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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.

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One-Day Molecular Pathology Diagnostics and Translational Research Symposium

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E-Posters
One-Day Computational Pathology Symposium
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ABSTRACTS

33rd European Congress of Pathology – Abstracts

Oral Free Paper Sessions

OFP-01 | Autopsy Pathology

OFP-01-001
Myocardial pathology in pregnancy - an autopsy study
P. Zare*, P. Vaideeswar
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Background & objectives: Peripartum cardiomyopathy (PPCM) is an idiopathic left ventricular systolic dysfunction leading to cardiac failure in last trimester of pregnancy or in the postpartum period. Aim is to identify the clinical presentation and pathological features of PPCM among the maternal deaths.
Methods: We conducted a retrospective autopsy study of pathologically diagnosed cases of PPCM in maternal deaths in tertiary centre from 2012 to 2020. Analysed details were demographics, duration and type of symptoms, clinical diagnosis and investigations. The hearts were dissected by the inflow-outflow method. Samples were taken from right and left ventricular myocardia and examined by routine and/or special staining techniques.
Results: Among the 425 autopsies performed, 25 patients (5.8%) were diagnosed as PPCM on clinico-pathological basis. The mean age was 26.9 years. Among these, 5 (20%) patients were clinically diagnosed as PPCM or dilated cardiomyopathy, where an echocardiology showed an ejection fraction <45%, presented with dyspnoea and had associated pregnancy-related disorders like eclampsia and acute fatty liver. In the remaining 20 patients (80%), the diagnosis was made on the assessment of cardiac pathological features. The patients had varied clinical presentation associated with preeclampsia, puerperal sepsis and postpartum haemorrhage. Histologically, 12 hearts (48%) had myocarditis, while 13 (52%) had histological features of dilated cardiomyopathy. Among the latter, 7 hearts had mural thrombi.
Conclusion: Recent research has suggested the important initiating and driving factor for PPCM is the shift in angiogenic balance and development of anti-angiogenic environment. Even with the substantial advancement in understanding the pathogenesis of this relatively uncommon condition, this enigmatic entity significantly causes morbidity and mortality so cautious diagnosis is of paramount importance. This study is an attempt to highlight the pathological features of PPCM cases to aid further understanding of this condition.

OFP-01-002
Minimally invasive tissue sampling findings in 12 patients with COVID-19
N. Rakislova*, M.T. Rodrigo-Calvo, J. Ordi, E. Ortiz, L. Marimon, M. Ferrando
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Background & objectives: Complete autopsy is frequently not feasible in COVID-19. Minimally invasive tissue sampling (MITS) may be an alternative. We aimed to compare the MITS performance versus the complete autopsy in COVID-19 deaths and evaluate the safety of the procedure.
Methods: We conducted MITS to 12 adults who tested positive premortem for COVID-19. MITS was performed in a standard well-ventilated autopsy room, and the personnel used only reinforced protective equipment. In nine cases, a complete autopsy was performed after the MITS. A thorough histological evaluation was conducted, and the presence of COVID-19 was evaluated by PCR in a range of samples.
Results: The diagnoses of the MITS matched almost perfectly those of the complete autopsy in COVID-19-associated deaths. In nine patients, COVID-19 was in the chain of events leading to death, being responsible for diffuse alveolar damage and mononuclear T-cell inflammatory response in the lungs. No specific COVID-19 features were identified by MITS nor complete autopsy in any organ. Three deaths were not related to COVID-19. All the personnel involved in the MITS tested repeatedly negative for COVID-19.
Conclusion: MITS is a useful tool to evaluate COVID-19-related deaths in settings where complete autopsy is not feasible. The results of this simplified and safer technique are comparable to those of the complete autopsy.

