteofibrous dysplasia (OFD) is a rare benign paediatric fibro-osseous neoplasm exclusively affecting lower limbs. Rare familial OFDs showed MET gene mutation, however, the majority of OFD genetics remain unknown. Here, we present a rare neonatal OFD case with novel mutations.
Methods: This is a case report for a female infant with lower limb bone mass. Ancillary tests for the mass included: immunohistochemistry, florescence in situ hybridization (FISH) and next generation sequencing (NGS) for DNA sequence variants, copy number variation and fusion.
Results: A 4-month-old female presented with a clinically alarming leg swelling noticed shortly after birth with reduced limb movement. Radiologically, a heterogeneous lobulated corticomedullary lesion at the tibial diaphysis was noted. A biopsy revealed a fibro-osseous lesion with osteoid trabeculae rimmed with reactive osteoblasts within bland fibroblastic proliferation. ETV6 gene rearrangement was negative ruling out congenital fibrosarcoma. NGS was performed to identify if the lesion harbours GNAS or MET mutations. GNAS gene was intact. Combined with the histologic features, a diagnosis of OFD was favoured. Alongside the intact MET gene, mutations in DDR2 and CDK12 genes were detected. The patient was managed conservatively and showed tumour size reduction with preserved function.
Conclusion: We reported a rare neonatal presentation for OFD with novel DDR2 and CDK12 gene mutations. To the best of our knowledge, this is the first reported OFD with these gene mutations.

E-PS-25-003
Heterotopic mesenteric ossification, a distinctive pseudosarcomatous feature
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Background & objectives: Heterotopic mesenteric ossification is a rare and benign form of ossification, usually related with previous abdominal surgery or trauma and may be histologically confused with malignancy, especially extraskeletal osteosarcoma. 52 cases have been reported in the literature until today.
Methods: We presented a 76-year-old male patient who developed ileus due to small bowel perforation, after abdominal surgery because of adenocarcinoma of colon. Macroscopic examination revealed perforation on bowel wall and 2 cm diameter, white, hard, irregularly limited mass on mesenteric area of the ileum.
Results: Microscopically, there was an irregularly limited nodular lesion in the mesentery consist of (myo)fibroblastic spindle cells, proliferative osteoblastic cells producing osteoid lace-like, fat necrosis and haemorrhage. There was no bone formation. The proliferating (myo)fibroblasts and osteoblasts were mitotically active but cytologically bland and there were no necrosis and atypical mitosis. Immunohistochemically, osteoblastic cells were positively stained with SATB2, negatively with cytokeratin.
Conclusion: This is a very rare pathology and awareness on this reactive process will prevent pathologist to misdiagnosis this lesions as sarcomatous

E-PS-25-004

Ossifying fibromyxoid tumour: a case report with a review of the literature

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Background & objectives: Ossifying fibromyxoid tumour (OFMT) of soft tissue is an extremely rare mesenchymal tumour of intermediate malignancy and uncertain line of differentiation. It most commonly arises in extremities. The aim of our work is to recall its anatomo-clinical features.
Methods: We report the case of a 57-year-old man who presented with a three-year-history of painless, subcutaneous mass that involved the scapular region.
Results: Macroscopically, the excised tumour measured 10 cm in size and was well circumscribed. On a cut section, it was tan-white coloured and had a firm texture. It was centred by an ulceration and contained calcifications. Microscopically, the tumour was composed of uniform round or spindle cells arranged in nests and cords and deposited in a variably myxoid and collagenous stroma. The cells had a pale nuclei with small amounts of eosinophilic cytoplasm. There was an incomplete shell of lamellar bone found at the periphery of the tumour. Immunohistochemically, tumour cells expressed strongly vimentin and S-100 protein. The patient was diagnosed with ossifying fibromyxoid tumour of the scapula.
Conclusion: The OFMT is a rare tumour with a variable behaviour. The majority of these tumours are histologically benign. However, recurrence and metastasis are reported in rare cases.

E-PS-25-005

Desmoplastic small round cell tumour: report of two cases

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Background & objectives: Desmoplastic small round cell tumour (DSRCT) is a rare malignant tumour that typically involves the abdominal or pelvic peritoneum of young males and pursues an aggressive clinical course. Herein, we spotlight the clinical, morphological and immunohistochemical features of this disease.
Methods: We report two cases of DSRCT diagnosed in our department. It was a 30-year-old men and a 10-year-old boy. Both cases showed typical DSRCT findings in terms of localization of the lesions and histopathology.
Results: The two patients presented an atypical abdominal pain. Imaging revealed large intra-abdominal masses with multiple peritoneal nodules. Biopsy was performed and showed, in both cases, a proliferation of small round cells arranged in nests separated by a slightly cellular fibrous tissue. These cells have a scanty, poorly delimited cytoplasm and monomorphic hyperchromatic nuclei. Mitoses are rare. Some cells had a rhabdoid appearance. An immunohistochemical study showed an intense and diffuse positivity of tumour cells with dot-like staining with desmin and negativity with myogenin. Based on the histological and immunochemical features of the tumour, the diagnosis of DSRCT was made.
Conclusion: DSRCT is highly aggressive neoplasm, characterized by a specific t(11;22) (p13;q12).This tumour must be differentiated from other small round cell tumours. The treatment is based polychemotherapy, aggressive surgery and radiation therapy.

E-PS-25-006

Chondroblastic osteosarcoma with heterologous rhabdomyosarcomatous differentiation

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Background & objectives: Malignant mesenchymoma describes a tumour composed of two or more unrelated malignant mesenchymal components. Its prevalence depends on the location and is much more common in soft tissue than bones. Herein we report a rare case of bone malignant mesenchymoma.
Methods: A 72-year-old male patient with a history of myasthenia gravis was admitted to the hospital with symptoms of progression of the disease. A thoracic computer tomography was conducted and revealed large tumour of the right eighth rib. Core needle biopsy followed by standard pathological evaluation and ancillary genetic tests were performed.
Results: The biopsy showed pleomorphic neoplasm with complex morphological pattern. Foci of chondroblastic (S100 and SOX9 positive), osteoblastic (SATB2 positive) and rhabdomyoblastic (desmin and myogenin positive) differentiation were present. Due to the fact that all three components showed malignant features and no IDH1 and IDH2 mutations were detected, final diagnosis of chondroblastic osteosarcoma with heterologous rhabdomyosarcomatous differentiation was made. Next generation sequencing (NGS) using FusionPlex Kit did not reveal any genomic abnormalities.
Conclusion: Although malignant mesenchymoma of bone is a very rare tumour, such entity should be kept in mind in case of complex bone neoplasm. It is also important to underscore that chondroblastic osteosarcoma undergoing heterologous differentiation is a different entity than a dedifferentiated chondrosarcoma. In keeping with complex genomic alterations reported in osteosarcomas with absence of common genetic lesions our NGS analysis has not revealed any potentially targetable molecular alterations.

E-PS-25-007

A perivascular epithelioid cell tumour (PEComa) in the retroperitoneum, with a pattern recalling lymphangioleiomyomatosis of the lung – a case report

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Background & objectives: PEComas encompass a wide group of rare neoplasms, more so in the retroperitoneum. May be related with congenital syndromes and may even progress. They can have many morphological patterns but have a perivascular arrangement throughout. Also, have a characteristic immunophenotype.
Methods: We describe a case of a 38-year-old woman, admitted to the hospital with a spontaneous pneumothorax. During work-up, TC revealed a retroperitoneal, solid mass and an endoscopic ultrasound-guided fine-needle aspiration cytology (EUS-FNAC) was performed. Afterwards, she underwent excisional surgery.
Results: EUS-FNAC revealed groups of monotonous spindle cells. The pathology specimen with a lacerated surface, measured 42mm in greatest dimension. On histology, we observed a mesenchymal neoplasm, comprised of spindle cells with granular, light eosinophilic cytoplasm, oval nuclei and small nucleoli, organized in fascicular pattern and interconnected with vascular channels. These were immunorreactive for Podoplanin and the spindle cells marked for smooth muscle and melanocytic antibodies, confirming the diagnosis of a PEComa with

lymphangioleiomyoma pattern. We counted 2 mitosis per 50 HPF, without other high grade features. Due to an incomplete surgical margin, invasion and neoplasm's complete size were not assessable, thus lacking features to apply the Folpe criteria for malignancy.
Conclusion: PEComas with lymphangioleiomyoma pattern can arise in the retroperitoneum, even without clear context of lymphangioleiomyomatosis. Careful follow-up should be performed due to potential progression to the lung.

E-PS-25-008
Vancomycin soaking of anterior cruciate ligament autograft reconstruction enhances elastic fibres
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Background & objectives: ACL rupture a frequent injury in sports and infection is rare (0.14-1.8%); coagulase-negative staphylococci accounts90% of cases associated to contamination by commensal bacteria of patient's skin during graft preparation. Intravenous antibiotic prophylaxis impregnation of autografts with vancomycin have been applied.
Methods: A prospective case-control study was carried out to preview histopathological changes that plasty can undergo after ACL vancomycin impregnation. Tendons collected during surgery were used and surplus segments were submitted to histopathological study and elastin impregnation. Two samples from each tendon of nine patients were analysed, with and without vancomycin impregnation.
Results: The normally kept ACL segment presented HE hyaline substance with delicate wavy elastic impregnation compared with vancomycin impregnated ACL where considerable reinforcement of elastin waving and apparent retraction were seen.
Conclusion: Vancomycin as bactericidal against skin commensal bacteria has shown evidence of low toxicity on chondrocytes and osteoclasts with releasing rate into tissues over time. Although post-ACL reconstruction infection is a rare complication, it can have catastrophic effects, plasty failure and joint function compromise. Studies are needed to clarify vancomycin effects on graft integrity beyond infection concern. Without considering patients age, the observed elastic waving might be concurrent to ACL after-surgery preserved function.

E-PS-25-009
Unusual intraneural tumour harbouring EWSR1-NFATC2 fusion: a case report
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Background & objectives: The EWSR1-NFATc2 fusion characterizes a rare subset of Ewing-like sarcomas with a unique morphology, occurring predominantly in bone. We present an unusual case of an intraneural EWSR1-NFATc2 associated sarcoma highlighting clinical, histological and molecular features and potential diagnostic pitfalls.
Methods: We retrospectively reviewed the histology, radiological and molecular findings of a patient diagnosed with an intraneural EWSR1-NFATc2 associated sarcoma at our institution, and review the recent literature on EWSR1-NFATc2 associated tumours. DNA was extracted from fresh frozen tumour and matched normal tissue for whole genome sequencing (WGS) under the 100,000 Genomes Project, and the data analysed using standard bioinformatics pipelines.
Results: A 35-year-old female presented with a 6-month history of a painful lump on the left forearm, arising from the radial nerve on MRI. Initial biopsy showed a round cell tumour with no distinguishing features. On further open biopsy, tissue was submitted for histopathology and WGS as part of the 100,000 Genomes Project. Histopathology revealed an epithelioid to spindle cell lesion with scattered EMA and S100 expression. FISH studies demonstrated a deletion of the 3' of the EWSR1 locus. The tumour was classed as an unusual epithelioid tumour possibly representing a malignant peripheral nerve sheath tumour with perineural differentiation. WGS analysis subsequently revealed an EWSR1-NFATc2 fusion, refining the diagnosis.
Conclusion: This case expands the spectrum of morphological and clinical features associated with sarcomas harbouring an EWSR1-NFATc2 fusion and highlights the role of molecular and genomic studies in the workup of Ewing-like sarcomas.

E-PS-25-010
Synovial sarcoma of the hand with osteoid and bone formation: a case report and therapeutic implications
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Background & objectives: Synovial sarcoma (SS) is a rare soft tissue sarcoma of uncertain differentiation, affecting mostly young patients. It displays a specific chromosomal translocation t(X;18)(p11;q11) that provokes a SS18-SSX fusion gene. SS of the hand has distinct clinical behaviour and treatment opportunities.
Methods: Man, aged 29, presented with a swelling of the right palmar aspect of his hand. Radiologically, a soft tissue palm mass was detected without any relationship or erosion to adjacent bones. CT of thorax, CNS and abdomen (-). After surgery: multinodular, compact, centrally cystic, whitish/grey tumour, measuring 5,5X5cm. Paraffin-embedded tissue was stained with hematoxylin-eosin and immunohistochemistry. Molecular analysis was performed.
Results: Microscopically, a neoplasm, composed of spindle cells arranged in a fascicular or "herring-bone" pattern, was revealed. The cells were ovoid, fairly uniform with hyperchromatic nuclei and inconspicuous nucleoli. Mitoses: 19/HPF(X40). Necrosis: (+ in <50% of tumour). Focally, calcification, osteoid and woven bone formation was present, resembling osteosarcoma, osteogenic or extraskeletal. The differential diagnosis comprised mainly osteosarcoma, clear cell sarcoma of soft parts, malignant solitary fibrous tumour, MPNST and synovial sarcoma. Immunohistochemistry: Vimentin(+), EMA(+/-), CKAE1/AE3(+ in single cells), bcl2(+), CD99(+), TLE-1(+), S100(+), MelanA(-), HMB45(-), CD34(-), Desmin(-), Ki67(8-10%). Molecular findings: formation of a SS18-SSX fusion gene. Diagnosis: Monophasic synovial sarcoma with osteoid and bone formation, grade 3 according to FNCLCC.
Conclusion: Adequate margins of excision are necessary to reduce the risk of local recurrence. Limb-sparing surgery is possible in most patients, as in our case. Adjuvant radiotherapy can improve local control of high-grade SS of the limbs, but not survival.

E-PS-25-011
Malignancy in giant cell tumour of bone: a case of rapid transformation in an unprecedented site
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Background & objectives: Giant cell tumour of bone (GCTB) is a benign, locally aggressive neoplastic process taking place in the bone. Malignancy in giant cell tumour of bone "MGCTB" is rare and has never been reported in small bones of extremities.

Methods: We presented a case of a 43-years old male who was admitted initially with right big toe swelling. Radiology at that time showed an expansile multiloculated intramedullary lesion in the proximal and distal phalances.
Results: First biopsy result was giant cell tumour of bone. 6 weeks later the patient presented with swelling and pain of same toe and radiology showed significant increase in size of the lesion as well as soft tissue involvement. Amputation was done and histological examination yielded a diagnosis of malignancy in giant cell tumour of bone (MGCTB). Up to our knowledge this entity was not reported in this anatomical site before.
Conclusion: Although malignant transformation of giant cell tumour of bone is rare, however it can occur in a rapid manner. Thorough follow-up surgically and radiologically are needed, as well as pathologist's vigilance especially in recurrent cases.

E-PS-25-015
Primary undifferentiated pleomorphic sarcoma of the left ventricle
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Background & objectives: Primary cardiac tumours are rare, with autopsy incidence up to 0.3%. Depending on the tumour location, can present a variety of cardiopulmonary symptoms, the left sided ones are the most common including pulmonary congestion, mitral stenosis and pulmonary vein obstruction.
Methods: A 15 year old female without any cardiological or family background of interest, with palpitations and pre-syncope consults the emergency department. In Transthoracic echocardiography presents a 35 mm mass in right ventricle, which depends on the interventricular septum, obliterating the cavity with extension to right ventricular outflow tract, with left ventricule collapsed and minor pericardial effusion.
Results: The tumour's biopsy and the following cardiectomy specimen obtained after a cardiac transplant procedure, shows in the histologic analysis a poorly-differentiated hypercellular mesenchymal neoplasm, with spindle cell predominant population with pleomorphic nuclei showing fine chromatin and prominent nucleolus, amphophylic cytoplasm, infiltrating the right ventricle myocardium with a messy arrangement in a storiform collagen stroma, with a minority myxoid component. No heterologous or epithelial differentiation is observed. Immunohistochemistry staining shows positive immunoreactivity for S100 (focal), SMA (focal) and MDM2; FISH study shows MDM2 gene amplification. The final histological diagnosis was a primary cardiac undifferentiated pleomorphic sarcoma Grade 3 FNLCC, with pathologic stage pT1b N0 M1 (cerebral metastasis with no histological confirmation).
Conclusion: Primary cardiac undifferentiated pleomorphic sarcoma is an extremely rare condition. With no gender predilection and a mean age of presentation around 45 years. Cases in paediatric age are uncommon. Cardiac sarcomas tend to be clinically aggressive with a poor prognosis.

E-PS-25-016
Childhood primary mediastinal leiomyoma
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Background & objectives: Benign mesenchymal tumours of the mediastinum are rare, representing only 1- 6% of all mediastinal masses. Primary mediastinal leiomyomas are extremely rare, its aetiology still remains unknown. Up to the present approximately 15 cases of leiomyoma that developed from spindle cells in the wall of small vessels in the soft tissue of the mediastinum wall has only been described in the English literature.
Methods: In this case report, we will be describing a 12-year-old child having a primary tumour of mediastinum, suspicious for malignancy. Chest computed tomography demonstrated a giant solid mass in the anterior mediastinum with cystic-liquid content. He underwent a complete surgical tumour resection. Gross pathologic examination of the mass revealed a whorlled, tan- white, homogenous, rubbery soft tissue mass surrounded by a thin membranous capsule. Histologically, the lesion consisted of monomorphic spindle cells with blunt-ended nuclei, with mild nuclear atypia and mitoses.
Results: Immunohistochemical examination was used including these antibodies: CD117 (-); DOG1 (-); CD34 (-), S100 (-); HMB45(-); MelanA (-), Ki 67(4%), sma(+), desmin(+) and PLAP(+).
Histological and immunohistochemical findings represented benign mediastinal leiomyoma.
Conclusion: PML is extremely rare and has only been described in a few cases in the English literature up to the present. In children these findings are even less common. Here, we report case of the PML occurring in a child, which serves as a supplement to the spectrum. Although its quite rare, PML should be considered as one of the differential diagnoses of an unexplained mediastinal mass.

E-PS-25-017
Lipoblastoma of the temporal-occipital region: an uncommon presentation in an older African child
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Background & objectives: Lipoblastoma is a rare, benign, adipocytic tumour encountered almost exclusively in infancy and early childhood; usually noted during the first three years of life. Presentation after the first decade of life is very rare.
Methods: The most common locations for this tumour are the limbs and the trunk. Occurrence in the head and neck region is uncommon. Not many cases in the temporal-occipital site have been reported. Surgical excision is considered curative and prognosis is excellent. Yet, recurrence rates of up to a quarter of cases have been reported, especially with the diffuse variety.
Results: We present a case of a 12-year old boy admitted into our hospital with a painless slow-growing mass in the left temporal-occipital region. A similar mass at the same site as the present one was said to have been surgically excised - not subjected to histologic evaluation though - two years prior to the emergence of the current mass. The child had no other comorbidities, nor any significant past medical history. Routine laboratory investigations were essentially normal. Surgical resection of the tumour was done. Histopathologic examination findings on the lesion were consistent with lipoblastoma. The possibility of a recurrent disease was entertained. The child recovered well; post-operative course was uneventful.
Conclusion: Although rare, lipoblastoma should be considered in the differential diagnosis of benign head and neck soft tissue tumours in African children and early adolescents.

E-PS-25-018
First description of lipomatous ganglioneuroma in precoccygeal location
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Background & objectives: Lipomatous ganglioneuromas are exceedingly rare benign tumours of neural crest origin. The reported tumours were located mediastinal, retroperitoneal, or paravertebral (1). Although a few cases of presacral ganglioneuromas have been published (2), a precoccygeal lipomatous ganglioneuroma has not been reported.

Methods: A 26-year-old man presented with sacral pain. MRI displayed a precoccygeal mass (52 x 48 x 49mm) with inhomogeneous and partial lipomatous signal. Differential diagnoses included neurogenic tumours like schwannoma, neurofibroma and malignant peripheral nerve sheath tumour (MPNST). Due to the lipomatous appearance on MRI also lipoma, liposarcoma and spindle cell lipoma were considered. An open biopsy was taken.
Results: Histology revealed a ganglioneuroma accompanied by various proportions of mature adipocytes without any atypia. The neurogenic component displayed mature Schwann cells arranged in a fascicular architecture and a background of a collagenous stroma. The Schwann cells were spindle-shaped with serpentine nuclei and a pale eosinophilic cytoplasm. Palisading or a myxoid stroma reminiscent of schwannoma was not present. Nuclear atypia, mitoses, necrosis, or vascular invasion were absent. Scattered mature ganglion cells with large nuclei, a prominent nucleolus, and abundant granular cytoplasm were present.
The schwannian cells were immunohistochemically positive for S100, GFAP and nuclear positive for SOX10.
The tumour was not resected, and the patient will be followed up.
Conclusion: To the best of our knowledge, less than 10 lipomatous ganglioneuromas have been reported in the literature. Herewith, we describe the first neoplasm of this entity in precoccygeal location.
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E-PS-25-019
Foamy-cell cutaneous angiosarcoma with aberrant S100 expression
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Background & objectives: Cutaneous angiosarcoma (CA) represents 0.1% of all head&neck malignancies, is more prevalent in elderly males and has a poor prognosis. Less than 10 cases of foamy-cell variant of CA are described in the literature; none with aberrant S100 immunoexpression.
Methods: 28-year-old female with a painful scalp nodule, suspicious of epidermoid cyst. Surgical specimen revealed a elastic, rose-white, well-circumscribed nodule. Morphologically it was composed by intradermal proliferation of plump, rounded cells with vesicular nuclei, small nucleoli and clear/foamy cytoplasm, growing in cohesive sheets/nests with focal irregular shaped vascular channels. Pleomorphism was scarce, mitotic figures were present and no necrosis was found.
Results: Immunohistochemistry showed diffuse positivity for ERG1, FLI1 and focal positivity for CD31. Multifocal intense positivity for S100 was seen. CD34, MelanA, HMB45, SMA, CKs and CD68 were negative. The presence of conventional vasoformative areas, some lined by foamy cells, and immunoreactivity for vascular markers allowed the diagnosis of foamy-cell CA. Wide excision and lymph node dissection was performed. The patient is currently alive with residual disease and lymph node metastases.
Conclusion: Angiosarcoma accounts for less than 2% of sarcomas and has a wide range of morphological variants. Foamy-cell CA is extremely rare, with only a few cases described in the literature. Due to a deceptively bland appearance, differential diagnosis encompasses both benign and malignant neoplasms, specially when vasoformative areas are not immediately apparent.
An unusual immunohistochemical profile adds difficulty to the diagnosis. To the best of our knowledge, this is the first case of foamy-cell CA with aberrant expression of S100.

E-PS-25-020
Posterior mediastinum PEComa with aggressive histological features: a case report
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Background & objectives: PEComas are a growing family of tumours composed of histologically and immunohistochemically distinctive perivascular epithelioid cells, showing melanocytic and smooth-muscle markers. Herein we report a case of a PEComa in posterior mediastinum, displaying aggressive histological features.
Methods: A 36-year-old male patient, locksmith, without previous relevant medical history, was admitted in hospital due to a "heavy" chest sensation and dyspnoea, with nocturnal worsening. MRI revealed a well circumscribed posterior mediastinum mass, 9,5cm of largest diameter without contrast enhancement. Surgery was performed.
Results: Grossly, a 221g solid yellow mass with 9,5cm of greatest dimension. Microscopically the neoplasm consisted of polygonal, epithelioid or spindle shaped cells with large granular eosinophilic cytoplasm and prominent nuclear atypia. Multinucleated and bizarre cells were identified, frequently featuring lipidic vacuoles. Occasional atypical mitotic figures were identified and tumoral necrosis was also present. Immunohistochemistry revealed multifocal expression of the melanocytic markers Melan-A and HMB45 and the myogenic marker desmin. No expression of cytokeratins, smooth muscle actin, S100 protein or SOX10 was observed. Our diagnosis was PEComa with aggressive histological features. Adjuvant local radiotherapy was performed. At follow-up, the patient is alive and free of disease 7 months after surgery.
Conclusion: We report a rare case of a posterior mediastinum PEComa, displaying aggressive histological features, according to the criteria proposed by Folpe et al. So far only 15 cases of PEComa were reported in the English literature, all displaying a benign behaviour.

E-PS-25-021
Atypical presentation of tenosynovial giant cell tumour: a challenging diagnosis especially on biopsy
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Background & objectives: Tenosynovial Giant Cell Tumour (TSGCT) is a locally aggressive tumour mainly affecting the knee and hip joints. The present study highlights detailed cytomorphological features, differential diagnosis and diagnostic pitfalls of an unusual presentation of TSGCT, mimicking sarcoma.
Methods: We present a case of foot TSGCT in 33-year-old man diagnosed in our department.
Results: A33-year-old man presented with foot swelling. MRI suggested synovialosarcoma. On biopsy specimen, the tumour grows as diffuse, expansile sheats. The tumour was composed of large cells with pale to eosinophile abundant cytoplasm. Nuclei were reniform, with prominent nucleoli. Excision was performed. Histologically, the lesion was well-demarcated without infiltrative growth. There were two types of regular mononuclear cells: small in size histiocyte-like and larger epithelioid cells. There were extremely rare multinucleated osteoclast-like giant cells. Focal necrosis was seen. Peripheral soft tissue and chirurgical limits were normal. There was neither pleomorphism nor infiltrative character nor mitosis. A large panel of antibodies was done showing positivity with CD68. Final diagnosis was TSGCT.
Conclusion: the occasional predominance of large cells may obscure the typical features of a TSGCT and lead to a diagnosis of sarcoma.

E-PS-25-022

Multiple intra-peritoneal liposarcoma: a challenging diagnosis

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Background & objectives: Multiple intra-peritoneal liposarcoma (MIPL) is an extremely rare entity. We present a case of MIPL which was difficult to diagnose pre-operatively and discuss several differential diagnosis.
Methods: We report the case of 67-year-old women who presented with multiple abdominal hard masses. A CT-scan of the abdomen revealed numerous masses in the abdomino-pelvic cavity, which was characterized by two components, a fatty density and a non-adipose solid portion. It showed also thickening of the antro-pyloric, duodenum and colonic wall.
Results: Digestive endoscopy revealed submucosal masses protruding in the gastric and colic lumen. Endoscopic and CT-guided biopsies were realized and several diagnoses were suggested: inflammatory myofibroblastic tumour and desmoid fibromatosis. A laparotomy was performed to obtain a definitive diagnosis. Numerous fatty nodules and masses were identified within the greater omentum, the mesentery and the mesocolon. The complete resection was impossible to perform due to the large number of nodular lesions and the involvement of the gastro-intestinal wall. Histological analysis of an omentum mass revealed mature adipocytes and scattered hyperchromatic pleomorphic cells. Immunohistochemically, tumour cells were positive for MDM2. FISH demonstrated MDM2 gene amplification. The final diagnosis was of a MIPL.
Conclusion: A pre-operative diagnosis of a MIPL may be challenging due to the rarity and lack of awareness of the tumour. The location and the multiplicity of these tumours in the present case make it unique. Although uncommon, liposarcoma should be considered in the differential diagnosis for masses involving the gastrointestinal tract, particularly if there is significant or unusual involvement of the surrounding adipose tissue.

E-PS-25-023

Pulmonary artery intimal sarcoma: a case report

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Background & objectives: Intimal sarcoma (IS) is an uncommon, poorly differentiated malignant mesenchymal neoplasm, typically affecting larger vessels. Symptoms and imaging of pulmonary IS mimic pulmonary thromboembolism (PE). We report a case of IS of the right main pulmonary artery.
Methods: A 59 year old female presented to the primary care with chest pain and shortness of breath. She was thought to have possible central right PE but imaging was not typical. Repeat CT scan and EBUS revealed a high-grade sarcoma. Subsequent right pneumonectomy showed a solid mass within the main pulmonary artery.
Results: Histology demonstrated a cellular neoplasm originating from the arterial wall and occluding the lumen. The morphology was of a poorly differentiated, mainly patternless, neoplasm, with areas of necrosis, and easily identifiable mitoses. Focally intersecting bundles of spindle cells, as well as more epithelioid and multinucleated giant cell forms were noted. Nuclear pleomorphism was prominent. On immunohistochemistry the tumour was positive for desmin, SMA, focally for EMA. It was negative for AE1/3, caldesmon, CD31, CD34, S100, Melan A, HMB45, CD117 and DOG1. EGFR polysomy was identified. MDM2 was not amplified. The diagnosis of intimal sarcoma was made. The lesion was excised by a narrow margin. The patient underwent post-operative radiotherapy.
Conclusion: The pulmonary artery IS is a rare aggressive tumour, often mimicking PE. Rapid recognition is paramount in order to proceed promptly with the initiation of therapy. Unfortunately, prognosis is poor, although our patient remains clear of tumour thirteen months post-surgery.

E-PS-25-024

Malignant solitary fibrous tumour of thorax presenting with distant metastasis: report of a case and literature review

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Background & objectives: Solitary fibrous tumour (SFT) of the pleura is a rare neoplasm. SFTs are generally benign and asymptomatic with 10-year survival of up to 98%. Approximately 10% of these have a malignant potential, leading to local recurrence or metastatic spread.
Methods: A 56 year old man presented with a left hemithorax mass in March 2017.The resection revealed a spindle cell neoplasm of 15.0 cm consistent with SFT with poor prognostic features. These included size > 10 cm, numerous (08/10 HPFs) mitoses, cellular atypia and involved margins. The patient was lost to follow up after surgery.
Results: In October 2019 the patient presented with bone pains. Radiology revealed iliac bone, pancreatic, liver, bilateral lung and brain metastasis. Core biopsy from iliac bone revealed SFT metastasis. On immunohistochemistry the STAT6 and CD34 were positive. Two months later the patient developed a soft tissue swelling in ring finger of right hand. Fine needle aspiration was performed. The cytomorphological features revealed metastasis of malignant SFT
Conclusion: SFTs can rarely behave in a malignant fashion. Identification of poor prognostic features on gross examination and microscopy is important as these lesions need aggressive management accordingly.

E-PS-25-026

Primary leiomyosarcoma of femur: a rare entity- case report and review of literature

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Background & objectives: Primary osseous leiomyosarcoma (POL) is a very rare sarcoma, accounting for <0.7% of all primary malignant bone tumours. It shows histological and immunohistochemical smooth muscle differentiation. We report this case to highlight clinical and pathological features of this rare entity.
Methods: We report the case of a 48 year-old women presented a thigh tumefaction evolving for a year. Imaging showed an osteolytic lesion of the lower extremity of the left femur.
Results: A biopsy of the lesion showed densely cellular malignant mesenchymal proliferation focally necrotic. It was made by bundles of smooth muscle cells with hyperchromatic nuclei of moderate to severe atypia with fairly numerous figures of mitosis. The immunohistochemical study showed an intense and diffuse cytoplasmic positivity of tumour cells with the smooth anti-muscle. Desmin was focal positive. The diagnosis of POL was made. The patient received neo-adjuvant chemotherapy and had a knee block resection. Macroscopically, the tumour measured 10 cm in size and was located in the distal part of the femur. Histologically, tumour showed chemotherapy effects estimated at 20%. The bone and muscle surgical limits were unscathed.
Conclusion: POL affects long bones mainly at the knee region. The treatment of choice is surgical resection. The role of chemotherapy and radiotherapy has not yet been established. Although the tumour stage and histological grade have an impact in disease-free survivals.

E-PS-25-027

Metastatic lung adenocarcinoma histologically mimicking primary osteosarcoma

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Background & objectives: Osteosarcomatous differentiation of lung adenocarcinoma is rare and usually related to prior therapy. We report two cases of solitary bone tumours morphologically mimicking osteosarcoma but with the immunoprofile of lung adenocarcinoma arising in patients without evidence of a primary elsewhere.
Methods: Both cases occurred in patients >75 presenting with radiologically non-specific solitary bone lesions. Biopsies showed malignant bone-forming tumours morphologically identical to conventional osteosarcoma. Immunohistochemistry showed strong diffuse positivity for markers characteristic of lung adenocarcinoma. Subsequent staging did not identify a primary lesion. Both tumours underwent molecular testing to determine systemic treatment options.
Results: Cytokeratin expression is rare in osteosarcomas and should not show strong diffuse positivity of all broad spectrum CK's, EMA as well as site specific markers as reported here. Furthermore, in this age group there is a high incidence of carcinoma whilst osteosarcoma is rare. We favour these tumours represent metastatic carcinoma presenting as solitary bone lesions. To our knowledge this is the first report in the literature to describe carcinoma with complete osteosarcomatous differentiation morphologically, and the immunoprofile of a lung primary.
Conclusion: We suggest that in this age group immunohistochemical testing of bone-forming malignancies should be undertaken routinely to avoid missing these cases and thus the patients missing out on systemic therapies that may be potentially available to them.

E-PS-25-028
Clinicopathologic features of intraabdominal inflammatory myofibroblastic tumour with transformation to sarcoma
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Background & objectives: The aim of study is determining the relation between pathological features of and clinical outcomes of IMT.
Methods: A review of pathohistological and FISH dates, ICH-stainings (ALK D5F3, SMA, PanCytokeratin AE1\AE3, Calponin, Desmin, EMA CD117, DOG1, CD34, SOX10, Melan A, HMB45, MITF, CD34, GFAP, Myogenin, Ki67) from 31 years old man was carried. FISH: A split signal indicates pericentric inversion (2)(p23q13), showing ALK/RANBP2 gene rearrangement. The primary 5 cm tumour grew into the wall of the colon.
Results: Right hemicolonectomy was performed. Histologically: fascicular type of growth from spindle-shaped and ovoid myofibroblast-like cells, with cells with macronucleols, 12 mitoses in 10 hpf, haemorrhages, necrosis, calcifications, a pronounced inflammatory component with a predominance of lymphocytes and plasmocytes. IHC revealed cytoplasmic type of expression of ALK, focal positive expression of SMA, PanCytokeratin AE1\AE3. Others reactions were negative. 3 months after on CT scans: in the small pelvis neoplasm 59x44mm is determined, associated with loops of the ileum, expansion and thickening of the ileum wall. Recurrent tumour and 3 foci up to 4 cm on the peritoneum were resected. Macro: node 11x9x6cm, grey tan mass with fleshy cut surface, with necrosis.
Conclusion: Variable of histologic patterns in primary intraabdominal inflammatory myofibroblastic tumour was found (resembling nodular fasciitis , loose myxoid stroma and densely hyalinized stroma) and in recurrent tumour and peritoneum implants epithelioid myofibroblast-like cells types were prevailed highly atypical polygonal cells with oval nuclei, prominent nucleoli, Reed-Sternberg like cells, atypical mitotic figures up to 20 in 10 hpf, associated with aggressive clinical course.

E-PS-25-032
Unusual bone presentation of clear cell sarcoma with immunohistochemistry and molecular confirmation
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Background & objectives: Clear cell sarcoma occurs in the soft tissue in association with tendons and aponeuroses. The neoplastic cells express a variety of melanocytic markers. The differential diagnosis from a conventional cutaneous melanoma is made by molecular findings: EWSR1-ATF1 fusion transcript.
Methods: We report the case of an 11-year-old boy with a lytic bone lesion located in the distal femur epiphysis, simulating a chondroblastoma. The biopsy revealed a malignant tumour with sarcomatous features probably metastatic. The pathologic material was sent to us in consultation for ancillary studies.
Results: Immunohistochemistry was positive for all melanocytic markers: HMB45, S-100, Melan A, SOX10, Tyrosinase, MiTF. It was suspicious of malignant melanoma metastasized to bone, but no other primary tumour could be found by complex imagery. Molecular analysis was performed in another laboratory and it was positive for gene rearrangement: EWSR1-ATF1 t(12;22)(q13;q12). The revised diagnosis was primary clear cell sarcoma of bone.
Conclusion: Clear cell sarcoma of bone is rarely reported, almost never in this age group and in this location. The ancillary methods, immunohistochemistry and molecular findings were essential for the final diagnosis excluding metastatic melanoma.

E-PS-25-033
Intraosseous schwannoma of the mandible: a rare case report and review of the literature
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Background & objectives: Schwannomas are slow-growing nerve sheath tumours derived from Schwann cells. Intraosseous schwannoma is a rare entity. In the current medical literature, there are 44acceptable cases of intraosseous schwannoma of the jaws, 39 of the mandible and 5 in the maxilla.
Methods: In this case report we report a case of a schwannoma of the mandible in a 51-year-old female, who presented with swelling involving the mandible. Radiographs revealed a well-defined expansion. The lesion was treated by resection.
Results: Microscopic examination revealed compact hypercellular areas with spindle cells and nuclear palisading. The stroma showed myxoid features with thickened hyalinized vessels. There was no mitotic activity. Immunohistochemically schwannomas show positive diffuse staining for S100, SOX 10, SMA, and focal forCD 34 with Ki-67 proliferation index around 1% at the highest level. In the presence of these findings, histopathologic diagnosis of the patient was reported as intraosseous schwannoma.
Conclusion: The clinical and radiographic features of schwannomas mimic benign odontogenic tumours, which can be misleading. The optimal treatment is surgical resection with follow-up examinations. Recurrence was reported only in five cases in mandible, which was attributed mainly to malignant cases.

E-PS-25-034
Vaginal undifferentiated sarcoma giant cell rich with lung metastasis
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Background & objectives: We would like to present our case of rare neoplasm in unusual localisation.
In 07.10.2019 73-year old patient was administrated to Oncological Center due to vaginal bleeding and subabdominal pain since few weeks priory.
Methods: Gynaecological examination showed a tumour on anterior wall of vagina with 30 mm ulceration that narrows canal. Also, imaging techniques (CT and PET scan) showed a tumour in lung.