OFP-01-003
Pandemics of our times: AH1N1 influenza versus COVID-19 – features of fatal cases in Romania
C. Popp*, L. Nichita, M. Neagu, C. Constantin, C. Dumitru, M. Buşcă, M. Cioplea, L. Sticlaru, A. Cioroianu, C. Mogodici, S.A. Zurac
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Background & objectives: During the last two decades, we faced two severe pandemics of air-borne infections: 2009-2010 pandemic of AH1N1 influenza (AI) and the present COVID-19 pandemic. Both diseases had a high mortality, but there are significant differences of characteristics between fatal cases.
Methods: We examined records from 97 consecutive fatal cases of AI that underwent post-mortem examination in our department in 2009 and 2010 and from 125 consecutive fatal cases of COVID-19 from our hospital (only 8 of them underwent autopsy). Demographic, clinical and pathological data were compared.
Results: Significant differences (AI versus COVID-19) were found between sex ratio (M:F of 1.7:1 versus 1.1:1), age (medium age of 42.01 versus 69.91). Pregnancy and post-partum period was a risk factor only for AI (9 out 36 women versus none in COVID-19 group). Obesity was frequent in both groups: (20.6% versus 21.6 considering that Romania has an obesity incidence of 9.4%). Some comorbidities were found in both groups (AI versus COVID-19): diabetes (10.3% versus 39.2%), malignancies (6.2 versus 22.4), and cardiovascular diseases (20.6% versus 63.2%). Histologic findings showed differences regarding thrombosis: only 6 out 97 cases of AI and all 7 cases of COVID-19, while DAD was more extensive in AI.
Conclusion: AI fatal cases were younger, healthier persons with very few severe comorbidities. While pregnancy and post-partum period is a risk factor for death in AI, obesity was equally affecting both groups. Knowing these characteristics, we can better tailor prophylaxis and

surveillance of population during infectious pandemics, reducing the number of fatal cases.

OFP-01-004

Multiple organ pathology in SARS-COV-2: reports of 232 autopsy cases

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Background & objectives: Pathological anatomy of SARS Cov-2 infection is still being investigated.
Methods: We report data of 232 autopsy of patients died from the COVID-19 infection confirmed by PCR during life and/or by examining paraffin blocks of lung tissue. Majority of patients were more than 65 years and had comorbid conditions (diabetes mellitus, obesity, ischemic heart disease and etc). Using macro- and microscopic studies, specific features of pathological processes in organs were identified.
Results: Lungs - diffuse alveolar damage, disseminated coagulopathy; lymphocytic alveolitis, viral-bacterial pneumonia, interstitial fibrosis and disregeneration changes of the lung epithelium; heart – lymphocytic endomyocarditis and coronoratis with thrombosis, ischemic damage of cardiomyocytes; brain – degeneration of neurons, vesculitis, edema and encephalitis in 3 cases; kidney – collaptoid glomerulopathy and tubulonecrosis; liver – steatohepatitis, foci of necrosis; endocrine system – adrenalities, lymphocytic thyroiditis, insulinitis; skin and skeletal muscle tissue – vasculitis. Coagulopathy associated to SARS Cov-2 was found in all organs.
Conclusion: The obtained data reveal the mechanisms of organs damage and individual aspects of COVID-19 pathogenesis. The thanatogenesis of the disease and the main causes of death are discussed, including acute cardiopulmonary failure, acute renal failure, pulmonary thromboembolism, shock involving multiple organ failure and sepsis.
The critical importance of autopsy is emphasized, which provides valuable information on the morphological substrate for this infection closely associated with possible clinical manifestations.

OFP-02 | Breast Pathology

OFP-02-001

A multi-feature AI-based solution for cancer diagnosis in breast biopsies: a prospective blinded multi-site clinical study

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Background & objectives: This study aimed to clinically validate the performance of a multi-feature AI-based solution on detection of invasive and in situ ductal carcinoma or atypical ductal hyperplasia against rigorous ground truth (GT) established by multiple blinded expert pathologists in breast biopsies.
Methods: Performance of the AI solution was prospectively tested on breast biopsies from 2 medical institutions in different geographies. AI results were compared against the ground truth (GT) established by consensus of two subspecialist breast pathologists. The study endpoints were detection of invasive carcinoma (IDC, ILC) and DCIS/ADH. ADH and DCIS low grade were pooled together because of similar clinical management.
Results: Six pathologists participated in the study and reported on 417 breast biopsies (872 H&E slides), including 135 invasive, 137 DCIS/ADH, and 145 benign diagnoses. 10 (2.4%) cases had discrepancies on invasive diagnosis, and 15 (3.6%) cases had discrepancies on DCIS/ADH diagnosis between the two specialist pathologists necessitating a third assessment by a specialist to establish GT. 4 of these cases also necessitated a committee decision since there was no majority even after 3 reviews. The AI solution demonstrated high performance when compared with the GT with AUC as high as 0.994 for the detection of invasive carcinoma, with specificity and sensitivity up to 95.4% and 98.4% respectively.
Conclusion: This blinded multi-site study reports the successful clinical validation of a multi-feature AI-based solution in detecting and automatically imparting clinically relevant diagnostic parameters regarding invasive and in situ breast carcinoma, offering an important tool for computer-aided diagnosis in routine pathology practice.