That part of the tumour from vagina and the tumour resected from lung were fixated in formalin and examined in hematoxylin & eosin sating and other diagnostic techniques were used.
Results: Samples from both tumours (vaginal and pulmonary) showed epithelioid neoplasm with necrosis and execs of multi nuclear osteoclast-like giant cells and over 50 mitotic figures per 10 high power fields.
Immunohistochemical stains showed: vimentin(+), CKAE1/AE3(-), Ck5/6(-), CD68(+) in multinuclear cells, p63(+) focaly, desmin (-), ER(-), Myogenin(-), SMA(+), EMA(-), s100(-), CD34 (-).
Sanger sequencing for H3F3A mutation was negative.
Diagnosis of undifferentiated sarcoma giant cell rich was made in both samples.
Conclusion: Sarcomas constitute less than 3% of all vaginal malignancies, rhabdomyosarcomas represent the most commonly reported sarcoma at this location. Undifferentiated pleomorphic sarcoma with giant cells is diagnosis from exclusion. Our case is rear entity situated in unusual localisation.

E-PS-25-035
Squamous cell carcinoma of the lung presenting as soft tissue mass: case report and literature review
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Background & objectives: Soft-tissue (ST)-metastases in patients who die from metastatic-carcinomas are rare (0.75-9%). Reported overall prevalence of ST and muscle metastases among lung-cancer-patients is 2.3% and 0-0.8% respectively. Lung, kidney and colon are the most common primary carcinoma sites leading to ST metastases.
Methods: 68-year-old-Caucasian-smoker-male with type-II-diabetes, with painful, gradually enlarging gluteal mass for 3-months. Otherwise asymptomatic.
Macroscopic evaluation: solid/poorly demarcated/nodular mass attached to adipose and skeletal muscle tissue, 8.7cm in maximum diameter.
Microscopic-examination: adipose tissue and striated muscle diffusely infiltrated by poorly-differentiated-neoplasm with areas of keratinization and necrosis.
Differential-diagnosis: metastatic poorly-differentiated squamous-cell-carcinoma-(SCC)-vs-ST sarcomas (e.g.synovial-sarcoma with squamous differentiation).
Immunohistochemistry: positive for CK5/6-p63-EMA-AE1/AE3-a1 antitrypsin. Negative for Vimentin-Desmin-CD99-TLE1-SMA-MDM2-CDK4-CD34-s100.
Results: Morphological and immunohistochemical findings were indicative of poorly differentiated SCC of unknown primary.
Following the histological diagnosis, the patient underwent brain, chest and abdomen CT scans, as well as bone scan, that revealed a lesion at the upper lobe of the left lung measuring 5.7cm in maximum diameter, ipsilateral lymphadenopathy, pericardial effusion and bone metastases.
Further immunohistochemical testing showed the tumour to be PD-L1 negative, while molecular analysis showed absence of EML4-ALK and NPM1-ALK inversions and of EGFR mutation.
The patient is currently being treated with Carboplatin/Paclitaxel and Pembrolizumab.
Conclusion: Most common symptoms of ST-metastases are pain and palpable mass.ST sarcomas are usually painless.ST metastases are associated to poor prognosis and advanced stage of disease. Any painful ST mass should raise suspicion for metastatic disease even in otherwise asymptomatic patients.

E-PS-25-036
Myxoid liposarcoma with cartilaginous heterologous component – a rare differentiation phenomenon
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Background & objectives: Myxoid liposarcoma (MLS) is the most frequent liposarcoma molecularly defined with DNA damage-inducible transcript 3 (DDIT3) gene rearrangement. MLS shows a typical mixture of lipoblasts, uniform round-cell mesenchymal cells and myxoid stroma with characteristic arborizing "chicken-wire" capillary vessels.
Methods: A 46-year-old male with a tumour localized in the posterior compartment of the right thigh, 16 cm in the largest dimension, without skin infiltration was admitted to Maria Sklodowska-Curie National Research Institute of Oncology for diagnostics and treatment.
Results: Initial biopsy revealed high-grade MLS with round cell component above 10% and DDIT3 rearranged in 87% of tumour cells. The patient received 3 cycles of chemotherapy [doxorubicin and ifosfamid] and preoperative radiotherapy. The surgically resected tumour presented response score C according to EORTC-STBSG protocol with abundant chondroid differentiation areas. The fluorescence in situ hybridization confirmed the *FUS-DDIT3*signature. The diagnosis of MLS with a cartilaginous component was established. After 6 months patient remains with no evidence of disease (NED).
Conclusion: Up-to-date only 8 cases with cartilaginous differentiation and 2 cases with rhabdoid features were described. Previously described MLSs were found among males, with median age 43 years, thigh involvement and median size 11cm. Moreover, the NED was from 6 to 45 months indicating that cartilaginous differentiation may be a good prognostic factor. Microscopically, in the differential diagnosis the chondroid lipoma, extraskeletal chondroma, and extraskeletal myxoid liposarcoma should be included.
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E-PS-25-038
A perivascular epithelioid cell tumour – rare and unique, posing a great diagnostic challenge: case report of male patient with pelvic mass
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Background & objectives: The aim of this work is to demonstrate the challenges in diagnosis of pelvic lesions in males. A wide range of tumours should be kept in mind to achieve correct preoperative diagnosis of PEComa (perivascular epithelioid cell tumour).
Methods: We present a case of 69 years old man admitted in the hospital with a tumour mass bulging into the rectal lumen, suspicious for GIST. MRI scan revealed tumour measuring 65/65/88 mm, located between prostate and front rectal wall.
A preoperative biopsy was performed, followed by surgical excision. The biopsies were routinely fixed, processed and stained with immunohistochemical /IHC/ analysis.

Results: The diagnosis of malignant PEComa was made on the preoperative tru cut biopsy - fragments from 3 to 9 mm. The routine histology revealed spindle cell with pale cytoplasm and nuclear polymorphism, foci of necrosis. IHC showed negative reaction for CD 34, CD 117, PSMA, CK AE1-AE3, S-100 protein, SOX 10 and DOG1 and positive reaction for SMA, HMB 45 and Melan A.
The surgical material was firm, fleshy appearance. Histology revealed perivascular arrangement with a lot of necrosis and high mitotic count (16/10 HPF).
6 months later the patient died of metastasis in the retroperitoneal and pelvic lymph nodes and peritoneal dissemination.
Conclusion: Prognosis of the PEComa depends on the size of the lesion and the risk category. Histopathology and immunohistochemistry are mandatory for proper diagnosis.

E-PS-26 Thymic and Mediastinal Pathology

E-PS-26-001
Large mediastinal teratoma, a differential for chronic chest pain
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Background & objectives: A case of a large mediastinal teratoma in an 18-year old girl who presented with an 8-month history of recurrent stabbing chest pain which radiated to the back and left upper limb.
Methods: The remarkable investigations that were carried out include chest x-ray, chest ultrasound scan, chest computed tomography scan. Other investigations were unremarkable. A thoracotomy was done and a 10cm circumscribed mass was excised and sent to the histopathology laboratory for examination and diagnosis.
Results: Chest computed tomography scan revealed an oval, heterogeneously enhancing mass extending from the anterior mediastinum to the left middle zone of the lung field.
Gross histopathologic examination revealed a multicystic mass containing greasy, pale material. Microscopic examination revealed mature structures derived from the three germ layers.
Conclusion: The clinical presentation of mediastinal tumours varies from asymptomatic to life threatening symptoms. A high index of suspicion for mediastinal tumours in patients presenting with cardiothoracic symptoms is needed in early diagnosis and treatment.

E-PS-27 Uropathology

E-PS-27-001
A rare case of renal carcinosarcoma associated with nephrolithiasis
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Background & objectives: Introduction – Carcinosarcomas are biphasic tumours comprising of epithelial and mesenchymal components. Primary carcinosarcoma of the kidney/upper urinary tract is extremely uncommon.
Case presentation – An 50 year old female patient presented to urology clinic with a chief complaint of right upper quadrant pain. CT scan reported right renal severe hydronephrosis secondary to proximal ureteric stone. On U/S right kidney has multicystic mass seen. During surgical exploration, hard mass was found attached to the liver and upper pole of kidney
Methods: On pathology gross examination, Nephrectomy specimen received measuring 15x8.5x6.5cm overall and there is a multinodular mass on the upper pole of the kidney parenchyma with grossly breached capsule. On cut section, the mass is 8.5x6x5.5cm grey white solid with central focus of haemorrhage and necrosis. Three dark coloured stones were identified in the dilated pelvicalyceal system largest measuring 3.5x2.8x2.6cm. cont..
Results: There was a small papillary excrescence on the mucosa of the dilated calyx measuring 1x1cm. On histopathology, infiltrative nests and tongues of malignant squamoid cells with well-formed keratin pearls admixed with sarcomatoid stroma of intersecting fascicular and undifferentiated pleomorphic cells with heterologous chondroid differentiation was seen along with areas of necrosis. Histologic sections from papillary excrescences showed papillary projections of metaplastic and dysplastic squamous epithelium.
Conclusion: Conclusion - Carcinosarcoma of the kidney is a rare tumour of which little is known about. Current literature is almost exclusively a case report.

E-PS-27-002
Facial skin lesion as first manifestation of renal carcinoma
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Background & objectives: In rare cases, skin metastatic lesions may be the first manifestation of a visceral neoplasm. Renal carcinoma is one of these neoplasms, although renal carcinoma metastasis on the skin is not usual.
Methods: We present the case of a patient with renal carcinoma, diagnosed, after the investigation of a frontal skin lesion. The patient, a 63 years old female, presented with a skin nodule on the face.
Results: She underwent surgical excision of the lesion, followed by histopathological examination that, established the diagnosis of a clear cell renal cell carcinoma metastasis. The imaging investigation revealed the presence of a tumour in the right kidney and the patient underwent a nephrectomy. Histopathological examination confirmed the presence of a clear cell renal cell carcinoma of the right kidney. Although skin metastases from renal carcinoma are considered to be advanced manifestation of the disease, it is possible that the skin metastatic lesions occur before renal neoplasm is diagnosed.
Conclusion: Even in these cases however, the involvement of the skin is an indication that the disease has spread and the prognosis of such patients is poor. We present this case because of its rarity and we review the relevant literature.

E-PS-27-003
Another brick in the wall: one case of renal anastomosing haemangioma with immunohistochemical and clinical correlation
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Background & objectives: Anastomosing haemangioma (AH) of the kidney is a rare benign vascular tumour with histological features mimicking angiosarcoma.
A 64-year-old woman with type 2 diabetes mellitus and no history of kidney disease or renal malignancy presented for routine examination.
Methods: Physical examination and blood tests showed no abnormalities. Ultrasonography and CT scan revealed a 4x4 cm, well-defined, hypoechoic mass occupying the upper pole of right kidney, which enhances in arterial phase and has fast wash-out in the delayed phase.
Patient underwent surgical resection of the renal mass. Shortly after, she had a haemorrhagic episode corrected with resuspended red cell concentrate.
Results: Grossly, the partial nephrectomy showed a round mass, well-circumscribed, encapsulated, measuring 3.5 cm in diameter, with a red-brown cut surface.

At low magnification, the tumour is well-defined, partially encapsulated, with lobular architecture, invading the tumour capsule, but without infiltration of the adjacent renal parenchyma. At higher magnification, tumour consisted of anastomosing capillary-sized vascular spaces, lined by endothelial cells with mild focal atypia and uniform nuclei, without mitoses, resembling splenic parenchyma.
Immunohistochemistry was negative for PanCK, HMB45, D2-40 and PAX8. Endothelial cells were positive for CD31 and CD34.
Conclusion: Becoming aware of the existence of renal AH and recognizing its histological characteristics is essential for the accurate diagnosis in order to avoid overtreatment. Renal AH has a favourable prognosis and the preferred treatment option is tumorectomy with long-term follow-up.

E-PS-27-004
Inhabitual presentation of retroperitoneal angiomyolipoma simulating ovarian tumour
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Background & objectives: Extrarenal retroperitoneal angiomyolipoma (AMLs) are rare lesions which may mimic other retroperitoneal tumours and thus pose a diagnostic problem to the clinician. The aim is to describe a case of retroperitoneal angiomyolipoma misdiagnosed as ovarian tumour.
Methods: A 50 year old woman presented with a right, pelvic and painless mass. There was no familiar or personal history. The physical examination was clean. An abdominal ultrasonography was revealed an ovarian mass with large haemorrhagic and necrotic areas. Torsion of fibrothecoma was clinically suspected.
Results: Macroscopically, it was an 18 cm, encapsulated and dark brownish mass with large foci of necrosis and haemorrhage. The microscopic examination concluded to retroperitoneal angiomyolipoma, as tumour was composed of variable proportions of adipose tissue, spindle cells, epithelioid smooth muscle cells and abnormal thick-walled blood vessels. Large foci of haemorrhagic necrosis were seeing and a foreign body type inflammatory reaction was noticed too.
Conclusion: The retroperitoneal angiomyolipoma is a rare disease that belongs to family perivascular epithelioid cell tumours (PEComas). This tumour occurs sporadically or in patients with tuberous sclerosis. It is reported more in women aged between 22 and 80 year-old. The incidence of haemorrhagic shock and necrotic feature is higher than renal angiomyolipomas. For that reason, they may be sometimes misdiagnosed as ovarian disease. Only histology examination can lead to the diagnostic.

E-PS-27-005
Xp11;2 translocation renal cell carcinoma: pathological study of 6 cases
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Background & objectives: Xp11;2 translocation renal cell carcinoma (TRCC) is a recent and rare entity. It belongs to the groups of Mit (Microphthalmia Transcription factor) family (TRCC). The aim of our work is to recall its anatomo-clinical features and to discuss the differential diagnoses.
Methods: A total of six cases of Xp11.2 (TRCC), diagnosed over a period of 12 years, were evaluated. A review
of clinical records and histopathological reports as well as additional immunohistochemical study were performed in all cases.
Results: These were six female patients, with an average age of 18 years. The average diagnosis time was 11.2 months. The main symptomatology was low back pain. The physical examination found a palpable mass in one patient. The average size of the tumour was 4.6 cm. Surgical treatment was performed in 5 cases. In one case, the tumour was locally advanced and inoperable. No adjuvant treatment was indicated. The macroscopic appearance was variable. Histologically, tumours had a mixed architecture. The tumour cells had a clear and eosinophilic cytoplasm. Psammomas were found in three cases. Immunohistochemically tumour expressed TFE3, CD10 and PAX8 in all cases and P504S in 5 cases.
Conclusion: Papillary architecture with clear or eosinophilic cells and psammoma is evocative of Xp11.2(TRCC). The nuclear staining of the tumour cells with (anti-TFE3) confirms the diagnostic. Ideally, we complete by a molecular study which highlights the presence of the TFE3 rearrangement.

E-PS-27-006
TFE3 expression in papillary renal cell carcinomas and renal cell carcinomas with papillary component, in patients under 45 years-old
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Background & objectives: Xp11 translocation renal cell carcinoma(RCC) is a tumour defined by translocations involving the X chromosome(Xp11), which produces fusion genes that involve transcription factor E3(TFE3). We reviewed papillary RCC(PRCC) and RCC with papillary component cases, using TFE3 immunomarker and reclassifying them.
Methods: Out of 76 cases with a previous diagnosis of RCC made between 2000-2019 in a tertiary healthcare institution, in patients under 45 years-old, 10 were selected based on its classification as either PRCC or RCC with papillary component. All cases were submitted to an immunohistochemistry panel to confirm the tumours' primary renal origin and also TFE3 immunomarker.
Results: Immunohistochemistry studies showed positivity for TFE3 in 4 cases out of the 10 previously selected. There was a male predominance (3:1) and the mean age at diagnosis was 28 years old, with a mean tumour size of 9 cm.
Conclusion: Immunostaining for fusion products detectable in Xp11 translocation RCC only became available recently, demanding a high index of suspicion and awareness for this diagnosis. Increased availability of novel TFE3 immunomarkers are expected to improve diagnostic accuracy in the future.

E-PS-27-007
An unusual site for a prostatic adenocarcinoma metastasis
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Background & objectives: Calvarium metastases of prostatic adenocarcinoma are an uncommon finding. This study presents the case of a 69YO male who was admitted to the neurosurgery clinic 2 weeks after the onset of a left hemiparesis, mimicking the symptoms of a stroke.
Methods: Physical examination revealed a parieto-temporal, subcutaneous, immobile, mass. Cranial CT examination has revealed a iodine absorbing mass in the right cerebral hemisphere that dislodged the brain and invaded the superjacent bones. Further CT examination of the full body revealed a prostatic mass and multiple destructive lytic lesions in the axial skeleton and ribs. Bloodwork did not reveal anything unusual.
Results: The tumour was surgically removed and sent to Pathology. Based on the histopathological features in concordance with IHC reactions (positive for CKAE1/AE3, NKX3.1, EMA and negative for CK7, Synaptophysin, GATA3, CDX2, TTF-1, HER2neu and CK HMW), the diagnosis of prostatic adenocarcinoma metastasis was established. A mention must be made that there were no urological symptoms present prior to the examination.

Conclusion: After the removal of the tumour, the patient's health status improved and he was sent to a hospice with no follow-up available. Axial skeleton metastases from a prostatic adenocarcinoma are somewhat a common finding, whereas the calvarium is an unusual location for such entities. Calvarium metastasis that precede the primary tumour diagnosis of prostate cancer are rare, and unfortunately, a sign of an end stage disease.

E-PS-27-008

Molecular and immunohistochemical evaluation of BAP-1 in bladder and comparison with luminal-basal subtyping

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Background & objectives: Molecular subtyping has become increasingly important in bladder tumours. There are very few molecular and immunohistochemical studies about BRCA1-associated protein-1(BAP-1) in bladder. We aimed to evaluate BAP-1 expression molecularly and immunohistochemically and determine subtypes with GATA-3 and Cytokeratin5/6 immunohistochemical stains.
Methods: Tumour and normal tissues of 11 patients with known primary bladder tumours were taken freshly during the operation. We applied BAP-1 antibody with reverse transcription-PCR and Western Blot method. In addition,150 non-invasive and 150 invasive tumour paraffin blocks were selected from transurethral resection materials. GATA-3, Cytokeratin5/6 and BAP-1 immunohistochemical stains were applied and evaluated in total 300 cases.
Results: BAP-1 protein expression levels were increased in tumour tissues compared to normal tissues in Western Blot (9 of 11). In the immunohistochemical evaluation of BAP-1, the muscle invasive group (solid morphology) showed statistically significant severe expression. GATA-3 expression severity and percentage, showing luminal subtype, was statistically significantly higher in the non-invasive group. The expression severity of Cytokeratin5/6, showing basal subtype, was statistically significantly higher in the muscle invasive group.
Conclusion: In this study, molecular BAP-1 protein expression levels, which have not been studied in bladder before, were found to be higher in the tumour tissues than the normal tissues. It was concluded that immunohistochemical BAP-1 evaluation may also vary according to tumour grade and papillary morphology. Also, it was determined that GATA-3 and Cytokeratin5/6 immunohistochemical stains can be used for basal and luminal subtyping of bladder tumours and especially the degree of invasion is compatible with this subtyping.

E-PS-27-009

Tubulo-villous adenoma with invasive adenocarcinoma component of the female urinary meatus

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Background & objectives: Villous adenoma of the urinary tract is a very rare tumour; sometimes, may present a malignant component, either adenocarcinoma or urothelial carcinoma. We describe a case of villous adenoma associated with invasive adenocarcinoma developed in female external urethral orifice.
Methods: A 69-year-old woman was admitted at the Urology Department. Physical examination showed an exophytic lesion circumferentially anchored at the upper part of the urinary meatus. The patient had no significant past medical history. Gynaecological and gastroenterological exams were normal. Tumour resection was performed. The excised specimen was specifically processed through paraffin embedding technique for standard histological and immunohistochemical exams.
Results: Gross examination showed a polypoid, fleshy mass, of 1.2 cm diameter. Histopathology revealed an epithelial tubulo-papillary proliferation lined by normal and pseudostratified columnar epithelium showing nuclear crowding, hyperchromasia, and goblet cells, with focal areas of low- and high-grade dysplasia. Several zones of invasive adenocarcinoma were identified in lamina propria. The epithelial proliferation was CK 20 and CDX2 positive, CK7 negative; Ki67 varied from 30% (adenoma) to 90% (malignant component).
Conclusion: The final diagnosis was tubulo-villous adenoma associated with invasive adenocarcinoma, originating in the urinary meatus. The main differential diagnosis of villous adenoma of the urinary tract is a possible metastatic adenocarcinoma from adjacent anatomical sites (particularly from colon). The key elements of this case consist in the very rare location - the external urethral orifice, and the evidences for the malignant transformation.

E-PS-27-010

Immunohistochemical findings in vasitis nodosa - case report

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Background & objectives: Vasitis nodosa is a benign condition characterized by proliferation of ductules in the vas deferens' wall, most often after injury. Since these ductules occasionally show features resembling malignancy, they may be confused with an adenocarcinoma originating from the adjacent organs.
Methods: We report the case of a 50 year old male with post-vasectomy recanalization that was reintervened. The resected fragments of both vas deferens were submitted for examination.
Results: Small-sized ducts proliferated within the vas deferens' muscular wall around nerves and blood vessels. These ducts were lined by a single layer of cuboidal to columnar epithelium with clear to eosinophilic cytoplasm and round to spindle shaped nuclei with hyperchromasia and coarse granular chromatin. Glandular cells showed positivity for cytokeratins 7 and AE1/AE3, and PAX8. CD10 and AMACR reacted against the luminal surface. PSA, GATA3 and p63 were negative.
Conclusion: Although diagnosis of vasitis nodosa is straightforward with hematoxylin and eosin examination, immunohistochemistry may be useful in differentiating vasitis nodosa from adenocarcinoma from adjacent organs. Proliferating glands show a prostate cancer-like AMACR and p63 staining pattern, but PAX8 positivity and PSA negativity aid in distinguishing this entity from prostate cancer.

E-PS-27-011

Vasitis nodosa: a report of 5 cases

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Background & objectives: Vasitis nodosa is a benign proliferation of the vas deferens' ductular epithelium within the muscle coat and adventitia as a reaction to injury. Many pathologists are not familiar with this condition, confusing it with an adenocarcinoma from nearby organs.
Methods: We reviewed our institution's archives and found 5 cases of vasitis nodosa diagnosed between 2003 and 2020. Ages ranged from 41 to 52 years and had undergone vasectomy 9 months to 23 years before present surgery. Serial sections were stained routinely with haematoxylin and eosin.
Results: Two cases had vas deferens' segments removed for post-vasectomy recanalization and three cases had painful testes. At microscopic examination, all cases showed varying degree of ductular proliferation lined by cubic epithelium with focal and mild atypia in one of them. One case showed luminal spermatozoa. In all cases this ductular

proliferation spread around nerves and blood vessels and showed sperm extravasation.
Conclusion: Although vasitis nodosa is a benign condition, its morphology may be confused with malignant neoplasms. Nevertheless, a closer look to its features in patients with history of previous vasectomy may help to recognize this entity with routine haematoxylin and eosin stains.

E-PS-27-012
Urachal adenocarcinoma: about two cases
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Background & objectives: Urachal carcinomas are rare, representing only 0.01%of adult cancers and 0.17-0.34% of bladder cancers. These are very aggressive tumours with poor prognosis. These tumours are usually adenocarcinomas and occur at the dome or anterior wall of the bladder.
Methods: Our purpose is to analyse clinical, radiological and pathological characteristics of these tumours in two patients.
We reviewed the data of Urachal carcinomas diagnosed in the Urology Department of Sahloul University Hospital of Sousse (Tunisia) during 2015-2020.
There were two patients, a49YO man and a57YO woman. Both of them presented haematuria; isolated for him, associated with hypogastral pain for her.
Results: Uroscan showed a median tumour process of the bladder dome limited to the bladder wall for him, associated with lymphadenopathy for her. The extension assessment objectified a pulmonary metastasis for her. He underwent a partial cystectomy and the specimen showed histologically an urachal adenocarcinoma infiltrating all the parietal layers with tumour-free boundaries. Adjuvant Chemotherapy (CT) wasn't recommended behind the lack of standardized guides. Unfortunately, he recurred two years later and developed pulmonary metastasis for what he took CT but without response. The lady had an endoscopy-guided-biopsy which confronted to clinical and radiological data, the histological conclusion was in favour of urachal adenocarcinoma and palliative treatment was proposed for her.
Conclusion: Although it is effortless to distinguish urachal from non-urachal adenocarcinoma in cystectomy specimens, it is challenging to differentiate them on small biopsy specimens which requires a comparison with clinical, cystoscopic and CT data. Until now, surgery is the only effective treatment, and its results depend essentially on the stage of the tumour.

E-PS-27-013
Primary kidney angiosarcoma – a rare case report and review of literature
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Background & objectives: Primary angiosarcoma of the kidney is extremely rare, with less than 40 cases reported in the literature up to date. Most reports described the origin of angiosarcoma in a normal kidney, but it has been reported also in multicystic kidney.
Methods: We present the case of a 51-year-old male with right lumbar pain and macroscopic haematuria. CT examination revealed a poorly circumscribed, hypodense mass (5,8/3,6 cm) in the right renal pelvis, with invasion of the parenchyma, without disruption of the renal capsule, with hydronephrosis and a mass of 4,2/4,3 cm in the left adrenal gland (possible metastatic). Radical nephrectomy was performed.
Results: At grossing, we found a flashy, soft, red tumour, with an extensive area of central necrosis and haemorrhage. Microscopically the renal parenchyma was replaced by a malignant vascular proliferation with mitotically active (>10 and <19 mitoses/10HPF) pleomorphic endothelial cells, with spindled and epithelioid morphology and large hyperchromatic nuclei, prominent nucleoli, with extensive areas of necrosis (over 50% of the tumour). Immunohistochemical stains showed strong and diffuse positivity for vimentin, CD31, CD34, ERG, FLI1, actin, with a Ki67 index of 35% and negative for CK7, HMB45, S100, indicating that the tumour was angiosarcoma of the kidney.
Conclusion: Primary angiosarcoma of the kidney is a rare and aggressive neoplasm with poor patient outcome. Little is known about its prognostic features or response to treatment. Tumours under 5 cm in size appear to be associated with an improved outcome.

E-PS-27-014
A rare and interesting case of sarcomatoid urothelial carcinoma with heterologous elements of osteosarcoma
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Background & objectives: Urothelial carcinoma is the most common type of urinary cancer. However, sarcomatoid urothelial carcinoma is highly malignant and rare. In the urinary bladder, it only accounts for 0.1 to 0.3% of carcinomas
Methods: We present the case of a 68-year-old male with a history of prostatic transurethral resection for benign prostatic hyperplasia, who presented with macroscopic haematuria. Cystoscopy revealed blood cloths in the bladder and a tumour on la left-lateral wall of the urinary bladder, which was resected transurethral. The resected tissue was embedded in paraffin and examined on H&E.
Results: Microscopically the urothelial architecture was replaced by a malignant biphasic proliferation of high-grade urothelial carcinoma with papillary or nonpapillary pattern and spindle cell sarcoma with areas of heterologous differentiation of osteosarcoma, with filigree/lace-like disorganized woven bone (intimately associated with neoplastic cells) and many multinucleated osteoclast-like giant cells, with invasion in the muscularis propria and areas of necrosis. Immunohistochemical stains showed strong and diffuse positivity for GATA3 and CK7 in the urothelial carcinoma component; vimentin and SATB2 in the areas with heterologous differentiation of osteosarcoma; Ki67 index was positive in 90% of the tumoral cells.
Conclusion: Sarcomatoid urothelial carcinomas are biphasic malignant neoplasms exhibiting morphological/immunohistochemical evidence of epithelial and mesenchymal differentiation with the presence or absence of heterologous elements (osteosarcoma, chondrosarcoma and spindle cell sarcoma).

E-PS-27-015
Adult cystic nephroma – a rare member of the MEST family
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Background & objectives: Adult cystic nephroma is a rare tumour with a prevalence of <1%, included in the mixed epithelial and stromal tumours (MEST) family, predominantly cystic to variably solid, usually benign. Herein, we present a renal cystic tumour from our routine practice.

Methods: A 41-year old woman, without relevant clinical history, started with intermittent low back pain with three weeks of duration. Abdominal-pelvic computed tomography revealed the existence of a renal multilocular cystic lesion, with thick septations, and consequently was submitted to radical nephroureterectomy.
Results: Macroscopically, there was a well-circumscribed capsulated cystic multiloculated tumour with 8 cm, with non-communicating cysts with variable sizes and thick septa with translucent content, and focal spongy microcystic areas. Histologically, the cysts were lined by flat to columnar epithelium sometimes with hobnail features and eosinophilic to amphophilic cytoplasm, without atypia; the stromal component ranges from hypocellular and collagenous to hypercellular spindled areas, often with an ovarian stroma-like appearance, without atypia and mitoses; the stromal cells were immunoreactive for smooth muscle actin, desmin, CD10, oestrogen and progesterone receptors. These features were consistent with the diagnosis of adult cystic nephroma.
Conclusion: Adult cystic nephroma is a rare renal biphasic tumour with epithelial and stromal components, mainly benign. Rarely, it can have an aggressive behaviour, especially in malignant transformation cases. This tumour typically occurs in perimenopausal women with a mean age of 52 years, in contrast to our younger patient. The hormonal imbalance is an important etiological factor in the histopathogenesis of this tumour.

E-PS-27-017
Papillary prostate ductal adenocarcinoma mimicking papillary urothelial carcinoma in bladder transurethral resection
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Background & objectives: Prostatic ductal adenocarcinoma (PDA) is uncommon form of prostatic carcinoma histologically characterized predominantly by papillary and cribriform architecture. It can be diagnostically challenging when encountered in organs other than prostate. Here we present a papillary PDA mimicking papillary bladder neoplasm.
Methods: This case is about an 80-year old man who presented with nocturia and urgency. Computer tomography showed diffuse thickening of the bladder wall and polypoid structures projecting to luminal space. Therefore, he underwent transurethral resection (TUR) of the urinary bladder.
Results: Microscopic examination showed a tumour composed of focal cribriform and mostly of papillary structures with fibrovascular cores lined by tall, pseudostratified columnar epithelium with high-grade nuclei in keeping with the initial clinical diagnosis of papillary urothelial carcinoma. There was extensive crush artefact. In some areas papillary fronds were lined by single layer of cuboidal or hobnail cells with crowded, round-to-ovoid hyperchromatic nuclei reminiscent of a nephrogenic adenoma with papillary architecture. The tumour was negative for cytokeratin-7, GATA3, p63 and PAX8. Past disease history revealed high grade prostate acinar adenocarcinoma with ductal component. The additional immunostains showed tumour to be positive with NKX3.1, PSAP and PSA.
Conclusion: PDA should be always kept in mind when evaluating metastatic carcinomas showing papillary or cribriform architecture in elderly male patients. Unusual histological findings such as hobnail cells or tall columnar cells with high grade nuclei should raise the possibility of PDA when encountered in urinary bladder papillary neoplasms.

E-PS-27-018
Low-grade oncocytic tumour of the kidney, an emerging entity: a report of two cases and review of the literature
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Background & objectives: Low-grade oncocytic tumour (LOT) of the kidney is a recently described entity, which has well-defined histomorphological and immunohistochemical features. With established classifications, it does not neatly match definitions for either oncocytoma or eosinophilic chromophobe renal cell carcinoma.
Methods: We report two such cases which arrived at our institution in short succession; our objective is to increase awareness of this evolving lesion, and to summarise the recent literature. We describe the characteristic features of these oncocytic tumours and their immunohistochemical profile. A search of the literature using PubMed including the terms 'LOT', 'oncocytic tumour', 'hybrid tumour' is performed.
Results: Our first case is from a 50 year old male who had nephrectomy for an 18 cm unilocular cystic mass. The second case is from a 76 year old male, who underwent a partial nephrectomy. Microscopically, both tumours included clearly demarcated loose oedematous areas with microcystic spaces, as well as nests of oncocytic cells which lacked raisinoid nuclei. Immunohistochemistry showed both cases were strongly positive for cytokeratin 7 (CK7), and negative for cluster of differentiation 117 (CD117), consistent with previous published findings. In the literature, the tumours have been shown to have an indolent behaviour.
Conclusion: We have demonstrated the typical histological and immunohistochemical features of LOT. We hope through presenting these two cases, we will raise awareness of this entity and provide an aid in assessment of the 'unusual' oncocytic tumour.

E-PS-27-019
Systemic metastasis of signet ring cell carcinoma of the prostate - an autopsy outcome
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Background & objectives: Signet ring cell carcinoma (SRCC) of the prostate is a rare histological variant (2.5% of cases), firstly reported in 1979. We present an aggressive case of SRCC, with systemic metastasis and rapid fatal outcome.
Methods: A 60-year-old man diagnosed in 2018 with congenital hydronephrosis and prostatic adenoma associated with chronic urinary retention was admitted at the Urology Department for bilateral ureterohydronephrosis, staghorn calculi, acute urinary infection and PSA<0.1 ng/ml. Prostatic fine needle biopsy revealed benign prostatic hyperplasia with rich polymorphous inflammatory infiltrate in the glandular component. He died 27 days later; the autopsy was performed.
Results: The autopsy revealed multiple nodules in lungs, pericardium, liver, pancreas, small gastric curvature, peritoneum, bladder and prostate. The prostate and the involved organs contained typical signet-ring cells (SRC) characterized by abundant clear cytoplasmic vacuoles displacing and compressing the nuclei, that infiltrate as single cells or small clusters. SRC were diffuse and intense/moderately positive for PSA and negative for CK7 and CK20. p63 was negative in the tumour (internal control present).
Conclusion: The case particularity consists in the discrepancies between the morphological findings in biopsy specimen, the PSA low level and final histopathological diagnosis, the rarity of SRCC variant, the presence of systemic metastases, and the silent course of disease with rapid, fatal outcome.

E-PS-27-020
Renal leiomyoma
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Background & objectives: Renal leiomyoma is a rare benign tumour, (0, 3% of all primary renal cell neoplasms) with smooth muscle cell differentiation. It represents in most instances as an incidental finding.
Methods: A 56 year old female patient, was admitted to the hospital due to prolapse of the uterus. MRI revealed a compact exophytic lesion measuring 2,6x 2,5x 2 on the left kidney. On cut sections the later lesion was white, elastic, firm and well circumscribed with an oedematous central area of 1cm.
Results: On microscopic examination, the tumour was consisted of medium sized cells with mild nuclear atypia with no necrosis, arranged in a fascicular pattern. Mitoses were rare, <1/10 HPF. Perivascular hyalinization of the stroma and cystic degeneration were also observed. The immunohistochemical results showed positivity for smooth muscle markers (SMA, Vimentin, Desmin, H-Caldesmon, HHF-35) and negativity for the following: HMB-45, Mart-1, Synaptophysin, AE1/AE3 and Congo Red. The mitotic index Ki67 (Mib 1) was 1%. Surgical excision was the therapeutical approach.
Conclusion: Renal leiomyoma is a rare entity with indolent clinical behaviour. It should not be confused with angiomyolipoma (predominantly leiomyomatous type) which is positive for melanocytic markers, although capsular leiomyoma frequently contains a population of cells, strongly positive for melanocytic markers.

E-PS-27-021
The importance of the evaluation of non-neoplastic kidney in tumour nephrectomy specimens: a case report

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Background & objectives: Non-neoplastic changes are often identified in renal parenchyma of the nephrectomy specimens for renal neoplasms. They are often overlooked. However, they may be prognostic or therapeutic importance. The accurate pathologic evaluation of the non-neoplastic renal parenchymais important for subsequent patient management.
Methods: A 62-year-old male patient presented with right flank pain with a history of hypertension and chronic obstructive pulmonary disease. Computerized tomography revealed a 6cm mass in the right kidney
Results: After evaluation of the nephrectomy specimen the tumour was diagnosed as clear cell renal cell carcinoma. Diffuse and nodular mesangial glomerulosclerosis and arteriolar hyalinosis in the afferent and efferent hilar arterioles were seen in the non-neoplastic renal parenchyma. After the comment about the possibility of diabetic glomerulopathy in the pathology report the patient's diabetes mellitus was diagnosed.
Conclusion: Considering that the evaluation of nephrectomy specimens primarily focuses on the diagnosis, grading, staging etc. of the tumour in question, non-neoplastic lesions might be overlooked during the routine pathologic evaluation. Non-neoplastic lesions is an important tool in recognizing patients at risk for progressive renal disease after nephrectomy and could be an important step in providing early preventive and treatment measures, better medical care of patients undergoing nephrectomy for neoplastic processes.

E-PS-27-022
A case report of urinary bladder IMT as late complication of bone marrow alotransplantation

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Background & objectives: An inflammatory myofibroblastic tumour (IMT) is composed of myofibroblastic spindle cells and inflammatory cells that infiltrate stroma. IMT is rare tumour being important because of dd of malignant spindle cell tumours and as a late complication of bone marrow transplantation.
Methods: Here we report a case of a young patient (born 2000) after bone marrow alotransplantation (2006). due to lymphatic leukaemia (2002.) and with radiologic endovesical polypoid lesion (2014).
Results: Patient underwent twice to the transurethral resection of the livid fleshy bladder tumour and, at a later date, partial cystectomy because of relapse. Histology revealed highly vascularized, mesenchymal tumour with pronounced myxoid stroma and spindle cell proliferation with slightly enlarged and sparsely hyperchromatic cell nuclei without mitotic activity, scarce lymphoplasmacytic infiltration and expansive growth toward the muscle wall. Tumour cells show a diffusely positive immunoreaction reaction for vimentin and SM-actin, focally for pancytokeratin and CAM 5.2, but negative for ALK. Differentially diagnostic IMT, polypoid cystitis, myxoid and spindle cell neoplasms of the bladder were considered, without criteria for malignancy.
Conclusion: IMT should be considered in differential diagnosis for young patients presenting with bleeding bladder tumours and significant anaemia, especially after bone marrow alotransplantation as a late complication. IMTs of the urinary bladder mostly has benign disease course, and good prognosis can be achieved after surgical resection as in our patient.

E-PS-27-023
A case of mixed and unclassified sex-cord-stromal tumour with annular tubules

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Background & objectives: Sex cord-stromal tumours of the testis are rare and more commonly seen in the paediatric age group. Mixed and unclassified testicular stromal tumours are neoplasms of undetermined differentiation and contain mixed Leydig, Sertoli, and granulosa cells or merely entrapped germ cells.
Methods: We present a testicular tumour of a ten-month-old infant. At 3 months of age, the mother noticed swelling and enlargement of the right testis. Ultrasound examinations discovered a cystic and solid appearing mass. First, we received an intraoperative biopsy and after our diagnosis of a tumour, the orchidectomy was performed.
Results: Histology revealed lobular structures with cystic formations coated with proliferating Sertoli-like cells. Clusters of these immature cells were mostly surrounded by the basement membrane and the cells within the formation surround the hyaline, PAS-positive material forming annular tubules. The stroma was oedematous, immature, cells were fusiform and mostly PAS-positive. In cystic spaces, there was sparse mucin. Immunohistochemistry showed diffuse positivity for inhibin, vimentin, WT1, focally for CD99 and nuclear reaction for S100. Stroma was diffusely, strongly positive for SMA.
Conclusion: The final* diagnosis was a mixed and unclassified sex-cord-stromal tumour. However, this tumour also had some features of an ovarian sex-cord tumour with annular tubules which made it special and more interesting.

E-PS-27-025
Primitive neuroectodermal tumour: a case report of malignant transformation of teratoma of the testis

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Background & objectives: Teratomas can be differentiated into somatic elements and malignant transformation. Primitive neuroectodermal tumour is a rare entity that results from the malignant transformation along the ectodermal lines; its prognosis is extremely poor with highly aggressive clinical course.

Methods: We report the case of a 65 year old man with multiple bone lytic lesions and a 9cm mass in the left testis. The patient was submitted to orchidectomy.
Results: Gross examination showed a testis with a solid nodule constituted by a firm and white tissue with various cystic spaces, with 9x8x7cm. Histopathological examination revealed a well delimited neoplasia composed of mature teratoma predominantly with cartilaginous differentiation but also of immature teratoma with blastema-like areas and glandular structures without atypia. Glial differentiation was present. In the centre of this neoplasm, there was an irregular nodule constituted by cells with scant cytoplasm and hyperchromatic to granular nuclei.
Immunohistochemistry study showed positivity for synaptophysin, chromogranin A, NSE, CD56, vimentin, MAP 2 and focally for desmin, S100 protein, GFAP and CD99.
EMA, CK, SALL4, OCT4, GLypican-3, WT1, CD30, CD34, Fli-1, ERG were negative.
Conclusion: The diagnosis was testicular teratoma with malignant transformation into primitive neuroectodermal tumour with glial differentiation. Surgical resection is the recommended therapy for localized disease, because this neoplasia is resistant to radiation and chemotherapy. However, our patient died due to advanced disease at the time of the diagnosis with bone involvement leading to an unfavourable clinical outcome.

E-PS-27-026
Alpha-d-galactose-binding lectin (native frutalin) as diagnostic marker of prostate cancer in humans

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Background & objectives: Plant lectins are often used in structural and functional investigations of complex carbohydrates due to their ability to detect cellular changes in glycosylation patterns induced by pathological processes. Biological markers have a promising potential as diagnostic tools in cancer.
Methods: Biotinylated frutalin was tested as a histochemical probe and protein marker for the detection of human prostate cancer. The semi-quantitative determination of positivity was based on the following criteria: Weak (+, <10% positive cells), Moderate (++, 10-50% moderately or strongly positive cells), and Strong (+++, >50% moderately or strongly positive cells).
Results: To assess the ability of frutalin to recognize tissue prostate cancer cells and hyperplasia, twenty cases were selected by the histopathological findings. The 100% positivity in cases of Pca the negativity in cases of BPH. The images captured by professional use Axion Vision 4.5 software were analysed and the data on the optical density of marking, were treated statistically by the non-parametric Mann-Whitney test and showed statistically significant ($p < 0.0001$) in differentiating between cancer and benign prostatic hyperplasia. This use of biotinylated frutalin, as probes in histochemistry provides a specific recognition of cells in the tumour tissue. This fact differentiates the lectin staining technique using frutalin, the measurement of PSA-st.
Conclusion: In this study, biotinylated native frutalin proved to be an attractive alternative diagnostic tool for research on human prostate cancer, capable of differentiating benign prostatic hyperplasia from prostate cancer. The marker has potential for use in the diagnosis of prostate cancer in humans.

E-PS-27-027
A primary extrarenal renal cell carcinoma

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Background & objectives: We present a rare case of a renal cell carcinoma in the retroperitoneum in the vicinity of the left kidney, where both morphology and origin of the tumour were challenging to define.
Methods: The patient was a middle-aged man. Gross examination showed that the tumour measuring 10 cm in diameter, was connected to the left kidney through a branch of the renal vein. No connection to ureter was identified. The tumour was without any normal kidney tissue. No tumour was detected either in the left kidney, adrenal gland or in the right kidney.
Results: Histologically, tumour was heterogeneous both with tubular and papillary areas with clear and eosinophilic cells with some atypical cells with nucleolar ISUP grade 3/4. More solid parts with eosinophilic and oncocytic-like cells were seen. Tumour was positive for Pax-8 and showed heterogeneous staining for CK7, AMACR, CD10 and vimentin by immunohistochemistry. FH was retained. CK20, CD117 and cathepsin K were negative.
Based on these features tumour was diagnosed as an extrarenal renal cell carcinoma (RCC), unclassified. We consider this tumour to be an example of a primary extrarenal renal cell carcinoma, likely arising from mesonephric remnants.
Conclusion: This is to the best of our knowledge, the first case of an unclassified extrarenal RCC.
We would like to thank Dr. Argani at Johns Hopkins Hospital USA, for his support with this case.

E-PS-27-028
Urethral prostatic ectopic tissue with eosinophilic epithelial metaplasia: a case report

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Background & objectives: Prostatic ectopic tissue is rare in urethra. Eosinophilic metaplasia (EM) is a characteristic lesion for the benign prostatic epithelium. We present clinicopathological and immunohistochemical features of a case of prostatic urethral cyst in association with EM in ectopic prostatic epithelium.
Methods: We report a case of 20-year-old male with a history of circumcision and nocturnal enuresis up to the age of 13 years who is currently presented with pollakiuria and cystic formation at the level of urethral meatus.
Results: Histological investigation of the specimen shows microcystic lesion, lined by a prostatic epithelium. There are areas with prostatic epithelial EM. Both normal ectopic prostatic epithelium and epithelium with EM show PSA and NKX3.1 positive staining. Only epithelium with EM shows PAS and MUC1 positive staining.
Conclusion: We report for the first time the presence of EM in an ectopic prostatic tissue. Ectopic prostatic EM cells save their histochemical (PAS+) and immunohistochemical (MUC1+) features. Presence of EM may serve as additional proof of benign character of lesion.

E-PS-27-029
Merkel cell carcinoma metastatic to the testis: report of a rare diagnosis and review of the literature

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Background & objectives: Merkel cell carcinoma (MCC) is an uncommon, aggressive cutaneous neuroendocrine neoplasm, with high recurrence rates. MCC metastases to the testis are an exceptional occurrence, with only eight cases reported to date in literature. We hereby report the ninth.
Methods: We report the case of a 58-year-old man with history of MCC of the wrist and multiple recurrences. Thirty-seven months after the initial diagnosis, the patient started complaining of scrotal oedema. Further inspections disclosed a solitary, indurated, moderately echogenic nodule within the left testis. Laboratory workup was unremarkable, including

normal serum AFP, β-HCG and LDH. The patient underwent radical orchiectomy.
Results: Macroscopic examination revealed a 60×49×40mm white to tan, ovoid, solid, centrally necrotic mass, almost completely replacing the testicular parenchyma. On light microscopy, the mass corresponded to a highly cellular, monotonous proliferation of small, blue, round cells, exhibiting a solid growth pattern, extensively infiltrating the seminiferous tubules. Lymphovascular invasion was easily identified. On higher magnification, tumour cells were often arranged in an organoid/trabecular fashion, displaying scant eosinophilic cytoplasm, hyperchromatic enlarged nuclei, coarse chromatin, visible nucleoli and brisk mitotic activity. Immunohistochemistry revealed strong diffuse immunoexpression of neuroendocrine markers; dot-like paranuclear immunostaining for CK20 and CK8/18; negativity for CK7, CD45, PLAP, OCT 3/4, TTF-1 and PS100. A diagnosis of metastatic MCC was made.
Conclusion: Metastatic dissemination of MCC to the testis is a rare event. Clinical suspicion and accurate histopathological assessment, including immunohistochemistry, are necessary for correctly diagnosing this entity. Clinicians must be aware of this unusual pattern of dissemination, since orchiectomy can be curative.

E-PS-27-030
Periureteral amyloidosis that mimics neoplasm: a case report with review of literature
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Background & objectives: Amyloidosis is a group of disorders associated with extracellular amyloid deposit. Urinary tract amyloidosis is very rare and is of interest to physicians because it mimics urothelial cell carcinoma clinically, cystoscopically, and radiologically. We report a case of this disease.
Methods: A 76-years-old man presented with haematuria for 6 months. Subsequent Computed Tomography (CT) revealed a homogeneous soft tissue periureteral density mass as well as hydronephrosis. Ureteral carcinoma was suspected and nephroureterectomy was performed.
Results: Grossly, the segment of the ureter was surrounded by a lightly orange and firm tissue that extended to renal sinus fat. Ureteral wall was lightly thickened. Urothelial carcinoma was not identified.
Histology of the cross-section revealed markedly thickened soft tissue due to amorphous, pale eosinophilic, extracellular deposits extending to renal sinus fat and ureteric wall. The amorphous material exhibited apple-green birefringence on Congo-red staining. No follow-up information was available for this patient.
Conclusion: Despite the rarity of localized amyloidosis, urologists, radiologists and pathologists should be aware of this entity to avoid misinterpretation and overtreatment. Histological examination is a requirement for definitive diagnosis and proper management. When diagnosis of AL amyloidosis is made, it is important to pursue further work-up to evaluate for systemic amyloidosis. Primary localized amyloidosis has a benign clinical course and usually is cured by with complete resection.

E-PS-27-031
Ductal type of prostate adenocarcinoma is not always high grade
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Background & objectives: PIN-like ductal adenocarcinoma represents a rare entity of prostate ductal adenocarcinoma (PDA) which, in contrast to the other ductal variants, behaves similar to Gleason's score 6 (3+3).
Methods: We describe the case of a 67 year old male who was hospitalized due to obstructive urinary symptoms. His clinical examination revealed a slightly elevated serum prostate specific antigen, while the digital rectum examination was negative. A simple suprapubic prostatectomy was performed. A focus of limited "prostatic intraepithelial neoplasia (PIN)-like" ductal adenocarcinoma of Gleason's pattern 3 was detected.
Results: Histologically, several crowded, basophilic glands were observed in an area of 10mm, lined by more than 2 layers of cells, with hyperchromatic, cylindrical nuclei. Immunohistochemical analysis was negative for high molecular weight cytokeratin (CK903/34BE12) in these glands, thus confirming the absence of basal cells and differentiating it from high grade PIN (HGPIN). Contrary to the other, poorly differentiated variants of prostatic ductal adenocarcinoma (PDA) (cribriform, solid, single-cell), the "PIN-like" pattern behaves similar to Gleason's score 6 (3+3) (Grade Group 1) acinar prostate adenocarcinoma, lacking therefore of substantial metastatic ability.
Conclusion: It is important to recognize "PIN-like ductal adenocarcinoma" as a separate entity from the other ductal adenocarcinoma variants and from HGPIN due to major differences in clinical behaviour. In fact, the term "ductal" has been proposed to be omitted from this type of cancer. In conclusion, the option of active surveillance with close clinical follow-up, serial biomarker evaluation, imaging and biopsy can be considered as a safe management option.

E-PS-27-032
Renal hydatid cyst misdiagnosed and treated as a cystic renal tumour: a diagnostic pitfall
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Background & objectives: The hydatid disease is a parasitic infestation caused by the larval stage of Echinococcus granulosus. The renal hydatid cyst is uncommon compared to those hepatic or pulmonary. Most patients remain asymptomatic for years and hydatiduria is the only pathognomonic symptom.
Methods: We report a rare case of renal hydatid cyst misdiagnosed and treated as a renal tumour.
Results: A 45-year-old woman with no significant medical history presented with left lumber pain with haematuria. Magnetic Resonance Imaging (MRI) displayed a left renal mass with cystic and solid components, showing discreet enhancement. The mass was classified as Bosniak-IV. The diagnosis of renal malignant tumour was made. The patient underwent a lumbotomy. The mass was adherent to the perirenal fat. A nephrectomy with surrenalectomy was performed. The gross specimen showed a renal cyst (9x7x6cm). The cyst contained multiple internal smaller cysts recalling the appearance of the hydatid cyst. The microscopic study showed an acellular eosinophilic laminated membrane lined by a germinal layer. The diagnosis of renal hydatic cyst was made.
Conclusion: Although the renal hydatid cyst is relatively rare, this diagnosis must be considered in patients with renal cystic masses. Preoperative diagnosis is challenging, especially in type IV cysts which can mimic a renal tumour and lead to overtreatment.

E-PS-27-033
Bilateral synchronous testicular germ cell tumours with discordant histology: a case report
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Background & objectives: Synchronous bilateral testicular cancer (SBTC) is a rare occurrence, accounting for only 0.5-1% of new testicular cancers; most BTC develop metachronously. In most published case

series of SBTC, bilateral seminomas comprise the majority; discordant histology has been reported in 15-70%.
Methods: Discordant histology in SBTC can be challenging from the perspective of staging and management and is associated with poorer survival outcomes compared to patients with concordant histology. Here we present a case report of a 34-year-old patient who presented with a large left sided testicular mass.
Results: The patient was found to have bilateral testicular tumours on ultrasound, accompanied by elevated alpha-fetoprotein (946 kIU/L), human chorionic gonadotropin (59.8 iU/L) and lactate dehydrogenase (555 iU/L). He had no risk factors for testicular cancer, including cryptorchidism. He underwent a bilateral radical inguinal orchidectomy. Microscopically, Stage pT3 embryonal carcinoma was diagnosed in the left testicle and Stage pT1 classical seminoma in the right testicle, neither of which had any other germ cell component. The patient proceeded to adjuvant bleomycin, etoposide and platinum chemotherapy.
Conclusion: Nonseminomatous components in SBTC are often reported as a broad category; the occurrence of synchronous seminoma and embryonal carcinoma has rarely been described. We discuss the histological appearances, possible pathophysiology, and staging of this unusual presentation of bilateral testicular cancer.

E-PS-27-034
Desmoplastic small round cell tumour of paratesticular region
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Background & objectives: Desmoplastic small round cell tumour (DSRCT) is a rare, aggressive, and frequently fatal tumour, which is most often seen in adolescent and young adult patients. It has characteristic morphology, and the fusion of the EWSR1-WT1 genes is diagnostic for it.
Methods: We report a case of 27-year-old man with tumour swelling of right testical, who underwent unilateral orchiectomy.
Results: Histologically was the tumour composed of nests and anastomosing cords of small blue cells with scant eosinophilic cytoplasm, oval nuclei, prominent nucleoli and frequent mitoses. Comedonecrosis and monocellular necrosis with massive lymphangioinvasion were observed. A remarkable desmoplastic stromal reaction was a part of the tumour. Immunohistochemical examination with positivity of CK AE1/AE3, EMA, desmin, NSE, PLAP and negativity of WT1, Syn, Chrom, Trombomoduline, S100, HMB45, GFAP, CD117, CK5/6, CK7, CK20, AFP, CEA, BerEP4, CD30 and CD99 was also performed. The characteristic EWSR1-WT1 gene fusion was detected by the genetic examination.
Conclusion: Paratesticular localization of DSRCT is very rare and it can be present with an isolated mass or with metastatic disease. Orchiectomy and local surgery is preferred method of local control. Patients with DSRCT have very poor survival rate, but patients with DRSCT of paratesticular localization have better outcomes. However, our patient could not undergo full follow-up therapy due to numerous comorbidities. He died after fourteen months of reduced therapy.

E-PS-27-035
Low-grade oncocytic renal cell carcinoma: one case report
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Background & objectives: Low-grade oncocytic renal cell carcinoma (LORCC) is a rare entity, not yet recognized by the WHO classification. Its main differential diagnosis is renal oncocytoma. We report here a case of this tumour.
Methods: 56 year old woman who consults for right low back pain. The CT-scan shows a rounded, 48 mm tissue renal process. Macroscopic examination showed a lower polar renal neoplasm. Histological examination revealed a carcinomatous tubulo-alveolar architecture with solid foci. The tumour cells are oncocytic, with slightly atypical nuclei presenting mitotic figures.
Tumour cells expressed cytokeratin7 and did not express CKit.
Results: LORCC is an emerging renal neoplasm. The main differential diagnoses are oncocytoma and chromophobic renal cell carcinoma (RCC). The LORCC shows a solid architecture or similar to the oncocytoma with more marked nuclear atypia and mitosis. In the presence of nuclear atypia and mitoses without the irregular appearance of nuclear contours and peri-nuclear halots of chromophobic RCC, the LORCC is strongly suspected. The LORCC shows an IHC profile Ckit-/CK7+ against an IHC profile Ckit+/CK7+ in the eosinophilic variant chromophobic RCC and the onocytoma.
Conclusion: LORCC is an oncocytic renal neoplasm which has a specific morphology and immunohistochemical profile (CD117-/CK7+), not yet recognized by the WHO, but represents an emerging entity. Its main differential diagnosis is oncocytoma and considered indolent.

E-PS-27-036
Mucin production in atypical small acinar proliferation with prostatic intraepithelial neoplasia and in adenocarcinomas of the prostate
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Background & objectives: The combination of ASAP and PIN worsens the prognosis for carcinoma. Therefore, there is a need to clarify the morphogenetic relationship between PIN, ASAP and prostate carcinomas of various grades, which may be done by studying mucin production.
Methods: We evaluated prostate biopsy samples of 90 patients divided into 6 groups according to the morphological diagnosis: the combination of ASAP and PIN and the carcinomas of Grade Groups 1-5. Normal prostate tissue samples served as controls. We performed Pas-reaction, alcyan blue staining (pH 1,0; 2,5), and immunohistochemical staining with 34betaE12, D2-40, and P504S antibodies. We applied non-parametric statistical methods.
Results: The prevailing ASAP phenotype was D2-40 (−), 34betaE12 (−), and P504S (+). In ASAP with PIN, neutral mucins were detected in greater numbers than in adenocarcinomas. Acid mucins were detected in all 6 groups. The highest level of their expression was recorded in Grade group 1 adenocarcinoma [Me = 68 (23-75) and the lowest level was in Grade group 5 [Me = 50 (32-80)]. In combination of ASAP and PIN, acidic mucins were scarce, and their expression was the lowest in comparison with other groups [Me = 28 (16-34)] ($p = 0.0001$). Sulphated mucins were detected only in PIN foci. Sulphated mucins were absent in ASAP foci and in adenocarcinomas.
Conclusion: In PIN foci, sulphated mucins are characteristic components of the secretion localized in the apical part of the cytoplasm of the luminal epithelium. They are not typical of ASAP foci and adenocarcinomas of all grade groups.

E-PS-27-037
Succinate dehydrogenase (SDH)-deficient renal cell carcinoma (RCC): a case report of a rare subtype
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Background & objectives: SDH is the key enzyme that connects the tricarboxylic acid cycle and mitochondrial electron transport chain and inherited in an autosomal fashion in contrast to other mitochondrial complexes. SDH-deficient RCC is a newly described rare entity.

Methods: A-24-year old male who presented with haematuria was investigated. A mass lesion was detected in the left kidney by radiologic examination. The subsequent nephrectomy revealed an exophytic mass located at the superior part of the left kidney. The tumour was well-circumscribed and had a tan-brown-red cut surface. Haemorrhage and partial cystic change were noted.
Results: Microscopically, the tumour had a pushing border, entrapping benign tubules at the periphery. The neoplastic cells demonstrated a variably solid or nested architecture, had eosinophilic to clear wispy cytoplasmic vacuoles or inclusions that represented the large mitochondria. The nuclei had homogenous chromatin with inconspicuous nucleoli. The tumour stroma showed areas of hyalinization. The differential diagnosis primarily included eosinophilic variant of clear cell carcinoma, eosinophilic solid and cystic RCC and SDH-deficient RCC. Immunohistochemically the tumour cells express kidney-specific cadherin, SDH-A. Diffuse loss of expression for SDH-B was noticed in tumour cells. There was no concomitant TFE3 or cytokeratin 20 expression. Post-surgery PET-CT screening was negative for a residual or metastatic tumour.
Conclusion: The defining abnormality of SDH-deficient RCCs is double-hit inactivation of the SDH-related genes. Long term follow-up is recommended for syndromic manifestations such as pheochromocytoma/paraganglioma, GIST, pulmonary chondroma, or pituitary adenoma. Early surgical intervention is recommended. Targeted therapies for VEGF, mTOR and tyrosine kinase may be administered in cases with metastatic disease.

E-PS-27-039
Large nested variant urothelial carcinoma: a case report
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Background & objectives: Large nested urothelial carcinoma (UC) is a rare histologic variant of UC, characterized by an unusual, bland morphology resembling von Brunn's nests but infiltrating lamina propria and muscularis propria.
Methods: 75 year-old male patient who was diagnosed as Ta Low Grade UC and papillary urothelial hyperplasia in previous transurethral resection (TUR) materials. PET scan examination performed and revealed metastatic nodular lesions in the left internal iliac region and in the upper posterior portion of the bladder. During control cytoscopy, clinicians revealed multiple tumours on the base, opposite wall and dome.
Results: They completely re-resected the tumours by TUR. On microscopic examination of re-TUR specimen there were large round shaped nests/tubules in lamina propria and muscularis propria. Tumour cells had bland morphologic features with uniform, vesicular nuclei, small indistinct nucleoli. Focal mild cytologic atypia and rare mitotic figures were present in deeper tissues. Immunohistochemically tumour cells were negative with CK20 and wild type with p53. Ki-67 proliferating index was 6%.
Conclusion: The case was diagnosed as large nested variant urothelial carcinoma which lead to underdiagnosis on previous TUR specimen due to bland cytologic features. It has a clinical behaviour of high-grade conventional urothelial carcinomas. Because of histologic features, which can be mistaken for a benign neoplasm or non invasive UC with endophytic growth pattern.

E-PS-27-040
Primary testicular squamous cell carcinoma
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Background & objectives: We present a case of primary testicular squamous carcinoma (SCC). Primary testicular SCC is extremely rare, except for metastasis from other primary lesions.
Methods: The patient, 71 years old, presented with enlargement of the left testis and a clinical diagnosis of scrotal inflammatory disorder was considered.
Ultrasound of scrotum was performed, and the left testis measured 14cm in diameter. Blood examination revealed aFP and βHCG within normal range.
Results: We received a left radical orchiectomy. In cut sections the testis was occupied by a cystic neoplastic tumour with an outer smooth surface, filled with brownish watery fluid and whitish compact material, while testicular parenchyma remained only in the periphery. The whole tumour was embedded in paraffin blocks. Microscopically, the cyst was lined by multilayered squamous cell epithelium with a granular cell layer. Cutaneous appendages, bone or cartilage were not present. Immunohistochemical staining for PLAP and CD117 did not reveal germ cell neoplasia in situ (GCNIS).
The absence of GCNIS and of tissues of all three germ cell layers supported the diagnosis of SCC arising in an epidermal cyst.
Conclusion: In such cases, it is important to take into consideration all clinical information in addition to the histological results, in order to exclude distant metastasis and reach a correct diagnosis.

E-PS-27-043
Sertoli cell tumour of testis: a case report
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Background & objectives: Sertoli cell tumour is a sex cord-stromal tumour. They comprise less than 1% of testicular tumours.
We report a case of a Sertoli cell tumour of the testis to show its epidemiologic, clinical, pathological and prognostic features.
Methods: A 40-year-old men presented with a painless progressive swelling of the right testis. Orchidectomy was performed
Results: The macroscopic examination revealed a well-circumscribed, homogenous, solid firm and white mass measuring 2,5 cm. Histopathological evaluation revealed a nodular growth of tubules and occasional clusters and cords of tumour cells which are round, with eosinophilic cytoplasm and elongated nuclei. A mild nuclear atypia was found without mitoses. The stroma was fibrous. No necrosis or embols were detected. On immunohistochemistry, tumour cells were positive for inhibin, calretinin and were negative for PLAP, AFP and CD30. The final diagnosis was Sertoli cell tumour of the testis, NOS. Sertoli cell tumours must be distinguished from other rare tumours of the testis especially seminoma which is the main differential diagnosis.
Conclusion: Sertoli cell tumours of the testis are an uncommon entity with most of the cases being benign. The malignant forms are too rare. They may involve any age with an average of 45 years. Orchidectomy is the hallmark treatment. Microscopy and immunohistochemistry are definite ways of diagnosis.

E-PS-27-044
Spermatocytic tumour in a middle-aged adult: a case report of a rare testicular neoplasia and review of the literature
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Background & objectives: The spermatocytic tumour is an extremely rare testicular neoplasm that presents as painless testicular swelling and mass with a size ranging from 1,5cm to 28cm and negative serum tumour markers. It occurs predominantly in adults in the fifth decade.

Methods: We report the case of a 57-year-old male with a history of right scrotal enlargement in the last month. The ultrasonography study showed a large heterogeneous nodule replacing most of the right testicle parenchyma. Serum tumour markers were negative. The patient underwent radical orchidectomy. We received a 16g surgical specimen comprising a 7x5,5x4,5cm testicle.
Results: Upon section, a 4,6x4,2x4,2cm solid testicular-confined neoplasm was observed, well-circumscribed, with whitish pseudocapsule and greyish-fleshy and vaguely mucoid cut surface. The histological analysis revealed a solid pattern neoplasia, with an oedematous stroma, scant fibrovascular septa, composed predominantly of intermediate sized cells, with giant cells and small lymphocyte-like cells. The neoplasia was permeated by a scarce lymphoplasmacytic infiltrate, there were images of intratubular extension and no signs of lymphovascular invasion. The neoplastic cells were immunoreactive for SALL4 and CD117, focally positive for CKAE1/AE3, Glipican-3, CD10 and PLAP and negative for the expression of OCT4, CD30, α-Fetoprotein, Podoplanin, Vimentin, CAM5.2, CK7, CK19, CK20, CDX2 and NSE. There were no diastase-resistant PAS+ globules.
Conclusion: This case illustrates the main immunophenotypical features of this extremely rare testicular neoplasia, which is generally cured by radical inguinal orchidectomy and, consequently, has an excellent prognosis.

E-PS-27-046
Cavernous haemangioma of the verumontanum: an unusual cause of haematospermia in an African man
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Background & objectives: Haematospermia is a relatively uncommon symptom in urologic practice. Varied aetiologies have been ascribed to it especially inflammatory, traumatic and iatrogenic causes. It is usually benign and self-limiting but may indicate more serious underlying organic pathological changes.
Methods: Although a haemangioma is one of the most common soft tissue tumours, most of them are superficial lesions, with a predilection for the head and neck region. The incidence of tumours in the verumontanum is low and studies reporting such diseases are scarce. Here, we report a case cavernous haemangioma of the verumontanum presenting with haematospermia.
Results: Patient
A 44-year old man without any known comorbidity with a complaint of blood in his semen (ejaculate) and occasional initial haematuria over the preceding three years. Symptoms were initially intermittent but became more frequent and persistent.
He had no lower urinary tract symptoms, constitutional symptoms or history of childhood haematuria.
Physical examination was essentially normal. Routine investigations were within normal limits. Diagnostic urethrocystoscopy showed a polypoid growth at the summit of the verumontanum. He was treated by transurethral electro-surgical resection of the verumontanum. Histologic findings were those of cavernous haemangioma. He had an uneventful post-operative recovery and remained symptom free in the in over 1-year of follow up.
Conclusion: Haemangioma should be considered in the differential diagnosis of haematospermia, and although rare in this location, clinical behaviour may not be different from those in other sites.

E-PS-27-047
Xanthogranulomatous prostatitis: a case report
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Background & objectives: Xanthogranulomatous prostatitis constitutes a rare subtype of granulomatous prostatitis, which can mimic carcinoma clinically and rarely histologically, especially for the inexperienced eye. We report a case of a 59-years-old male who underwent transurethral resection of the prostate (TURP) .
Methods: A 59-years-old man underwent TURP for urinary obstraction. Medical history included hypothyroidism, hypertension, chronic viral hepatitis B. The prostatic volume was 76cc. Prior transrectal biopsy (TRUS-b) performed in another centre showed high prostatic intraepithelial neoplasia (HG-PIN). PSA level was not available. We received multiple pieces of prostatic tissue weighting 15 grams. The tissue was processed in 6 blocks.
Results: Microscopic examination revealed nodular prostatic hyperplasia, glandular predominant. In three slides there were four lesions, measuring 0,1-0,2 cm in diameter composed of nodular collection of foamy cells, admixed with other inflammatory cells, mainly eosinophils. Atypia was not present. Immunohistochemistry revealed KerAE1/AE3(-), PSA(-), PGM-1(+), CD68(+). There was also patchy, non-specific inflammation of the prostate stroma and areas of squamous metaplasia. The diagnosis was xanthogranulomatous prostatitis.
Conclusion: Xanthogranulomatous prostatitis is a rare type of granulomatous prostatitis which can confuse the inexperienced eye. The other types of granoulomatous prostatitis are infectious (caused by mycobacteria) and non-specific granulomatous prostatitis. The nodular appearance and the presence of other inflammatory cells are clue to the diagnosis. Immunohistochemistry can be helpful.

E-PS-27-048
Schistosomiasis of the urinary bladder in combination with the presence of a prostatic polyp: a case report
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Background & objectives: Human Schistosomiasis is a parasitic disease caused by trematodes of the genous Schistosoma. S.haematobium which is endemic to Africa and the Middle East, is the species that infects the genitourinary system. People acquire the disease though contact with water containing infected snails.
Methods: We present a case of a 54 year old immigrant who came to our hospital with haematuria and was subjected to biopsy because of cystic changes observed at the posterolateral wall of the bladder during cysteoscopy.
Results: Microscopically we observed urinary bladder fragments covered by urothelium, containing in the lamina propria and the muscularis propria calcified eggs of the S.haematobium which are highly immunogenic, surrounded by dense collagene. The deposition of the eggs of S.haematobiumin the bladder may induce an intense granulomatous host immune response but may also elicit a network of dense concentric calcifications as in our case.
A prostatic polyp containing benign glands within loose stroma, covered by columnar epithelium was also recognized. The glandular epithelium was PSA immunoreactive, confirming the prostatic nature of the polyp. The pathogenesis of such a polyp is related to chronic irritation. The origin of the polyp from the prostatic urethra or urinary bladder couldn't be determined.
Conclusion: The diagnosis of urinary bladder Schistosomiasis can be made by tissue biopsy as the histologic findings are pathognomonic. The diagnosis should be considered in patients with haematuria who have immigrated from or travelled to areas where this disease is endemic.

E-PS-27-049

Urinary bladder, a rare metastatic site for breast carcinoma: case report

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Background & objectives: Given the high prevalence of breast cancer and the mortality associated with metastatic disease, it is important to be aware of rare metastatic sites, such as the urinary bladder, with only 66 cases previously reported in the literature.
Methods: We present the case of a 72 years old woman admitted to the Urology Department for urinary symptoms occurring four years after a diagnosis of breast cancer. Cystoscopy revealed a suspicious growing mass in the bladder wall and TURB was performed. The specimen was sent to the Pathology Department.
Results: Microscopical examination revealed a normal urothelium on surface and an infiltrative tumour in the lamina propria and muscular layer. Tumoral cells were either arranged in cords, nests or isolated, showing abundant basophilic cytoplasm, sometimes with signet ring cells features. These findings were suggestive for a tumour infiltrating the bladder from outside. In immunohistochemistry tumour cells were positive for CTK7 and GATA 3, ER, Mammaglobin, and negative for GCDFP-15, E-Cadherin, PR, WT1, p63, HER-2. Gastro-intestinal origin of the tumour was excluded due to negativity for CTK20 and CDX2. The morphological aspect and the immunohistochemical profile lead to a diagnostic of a metastasis of breast cancer in the bladder.
Conclusion: Even though bladder metastasis from breast cancer are uncommon, this possibility must be taken into consideration in patients with a history of breast cancer. Clinical data and immunohistochemistry are mandatory for establishing a correct diagnosis.

E-PS-27-050

Case report: primary urinary bladder adenocarcinoma

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Background & objectives: Primary Urinary bladder adenocarcinoma is a scarce histological variant accounting 0.5-2% of all urinary bladder cancers, reported higher in males at 60year and Schistosoma infection populations. Haematuria, dysuria, bladder tenesmus, suprapubic pain and urinary urgency are some of the nonspecific symptoms.
Methods: We present 57years female with haematuria, lower abdomen pain treated as recurrent schistosomiasis for 6months. Abdominal ultrasound and cystoscopy revealed 10mm tumour right lateral wall of the bladder. Patient underwent transurethral resection, tumour confirmed as adenocarcinomas by Pathologist. Gastrointestinal tumours were eliminated through tumour markers CA 19-9, CA 125, alpha-fetoprotein, CEA and gastroscope, colonoscopy as were all within normal ranges.
Results: Urinalysis were positive for red blood cells, abdominal ultrasound and cystoscopy revealed a 10mm tumour right lateral wall of the bladder and the CT-scan of abdomen showed an extensive bladder wall thickened by the tumours. Patient underwent transurethral resection and tumour confirmed as Primary adenocarcinomas by Pathologist. Gastrointestinal tumours were eliminated through tumour markers CA 19-9, CA 125, alpha-fetoprotein, CEA and gastroscope, colonoscopy as were all within normal ranges. Immunohistochemical stains were done with the following makers: EMA, PAS and vimentin. Appropriate positive and negative controls were used. The tumour cells were positive for EMA and were negative for PSA and vimentin.
Conclusion: Adenocarcinomas account 2% of malignancies of the urinary bladder. Common in elder males but females should be considered. Most presents with haematuria, irritative symptoms and diagnosed by histopathology. Diseases is characterized by high degree of malignancy, invasion and difficulty in diagnosis.

E-PS-27-051

A rare case of testicular adrenal rest tumours in an adult

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Background & objectives: Testicular adrenal rest tumours (TART) is an important complication of congenital adrenal hyperplasia (CAH), now a rarely encountered pathology due to hormonal treatment. We herein report an unusual and challenging case of TART and discuss its clinical and histological particularities.
Methods: A 37-year-old patient with bilateral testicular masses underwent surgical resection of the left testicle and after three years of the right testicle and left spermatic cord, due to suspicion of malignant recurrence based on the clinical and imaging features. For the histological diagnosis we used HE and IHC stained slides (CD56, Vim, Inhibin-α, Calretinin, Syn, Melan A, AR, CD10, Ki67).
Results: Both lesions consisted of solid islands and trabecules of Leydig-like, polygonal cells with some nuclear pleomorphism, reduced mitotic activity, granular eosinophilic or clear cytoplasm, with areas of inflammatory-type necrosis and fibrosis which separate the tumoral islands, characteristics which in a adrenal tumour would represent aggressive features. The remaining parenchyma presented atrophic features. Based on family history, clinical and morpho-immunohistochemical features, we reached the final diagnosis of TART.
Conclusion: TART is a very rare lesion, the only one diagnosed in the last 20 years in our department. Having the particularity of a diagnosis at such an old age, we want to underline the importance of a differential diagnosis with a malignant Leydig cell tumour, because of the histological similarities of these two lesions, but different evolution and treatment options.

E-PS-27-053

Role of ureteroscopic biopsy in diagnosis of upper tract urothelial carcinoma

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Background & objectives: Most upper urinary tract urothelial carcinomas are invasive at the time of diagnosis, being associated with a poor prognosis. Accurate diagnosis is essential for management.
Our objective was to determine the performance parameters of ureteroscopic biopsy in our tertiary centre.
Methods: We retrospectively identified and reviewed relevant documents of patients who underwent endoscopic examination for a suspected upper tract malignancy from January 2012 to August 2017. Biopsy and resection pathology reports were analysed for the histological diagnosis, grade and stage. False negative samples were reviewed by an experienced uropathologist.
Results: Of 115 biopsies, all 68 biopsies reported as malignant were true positives (100%specificity). Of the 47 benign or non-diagnostic biopsy reports, 32 were true negatives and 15 were considered false negatives (82.3%sensitivity). Review of false negative cases found no diagnostic errors. Grade concordance was 52.6% for WHO1973 and 65% for WHO2004. Grade 1 and 3 biopsy results predicted 24% and 67% chances of having subsequent muscle invasive disease respectively.
Conclusion: In our centre, endoscopic biopsy of the upper urinary tract showed high diagnostic accuracy and specificity. The sensitivity was also reasonably high. False negative cases did occur, presumably due to sampling error. Although the grade concordance was marginally lower than other studies, it appeared to have no impact on the strong predictive value for pathological stage. Overall, pathological assessment of ureteroscopic

biopsies is a useful tool in the investigation and management of suspected upper urinary tract tumours.

E-PS-27-054

Histopathological study of five cases of sex cord stromal tumours of testis, with a short review of the current literature

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Background & objectives: Sex cord stromal tumours (SCSTs) comprise approximately 5% of all testicular tumours. Most of them resemble or recapitulate normal testicular components such as Leydig cells, Sertoli cells, and nonspecific stromal cells. They are divided as pure or mixed.
Methods: We conducted a retrospective clinicopathological study of five patients who were initially diagnosed with sex-cord stromal tumours at General Hospital Asklipieion Voulas from 2010 to 2019.
Results: There were two Sertoli cell tumours, two Leydig cell tumours and one malignant Leydig cell tumour.
Conclusion: Leydig cell tumour is the most common pure testicular sex cord stromal neoplasm. Malignant Leydig cell tumours are associated with older age. Sertoli cell tumour represents ≤ 1% of all testicular neoplasms and are rare in children. Most of (SCSTs) are biologically benign, but about 10 % may show malignant behaviour. The mainstay of treatment for SCST is orchiectomy. Malignant SCST generally are not sensitive to chemotherapy or radiotherapy.

E-PS-27-057

Schwannoma of the kidney: a case report

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Background & objectives: Schwannomas are tumours of the nerve sheath and are most commonly seen in the head and neck region, extremities and posterior mediastinum. Involvement of retroperitoneal parenchymal organs is extremely rare.
Methods: A 54-year-old man presented with left flank pain of four weeks duration. Magnetic resonance imaging revealed a renal tumour which is primarily located in the hilum of the left kidney. The patient underwent nephroureterectomy since the radiologic findings were suspicious for urothelial carcinoma of the renal pelvis.
Results: Macroscopically, the tumour was well circumscribed and lobulated, 7,5x7x5,5 cm in size, and located in the renal sinus with a light yellow cut surface. Microscopically, the tumour consisted of a solid proliferation of interlacing bundles of spindle cells without nuclear atypia, mitotic figures and necrosis. A peripheral cuff of lymphoid aggregates was seen. Small clusters of xanthomatous cells intermixed with the spindle cells were also observed. The tumour cells showed diffuse strong positivity for S-100 protein. CD68 was positive in xanthomatous cells. Pan-cytokeratin, CK7, CK8/18, SMA and desmin were negative.
Conclusion: Renal schwannomas are rare neoplasms which occur in the renal hilum in majority. Morphology of the tumour is similar to those seen elsewhere in the body. Recognition and awareness of these rare benign tumours would aid in the differential diagnosis of spindle cell tumours of the kidney and prevent their misdiagnosis as sarcomatoid carcinomas or primary renal sarcomas.

E-PS-27-059

Malignant kidney epithelioid angiomyolipoma: a case report

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Background & objectives: Epithelioid angiomyolipoma is defined as a "rare variant of angiomyolipoma that consists of at least 80% epithelioid cells" (WHO2016). Malignant behaviour has been reported but prognostic factors are largely undetermined. Herein we report a case of a malignant epithelioid angiomyolipoma.
Methods: A 40-year-old female patient without previous relevant medical history was admitted to hospital due to asthenia, anorexia, weight loss and periods of fever and night sweats. CT revealed a contrast-enhancing 17cm solid mass in the left kidney. Nephrectomy was performed.
Results: Grossly, a solid 17cm yellow mass in the kidney was observed infiltrating the perirenal adipose tissue. Histological examination revealed a tumour mainly composed of epithelioid cells with large granular amphophilic cytoplasm and prominent nuclear atypia, arranged in discohesive nests. Areas of spindle cells with frequent bizarre features and multinucleate giant cells with occasional lipidic vacuoles were observed. Frequent atypical mitotic figures, extensive necrosis and venous vascular invasion were identified. By immunohistochemistry, Melan-A and HMB45 expression was observed. Our diagnosis was epithelioid angiomyolipoma with aggressive features. At follow-up, lung metastasis was identified at 6 months post-surgery and vertebral metastasis at 10 months. Despite sirolimus treatment, death occurred 13 months after surgery.
Conclusion: Despite unequivocal evidence of malignant potential, the prevalence of aggressive behaviour in epithelioid angiomyolipomas is extremely variable across studies and prognostic factors are still in debate. The case herein presented is exceptional by its highly aggressive histological features and clinical course.

E-PS-27-060

Primary urethral adenocarcinoma in women: a single centre experience

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Background & objectives: Primary urethral adenocarcinoma can display a variety of morphological patterns. Different origins have been suggested, but with exception of the cribriform variant, no clear source has been determined. Our aim was to study the differences between these tumours.
Methods: We retrieved and reviewed the histological preparations of all primary urethral adenocarcinomas diagnosed at our institution in the time period between 1965 and 2019. Immunohistochemical techniques were made on the paraffin embedded samples. The cases were then classified according to their histological and immunohistochemical characteristics.
Results: We found five cases of primary urethral adenocarcinoma in women. The first represents an example of the cribriform variant, with expression of prostatic specific antigen (PSA) and prostatic acid phosphatase (PAP). Two cases were classified as columnar-mucinous variants. Another case was a typical clear cell adenocarcinoma arising from a urethral diverticulum. The fifth case was similar to the latter but was located within periurethral glands and expressed PAP.
Conclusion: Urethral adenocarcinoma can display multiple morphologic patterns. Each subtype has distinct immunohistochemical features. A careful examination of the anatomical relations of the tumour remains the best way to evaluate the most probable origin in each case.

E-PS-27-061

Cellular angiofibroma on corpus cavernosum

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Background & objectives: A 60 year old male, previously with prostate adenocarcinoma, presented with a lesion on right corpus cavernosum.
Methods: A well-circumscribed encapsulated whitish mass dimensioned 4.2x2.5x0.5cm was received. The specimen was fixed in 10% buffered formalin. Multiple sections were obtained, routinely processed and embedded in paraffin; 2–4 μm thick sections were stained with hematoxylin and eosin and immunohistochemical markers
Results: On microscopy, a well circumscribed encapsulated hypercellular neoplasm probably of mesenchymatic origin, was observed. The neoplasm was composed of uniform, small, spindle cells (fibroblasts/myofibroblasts) with minimal atypia. Mitotic activity was absent. The stroma was mainly collagenous-fibrotic and in some areas myxoid or oedematous. Dilated vessels with hyalinized wall surrounded by hypercellular areas were notable. No obvious extravasation of red blood cells was found.
Immunochemistry revealed positivity for the following markers: Vimentin, ER PR, CD34, FXIIIa .INI-1 expression was retained. All other markers (AE1/AE3, S-100, SMA, EMA, desmin, NF, MBP, SOX-10, C-KIT, CD31, MUC4, STAT-6, Calponin, Caldesmon, CD68, ALK, β-catenin, p16, RB1) were negative. Ki-67 was estimated ~7%.
Conclusion: Taking into consideration the morphological features and the immunochemical results as well as the location of the neoplasm, we favoured the diagnosis of cellular angiofibroma / male angiomyofibroblastoma like tumour, ICD-O code 9160/0 according WHO/2016.

E-PS-27-062
Proteasic profile of a mast cell population in kidney cancer
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Background & objectives: Approximately 250 thousand people become ill and 100 thousand people die from kidney cancer annually
Methods: The expression of tryptase and chymase in mast cells, associated with kidney cancer, was analysed. Five patients composed the group of patients with kidney cancer (6 patients was control group). Slices were studied on microscope ZEISS Axio Imager.A2 with system of image documentation, which included colour digital camera Camera Axiocam 506 colour and a monochrome camera Camera Axiocam 503 mono.
Results: The received data testify that development of cancer is accompanied by increasing of tryptase- and chymase- positive mast cells in kidney parenchyma. In case of detection of protease profile the significant increasing of chymase expression in population of mast cells takes place with the highest intensity in the peritumor region, where the number of mast cells with simultaneous expression of proteases increased.
Conclusion: The development of kidney cancer is accompanied by increasing of population of tryptase- and chymase- positive mast cells in organ. The assessment of expression level of tryptase and chymase reflects invasive ability of tumour tissue and may be presented as pathomorphological criteria of aggressiveness of kidney cancer.

E-PS-27-063
Eosinophilic solid and cystic renal cell carcinoma in a Li-Fraumeni syndrome setting
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Background & objectives: We report a case of a 10 year-old female with previous history of high grade glial neoplasia (2015), treated with RT/QT (temozolomide). Renal ultrasounds were performed (risk of therapeutic renal nephrotoxicity); multiple bilateral renal cysts (2018) and a cyst (upper-pole right kidney-2019) were detected.
Methods: Fine needle biopsy was performed, with the proposed cytological diagnosis of oncocytic papillary tumour with TFE3 nuclear expression. A partial nephrectomy was decided for treatment and diagnostic confirmation.
Macroscopically a subcapsular neoplasia was identified, with 14 mm, encapsulated, solid and tanned; multiple cortical cysts with less than 1cm were identified.
Results: Histologically the lesion had variable morphological patterns-predominance of solid pattern, focal cystic and papillary, with epithelial cells with ample, eosinophilic and granular cytoplasm, foci of cytoplasmic vacuolization or granular basophilic stippling, irregular nuclei, with small conspicuous nucleoli. These characteristics were also present in epithelial cells of the adjacent cysts.
Immunostains were performed, both neoplastic and cystic cells displaying diffuse expression of CD10, racemase,CK20 and Cathepsin K; focal expression of EMA and TFE3.To exclude the possibility of MIT-family translocations, FISH was performed(neither TFE3 nor TFEB gene rearrangements were identified)-rendering a diagnosis of eosinophilic solid and cystic renal cell carcinoma (ESCRCC).
Liquid biopsy for NGS reported only a pathological missense mutation in exon 7 of P53(c.733G>A).
Conclusion: To our knowledge it's the first case in literature of ESCRCC in Li-Fraumeni Syndrome.P53 mutation is not a frequent driver-mutation in epithelial kidney tumours, however, it was described in patients following QT/RT, raising controversy in interpreting the malignant potential of adjacent cysts.

E-PS-27-064
Primary renal schwannoma: a common tumour in an uncommon location
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Background & objectives: Schwannoma is usually a benign tumour, which arises from Schwann cells in nerve sheaths. The most frequent locations are the head, neck and limbs. It is uncommon in the urinary tract.
Methods: We present the case of a 47 year old man, without medical history of interest. A computer tomography detected a left kidney mass, suggestive of papillary renal carcinoma. A partial nephrectomy was performed.
Results: The surgical specimen was a 3.5 cm firm nodular lesion with a solid yellowish cut surface. Histological examination revealed a proliferation of spindle cells with eosinophilic cytoplasm, normochromatic nuclei without atypia and virtually no mitotic figures. The cells adopted a fascicular pattern with alternating hyper and paucicellular areas (Antoni A and Antoni B areas), with occasional palisading of nuclei (Verocay bodies). Dilated vessels with hyalinized walls were noted. A strong and diffuse expression of S-100 protein was observed by immunohistochemistry. The final diagnosis was a primary renal schwannoma.
Conclusion: Primary renal schwannoma is an extremely rare tumour with 35 cases described up to date. It is a slowly growing mass and usually an incidental finding. A high index of suspicion should be maintained when dealing with mesenchymal renal lesions.

E-PS-27-065
Small cell neuroendocrine carcinomas of the urothelial tract: a retrospective study
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Background & objectives: Small cell neuroendocrine carcinomas of the urothelial tract are rare tumours resembling their counterparts in lung and elsewhere. The aim of this presentation is to perform a retrospective evaluation of small cell carcinomas diagnosed in our Department.
Methods: Consecutive cases of small cell neuroendocrine carcinomas of the urothelial tract diagnosed during 2015-2020 in our Department of Pathology were evaluated retrospectively. There were 8 cases diagnosed in 5 years. Diagnosis was set with Hematoxylin – Eosin stains and supported by immunohistochemical assays (Synaptophysin, Chromogranin, CD56). Cell proliferation rate was extremely high (> 90%) for all cases.
Results: The mean age was 74,6 years and Male:Female ratio 6:2. The predominant site was the urinary bladder (75%) followed by the ureter (12,5%) and renal pelvis (12,5%). Six urothelial tract small cell neuroendocrine carcinomas (n=6) were infiltrating muscularis propria and two (n=2) were extending beyond. Also, in two cases (in the ureter and the urinary bladder) (n=2), several heterologous characteristics were observed, such as squamous cell carcinoma, poorly differentiated urothelial carcinoma NOS, chondrosarcoma and osteosarcoma In six cases (n=6) there was evidence of in situ and infiltrative urothelial cell carcinoma, whereas in two cases (n=2) the small cell neuroendocrine carcinoma coexisted as component of an otherwise typical urothelial carcinoma.
Conclusion: Most of small cell neuroendocrine carcinomas of the Urothelial Tract were localized in the urinary bladder and they extended into muscularis propria at the time diagnosis. Although high response rate to chemotherapy is observed for this type of tumours, overall prognosis is still poor (5- year survival rate of 8 to 16%). The presence of distant metastases may be the most important prognostic factor,

E-PS-27-066
A case of melanoma metastatic to urinary bladder
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Background & objectives: Melanoma is an aggressive malignancy known to widely metastasize to different sites. Metastases to mucosa are rare and such cases are often difficult to differentiate from primary melanomas or primary cancers of the corresponding organ.
Methods: Patient A., male, born 1945, was treated four times for cutaneous lesions (1996 – keratopapilloma, 1999 and 2004 – basal cell cancer, 2009 – trichoepithelioma). In 2010 a skin lesion clinically suspicious of melanoma was seen in the coronal region but after histological examination of the resected tumour sebaceous glands adenoma was diagnosed.
Results: In June 2011 the patient was admitted to oncourology department with macrohaematuria and bladder tumour was removed, histologically urothelial carcinoma grade III. In July 2012 right humerus bone metastasis was diagnosed. A subcutaneous lesion of the neck was found with malignant cells suspicious of melanoma on cytological examination. In core needle biopsy in December 2012 from supraclavicular lymph node urothelial carcinoma was diagnosed. As clinical data (one and lymph node metastases, non-muscular invasive bladder cancer) and histological data were controversial, histologic preparations were re-evaluated. Solid clear cell tumour with brown pigment in some cells, positive for vimentin and S100, was seen in skin, bladder and neck lesions, consistent with melanoma.
Conclusion: The presented case shows that melanoma metastases to urinary bladder are very difficult to diagnose due to rarity of such lesions.

E-PS-27-067
Ratio of membranous and cytoplasmic vimentin expression in prostate cancer
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Background & objectives: Vimentin is a marker of epithelial-mesenchymal transition (EMT) in various cancers. Cell surface vimentin was shown to mark cells with features of cancer stem cells (CSCs) irrespective of other CSC markers. We assessed ratio of Vim cytoplasmic and membranous expression.
Methods: 36 samples of prostate cancer (PCa) were stained immunohistochemically with rabbit polyclonal antibodies to Vim (ThermoFischer Scientific, 1:1000). Staining was assessed semiquantitatively using a light microscope, x200 magnification. Weighed staining index (WSI), taking into account the percentage of stained cells and the relative amounts of weak, moderate and strong staining, was used for separate membranous and cytoplasmic staining evaluation.
Results: 23 (63.9%) cases were stage pT3, 14 (38.9%) Gleason score 7 (4+3) or 8-10. Membranous vimentin staining was present in 29 (80.6%) cases, cytoplasmic – in 35 (97.2%). Among them in 0 and 3 (8.3%) cases membranous staining was more prevalent than cytoplasmic according to percentage of stained cells (in 5 (13.9%) cases equal scores) and WSI, respectively. In most cases the percentage of cells with membranous staining was much lower, but staining intensities were higher, than for cytoplasmic staining. No statistically significant correlations were found between prevalence of membranous staining and disease pT category, Gleason score or previous neoadjuvant hormonal therapy, this may be due to a small sample size.
Conclusion: Vimentin is mostly expressed in cytoplasm, but membranous staining can also be seen in practically all cases, mostly in a small proportion of cells. These cells with membranous expression may correspond to cells with CSC features, but this hypothesis needs further evaluation using conventional CSC markers or functional assays. Anyway, neoexpression of vimentin shows EMT in most PCa cases.

E-PS-27-068
Two cases of Wilm's tumour in adult patients
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Background & objectives: Nephroblastoma (Wilm's tumour, WT) is the most common renal malignancy in children. Sometimes it may be diagnosed in adulthood, mostly in younger patients. It is appreciated that the course and prognosis of WT in adults is worse than in children.
Methods: We present 2 cases of WT in adult patients, that were treated in Minsk City Clinical Oncological Dispensary (MCCOD).
Results: In a patient K., 28 years, a tumour of the right kidney, 160*65*113 mm was found, reaching the right lobe of liver. Surgery was performed, histological examination verified WT with lymphovascular invasion and spread outside the kidney. Synchronous metastases to abdominal and retroperitoneal lymph nodes, peritoneum, right lung and liver capsule were seen on additional examination. The patient died 3 months later.
Patient S., 35 years, was first admitted with papillary thyroid cancer (diffuse sclerotic variant) with bilateral metastases to cervical lymph nodes. In October 2013 tumour of the right kidney was seen, WT (mostly blastema and epithelial components) was diagnosed after nephrectomy. No signs of WT progression are seen.
Conclusion: These two cases show different patterns of WT course with quick lethal outcome in case of late diagnosis and long disease-free period in case of early radical treatment. This once more emphasizes the necessity of early diagnosis and different diagnostic procedures to differentiate WT from renal cell carcinoma.

E-PS-27-069
Renal carcinoma with angioleiomyoma-like stroma
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Background & objectives: Renal carcinoma with angioleiomyoma-like stroma represents one of the emerging/provisional entities in the 2016 WHO classification. The following case helps review, discuss and provides further insight into the diagnosis of this type of cancer.
Methods: A 77-year old lady, with a history of total left nephrectomy due to an angiomyolipoma, presented a solid tumour on her right kidney. The sample of the partial right nephrectomy, measuring 5.5 x 4.7 x 2.7 cm, showed a well-defined neoplastic lesion, with a white-reddish, heterogeneous coloration, measuring 3.5 x 3.4 x 2.7 cm.
Results: Histologically it`s constituted by atypical glandular structures immersed in a muscular-like stroma, accompanied by thick-walled vessels. Neoplastic epithelial cell cytoplasm was abundant, varying from light to pale, microvacuolated or eosinophilic. Immunohistochemical markers CK7, CK34βE-12 and vimentin were intensely and diffusely positive in the epithelium, with focal CD10+, demonstrating muscle differentiation in the stroma (actins HHF-35 and 1A4, caldesmon, desmine were positive), while HMB45 and Melan-A were negative. These types of tumours may be variants of clear cell carcinomas, or papillary clear cell renal cell carcinomas, but they may also represent a specific sub-group. Although their low malignant potential, when associated with tuberous sclerosis, they may present with affected lymph nodes.
Conclusion: The few cases reported, have not demonstrated the characteristic chromosome abnormalities such as (3p) deletion, (7) or (17) trisomies, therefore the relationship with the morphological spectrum of renal carcinoma with mutated TCEB1 cannot be established. Data is still limited.

E-PS-27-071
Divergent differentiation in invasive urothelial carcinoma - frequency in current practice and association with muscle invasive disease
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Background & objectives: Invasive urothelial carcinoma commonly shows divergent differentiation. Some of them may be clinically relevant. We evaluated the frequency of muscle invasive bladder cancer in our experience and its association with variant morphology.
Methods: All consecutive cases of invasive urothelial carcinoma from Imagepat Laboratory (Salvador, Bahia, Brazil) were included. All cases from January 2017 to October 2019 were reviewed. Overall, 45 cases had no divergent differentiation while 46 showed some form of variant morphology.
Results: The most common divergent differentiation was squamous which was present in 18/46 cases (39%) ranging from 5-95% of tumour area. The second most common was micropapillary – seen in 13/46 (28%), (range:<5-80%). Third, plasmacytoid was observed in 9/46 (20%) (range: 30-90%). These were followed by poorly differentiated 8/46 (17%) (range: 20-100%), glandular 5/46 (11%) (range: 10-50%), giant cell 3/46 (7%) (range: 30-100%), and sarcomatoid 2/46 (4%) (range: 30-90%). The frequency of muscularis propria invasion was 18/36 (50%) in patients with urothelial carcinoma with no divergent differentiation. This rate was lower than the rate seen in patients harbouring urothelial carcinomas with squamous component 12/14 (86%).
Conclusion: The rate of muscle invasive carcinoma did not differ between tumours without divergent differentiation and those with micropapillary, plasmacytoid and poorly differentiated morphology. Although common, squamous differentiation should be still recognized as a feature of aggressive disease.

E-PS-27-072
Effect of heavy metals on microstructural and microelemental changes in the rats urinary bladder
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Background & objectives: Global environmental pollution leads to the distribution of heavy metal salts (HMS) in the ecosystem and their impact on the organism.
To study the influence of the heavy metals (HM) accumulation on the ultrastructural changes in rat's urinary bladder (UB).
Methods: The rats were randomly divided into three groups: I–control, II – rats received a mixture of HMS (Zn, Cu, Fe, Mn, Pb, Cr) for 30 days, III – animals received HMS during 90 days. The UB structure and tissue chemical composition were studied using Scanning-electron microscopy with elemental analysis and atomic absorption spectrometer.
Results: The dystrophic, destructive, inflammatory and atrophic changes were founded in the UB wall during the experiment. The indicators of HMS accumulation were significantly ($p<0.01$) higher in several times on the 30th and 90th days (Zn–1.24/1.35, Cu–1.46/1.73, Fe–1.72/2.08, Mn–1.33/1.58, Pb–1.63/1.95, Cr–1.44/1.64) compared to control. Furthermore, the local accumulation of inorganic ions occurred in stromal and parenchymal components (their predominance in subepithelial and perivascular areas).
Conclusion: The long-term HMS intake has a negative influence on the UB (urothelium disorders (desquamation, epithelium thinning, nuclei architectonics changes, cytoplasmic contours loss); swelling of parenchymal and stromal components; disorganization and thickening of collagen, elastic and muscle fibres) which accompanied by increasing their concentration levels in the tissue. The study prolongation leads to decreasing accumulation intensity and compensatory mechanisms activation.

E-PS-27-073
Isolated granulomatous vasculitis of the epididymis
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Background & objectives: Testicular vasculitis is defined as inflammation and destruction of the blood vessels in the testis, which can be seen in either systemic or isolated diseases. Most commonly affected sites are a single testicle, followed by the epididymis and spermatic cord.
Methods: We report the case of a 66-year-old male presenting with pain in the left groin, extending to the upper scrotum and exacerbated with movement and coughing. Ultrasound examination revealed an abnormal mass in the left inguinal canal, interpreted as incarcerated inguinal hernia. Upon surgical exploration, the epididymis and tunica vaginalis appeared thickened and firm. A left orhiectomy was performed.
Results: Macroscopically, tunica vaginalis of the left orhiectomy specimen was tan-brown and diffusely thickened, as well as the epididymis. The spermatic cord appeared grossly normal. Histological studies showed the presence of multiple foci of granulomatous vasculitis, affecting medium-sized and small-sized arteries of the testicle, epididymis and tunica vaginalis, with fibrinoid necrosis and surrounding mixed inflammation including macrophages, small lymphocytes, plasma cells. Testicular parenchyma showed no histological alteration.
Conclusion: Testicular vasculitis is a rare entity, which can be easily overlooked. There is no consensus regarding the treatment of testicular vasculitis, although it is postulated that the excision of the affected organ is curative.

E-PS-27-074

Recurrent bladder schwannoma - a case report

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Background & objectives: We report a case of recurrent bladder schwannoma, two years after the initial TUR-B and diagnosis.
Bladder schwannoma is a rare entity with only a few reported cases in the literature.
Methods: A 69 year old gentleman was under active surveillance since two years subsequent to a diagnosis of bladder schwannoma in our hospital.
Transurethral resection of the same area was performed, and the material submitted for histological evaluation.
Results: Histology showed cellular schwannoma, identical to the previous trans-urethral resected material: richly cellular fascicles of spindle cells with a tendency to palisading. Antoni-A areas were recognized, but no "Verocay bodies" or Antoni B areas were identified. Mitotic activity was very low.
The tumour cells were positive for vimentin, caldesmon, SOX10, S-100 and p16, whilst EGFR, ACT, ACTSM, ALK1, CD34, CD31, NF, DESMIN, CKAE1/3, p63, CK34B, MELANA, EMA, PAX8, CD99, CD117, COLL4, NSE were negative.
This panel of immunostains help exclude, but also other soft tissue tumours, such as neurofibroma and malignant peripheral nerve-sheath tumour, inflammatory myofibroblastic tumour (inflammatory pseudotumor), leiomyoma or low-grade leiomyosarcoma, or primitive neuroectodermal tumour.
Conclusion: Bladder schwannoma is a very rare tumour. Transurethral resection is the usual therapeutic approach, but the patient must remain under active surveillance. A panel of immunostains can be used to help tin the differential diagnosis.

E-PS-27-075

Mucinous metaplasia and plasma cell balanitis of the corona of glans penis

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Background & objectives: We report the case of mucinous metaplasia of the squamous epithelium of the corona of glans penis associated with plasma cell balanitis.
A few cases of the same entity are being described in the medical literature.
Methods: A 72 years old gentleman with a medical history of plasma cell balanitis, presented with an erythematous lesion at the corona of the glans penis. A biopsy performed.
Results: Microscopically the squamous epithelium showed mild reactive changes, with areas of atrophy, parakeratosis, and spongiosis. A small area with mucinous producing cells was identified in the superficial layers of the squamous epithelium.
In the dermis, a band-like infiltrate of plasma cells and hemosiderin pigment-laden macrophages were presented, a picture of plasma cell balanitis.
The mucin-producing cells had a benign histological picture and they were CK7 and CKCAM , PAS and PAS-D positive while they were GATA3, GCDFP15, CK20, CDX2 and NKX3.1 negative.
This phenotype supports the metaplastic origin of these cells against the possibility of an extramammary Paget's disease or metastasis.
Conclusion: Pathologists should be aware of this entity in penile material, especially when there is a history of plasma cell balanitis in the background. Histology and a panel of immunostains can help pathologists to make the diagnosis.

E-PS-27-076

Diagnostic conundrum of patient with synchronous colorectal and renal tumours

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Background & objectives: Mucinous tubular and spindle cell carcinoma (MTSCC) is a renal carcinoma of low malignant potential with characteristic mixture of tubular and spindle structures amidst mucinous stroma. Its rarity and morphological overlap with adenocarcinoma of various origins can be a diagnostic challenge.
Methods: We present the case of a 63-year-old patient admitted to the surgical department for left flank pain and malabsorption. Imaging studies revealed synchronous colorectal and left renal tumours, raising the suspicion of metastatic colorectal carcinoma. Radical resection was subsequently performed. Multiple sections from the surgical specimens were routinely processed. Hematoxylin and eosin staining, histochemical and immunohistochemical tests were performed.
Results: On gross evaluation, two distinct tumoral masses were identified in the superior rectum and left kidney. The histological examination of the rectal tumour revealed a low-grade adenocarcinoma NOS, while the renal tumour presented a particular morphology, with tubular architecture, focal spindle cell areas and stroma with fibrous and mucinous appearance. The tumour cells were positive for CK7, cytokeratin 34βE12, EMA and Vimentin and negative for RCC, CD10, CK20 and CDX-2. The Ki-67 proliferation index was 5%. A diagnosis of mucinous tubular and spindle cell carcinoma was made.
Conclusion: This is, to our knowledge, the first reported case of synchronous colorectal carcinoma and MTSCC of the kidney. The latter is a rare renal neoplasm, accounting for less than 1% of renal cell carcinomas. While the occurrence of multiple primary cancers is an increasing phenomenon, patient management remains challenging. Morphological and immunohistochemical profiling are essential in differentiating MTSCC from secondary tumours, particularly in patients with relevant clinical and genetic background.

E-PS-27-077

Primary prostatic leiomyosarcoma: case report and literature review

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Background & objectives: Sarcomas of the prostate are rare, accounting for <0.1% of prostate malignancies. Leiomyosarcoma is the most common sarcoma of the prostate (38%-50%). Less than 200 cases have been reported worldwide.
Methods: 75-year-old-Caucasian-male with bladder-obstruction-symptoms for 6-months.
On-treatment for benign-prostatic-hyperplasia (BPH) for 2-years. Preoperative serum-PSA=0.534ng/ml.
Microscopic-examination of transurethral-biopsy-material-(TURP): infiltration of prostatic tissue by interlacing bundles-and-fascicles of spindle-shaped cells with elongated/pleomorphic/highly atypical/bizarre nuclei, brisk-mitotic-activity-and-necrosis.
Differential diagnosis: stromal tumours of prostate, specifically sarcomas.
Immunohistochemistry: positive for SMA/desmin/HHF35, weakly positive for vimentin, and negative for AE1/AE3/CD34/AR/PR. ki67 cell proliferation index was high, approximately up to 70% of the neoplastic nuclei.
Results: Morphological and immunohistochemical findings were highly supportive for primary leiomyosarcoma of the prostate gland.
Following the histological diagnosis, the patient was referred to a hospital in his hometown where he was programmed to perform an MRI scan and be treated with radical prostatectomy and chemotherapy.

Conclusion: Leiomyosarcoma-of-the-prostate is an aggressive neoplasm. Hard to be diagnosed clinically, as the presenting symptoms can be attributed to other benign-and-malignant conditions.
Combining surgery/radiation/and chemotherapy is considered to be the optimum therapeutic approach, although standardized guidelines do not currently exist.

E-PS-27-078
Large cell neuroendocrine carcinoma of the prostate: case report and literature review
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Background & objectives: Large cell neuroendocrine carcinoma (LCNEC) of the prostate is exceedingly rare and associated with poor prognosis and widespread metastases. However, because of the rarity of the disease, its course and optimal treatment are yet to be determined.
Methods: 85-year-old-Caucasian-male with urinary-retention-symptoms and history of prostate-cancer-Gleason-Score-7,on androgen-deprivation-therapy-(ADT) for 4-years.Preoperative-serum-PSA=0.03ng/ml.
Microscopic-examination of transurethral-biopsy-material-(TURP): infiltration-of-prostatic-tissue by highly cellular/poorly-differentiated-neoplasm with nested-and-glandular-pattern-of-growth and necrosis. Neoplastic cells have abundant-cytoplasm/large-nuclei/prominent-nucleoli, and brisk-mitotic-activity. Small-foci of conventional-prostatic-adenocarcinoma-Gleason-Score-9 are recognized, in-less-than 1% of the-examined-tissue.
Differential diagnosis: high-grade (Gleason-Score-10) conventional-adenocarcinoma-of-prostate, high-grade-urothelial-carcinoma, and neuroendocrine-tumour.
Immunohistochemistry for poorly-differentiated-neoplasm: positive for chromogranin/synaptophysin/CD56/TTF1/CDX2/p53.Negative for PSA/PSAP/ prostein/ PSMA/ GATA3/ p63/ CK7/ CK20/ b-catenin. ki67 was-expressed-in 40% of the neoplastic-nuclei. Immunohistochemistry for conventional prostatic adenocarcinoma: positive for PSAP/PSA (weak and focal staining)/p53.Negative for CDX2.
Results: Morphological and immunohistochemical findings were indicative of large cell neuroendocrine carcinoma. Taking into account the presence of conventional adenocarcinoma of the prostate and the patient's history, the prostate is the most possible primary site of the neoplasm. However, strong and diffuse CDX2 expression by the neoplastic cells renders the suspicion of a gastrointestinal tract primary.
Following the histological diagnosis, the patient was referred for further examination, not yet performed at the time writing this report.
Conclusion: LCNEC-of-the-prostate is a rare entity, which more frequently occurs in patients formerly diagnosed with prostatic-adenocarcinoma and treated with long-standing-hormonal-therapy. Further research is needed to determine if neuroendocrine-differentiation-of-prostate-cancer is a natural-outcome of the disease or a resistance mechanism to current therapies.

E-PS-27-079
Primary mixed adenocarcinoma and large cell neuroendocrine carcinoma in ureter: a case report
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Background & objectives: Primary adenocarcinoma (ADC) and primary large cell neuroendocrine carcinoma (LCNEC) are both rarely diagnosed in ureter with few cases reported in literature. We present a recent case report from our institution illustrating the unique characteristics of the disease.
Methods: We report a case of primary mixed ADC and LCNEC that arose in proximal ureter and renal pelvis of a 55-year-old Korean man. This patient has a history of simple nephrectomy of left kidney, ileocecal cystoplasty and augmentation cystoplasty with uretero-ileal implantation, that was undergone 30 years ago due to tuberculosis.
Results: After cystoplasty, the patient has percutaneous nephrostomy (PCN) on right ureter because of hydronephrosis and the accompanied end stage renal failure. Under the haemodialysis, contrasted abdominal and pelvic computed tomography (CT) was done and revealed a hypoattenuated mass in ureteral area. Radical nephrectomy of right kidney was undergone and the severe adhesion in Gerota's fascia was found in the operation. Histopathologic diagnosis finally revealed as mixed ADC and LCNEC by immunohistochemical (IHC) study. The ADC components showed mucinous features (positive for CK20 and CDX-2) and transited to LCNEC components (positive for chromogranin A and synaptophysin).
Conclusion: In summary, this case study showed that mixed ADC and LCNEC can develop in the upper genitourinary tract including ureter, renal pelvis and calyces, especially in the case of the patient who undergone ileocecal cystoplasty with ureter-ileal implantation.

E-PS-27-081
Metanephric adenosarcoma – a rare malignant tumour in a young male
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Background & objectives: Metanephric neoplasms encompass a spectrum of uncommon benign renal tumours including metanephric adenoma, metanephric stromal tumour and metanephric adenofibroma. There are few cases described in literature as metanephric adenosarcoma, with benign epithelial component and malignant stroma.
Methods: We present the case of a 20-year-old male with acute left lumbar pain after a trauma having imagistic characteristics suggestive of perirenal hematoma. After surgery, the left nephrectomy specimen was processed and examined by standard H&E technique and immunohistochemistry. Gross examination identified a subcapsular hematoma and a poorly circumscribed greyish white area localized in the renal parenchyma, measuring 2.5x2cm.
Results: Microscopically, the tumour showed a biphasic proliferation consisting predominantly of spindle cells, with high nuclear pleomorphism and high mitotic rate with atypical mitoses, large areas of tumour necrosis, associated with hypercellular epithelial component, with uniform tubular architecture. The stromal component resembled high grade sarcomatous tumour, which infiltrated the renal parenchyma, and the epithelial component was identical to metanephric adenoma. The histological aspects were suggestive of metanephric adenosarcoma. The epithelial component was positive for AE1/AE3, EMA and negative for WT1, CD10, CD34. The stromal spindle cells were positive for Vimentin, WT1, Desmin, Actin, P53, with high Ki-67 index (85%) and negative for Caldesmon, CD10, CD99, S-100, MYF4 and NSE.
Conclusion: We believe that the macroscopic aspect, histopathologic features and immunohistochemical profile of our case resemble the metanephric adenosarcoma. The particularity of this case is the incidental finding and the atypical presentation of an extremely rare malignant renal tumour in a young male who was initially evaluated for a post-traumatic perirenal hematoma.

E-PS-27-082
Bilateral multifocal papillary renal cell carcinoma, type 1: a case report
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Background & objectives: Papillary renal cell carcinomas (PRCCs) are the second most common renal cell carcinomas (RCCs) subtype and occurs in sporadic and hereditary forms, accounting for 10-15% carcinomas of the renal tubular epithelium.
Methods: The surgical specimens were bilateral nephrectomy materials formalin-fixed and paraffin embedded. The sections were stained with routinary H&E. Immunohistochemistry was performed.
Results: A 77-year-old male patient who applied with abdominal pain and prostatism symptoms. Laboratory tests revealed no significant abnormalities. By abdominal computed tomography revealed multifocal, solid masses with the largest size of 49 x46mm in bilateral kidneys. The patient underwent transperitoneal bilateral nephrectomy. In macroscopic examinations, the tumour was well circumscribed, grey-white, necrotic, solid and multiple, measuring 0.3-5.3cm. Microscopically neoplasm was formed small cuboidal cells arranged on single layer at papillary cores. Neoplastic cells were uniform, had scant pale cytoplasm, hyperchromatic nuclei. Papillary cores contained foamy macrophages. Many Psammom bodies and papillary adenomas were detected. Immunohistochemical reactions were as follows; tumour cells were positive for AMACR, CK7, Pax 8, EMA, Vimentin.
Conclusion: PRCC is a malignant tumour, with a tendency to present at a lower stage, but with a distinct potential for progression and aggressive. Type 1 variants are slow-growing neoplasm with a relatively favourable prognosis. Although generally correlated with familial cancer syndromes, bilateral RCCs are rare (3-5 %) in the epidemiology of the disease. For all these reasons, this rare entity should be kept in mind in differential diagnosis

E-PS-27-083
Seminoma presenting as a polypoid bladder mass: a case report
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Background & objectives: Germ cell tumours (GCTs) are uncommon in elderly males, and male GCTs arise predominantly in the testes. However, 2-5% of GCTs are of extragonadal origin. Extragonadal germ cell tumours (EGCTs) in adults are uncommon and are mostly encountered in male.
Methods: The surgical specimens were formalin-fixed and paraffin embedded tissues from transurethral resection material. The sections were stained with routinary H&E and immunohistochemistry was performed.
Results: A 55-year-old male patient who applied with urinary retention, dysuria and haematuria. Patient's physical examination did not reveal any significant abnormality. Laboratory tests revealed no significant abnormalities. A computed tomography showed a polypoid enhancing mass measuring 143x90mm arising from the right posterior basal aspect of the urinary bladder. A scrotal ultrasonography evaluation did not reveal any significant abnormality. The patient underwent cystoscopic biopsy. In macroscopic examination, measuring 2cm, white, fragmented tissues were detected. In microscopic evaluation, the tumour composed of uniform, round to polygonal cells with moderate to abundant partly clear cytoplasm, large nuclei with prominent nucleoli. Immunohistochemical examination showed diffuse positivity in the tumour cells with CD117, PLAP, SALL-4.
Conclusion: EGCTs are representing 2-5% of germ cell tumours. Mediastinum is the most common site of these tumours followed by retroperitoneum and central nervous system. We hereby present rare case of extragonadal seminoma which presented with a large polypoid intravesical mass.