OFP-02-002

Digital pathologist training program on the evaluation of PD-L1 expression by VentanaPD-L1 (SP142) in triple negative breast cancer

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Background & objectives: Unresectable locally advanced or metastatic triple negative breast cancer may presents expression of PD-L1≥1 in the immune cells. Pathologist training is critical for right interpretation of PD-L1 expression. We report the results of the training in Portugal for the Ventana PD-L1 test (SP142).
Methods: In each training there were 10 to 12 pathologists-during 1 day-using a novel digital training platform–Pathomation. The Sessions consisted of 1) consensual analysis of 10 known cases 2) self study - 4 known cases followed by trainer-led group discussion 3) pre test – 8 unknown cases followed by trainer-led group discussion 4) proficiency test – 28 cases followed by discordant case review with the trainer.
Results: Between March 7, 2019 and February 19, 2020, 6 training sessions were held including 64 pathologists from 30 institutions nationwide. 100% of the pathologists met the approval criteria of the Roche International Pathologist Training Program (score ≥85% on the Proficiency Test). The overall percent agreement, positive percent agreement and negative percent agreement at the Proficiency test was 97%, 97.5% and 96.5%, respectively.
Conclusion: The assessment of PD-L1 expression on IC is a new concept for pathologists. This training program showed excellent pathologist's concordance scores, establishing the feasibility and effectiveness of such trainings in triple negative breast cancer.

OFP-02-003

Correlation of tumour subtype with long-term outcome in small breast carcinomas: a Swedish population-based retrospective cohort study

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Background & objectives: Breast cancer (BC) is increasingly detected at stage 1, hence treatment decisions are more often influenced by tumour biology than stage. Our study aims to explore if there is any association between tumour subtype and outcome in these small tumours.
Methods: We classified samples from 445 women with unifocal, node negative BC <15 mm, treated 1986-2004 into surrogate molecular subtypes (Luminal A-like, Luminal B-like, Her2-positive, and triple negative breast cancer (TNBC)) by immunohistochemistry and in situ hybridization. Information on treatment, overall survival, breast cancer-specific survival (BCSS) and incidence of locoregional and distant metastasis were gathered from medical records.
Results: Median follow-up for women alive was 19.8 years and no patient was lost to follow up. Tumour subtype was not associated with overall survival. Luminal B-like and TNBC were associated with a two- and threefold higher incidence of distant metastasis at 20 years, in

comparison to Luminal A-like BC, respectively. Women with TNBC and Luminal B-like tumours had worse breast cancer specific survival but this was not statistically significant. Her2-positive subtype had no certain association with any outcome despite the fact that no woman received Her2-targeted therapy.
Conclusion: TNBC or Luminal B-like tumours behave more aggressively than Luminal A-like tumours, even at stage 1. Prospective studies are needed to clarify if this means these women benefit from adjuvant chemotherapy. Women with Her2+/ER+-tumours do not seem to have an increased risk of distant metastasis or death, absent targeted treatment.

Funding: Lions Cancer Research Foundation, Swedish Breast Cancer Association, Percy Falk Foundation, Northern County Councils Regional Federation (grant: VISARENORR750491 and VISARENORR931408), ALF funding from Region Västerbotten.

OFP-02-004
Cystic neutrophilic granulomatous mastitis: a retrospective reassessment of granulomatous mastitis patients
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Background & objectives: Cystic neutrophilic granulomatous mastitis (CNGM) is an increasingly recognised subtype of granulomatous mastitis often associated with Corynebacterium species. CNGM usually occurs in reproductive age women and typically characterised with pain, discharge, mass formation, nipple retraction and sinuses at unilateral breast.
Methods: A retrospective search for breast specimens with granulomatous inflammation from 2010 to 2020 was performed. Through this ten year period there were 108 female patients diagnosed with granulomatous mastitis whose slides were available for review. Haematoxylin and eosin slides were reviewed for typical histological features of CNGM. Slides which were suspicious of CNGM were stained with gram for microorganisms.
Results: Thirty-five (32,4%) cases were identified as CNGM with characteristic suppurative lipogranulomas that are composed of central lipid vacuoles rimmed by neutrophils and an outer cuff of epithelioid histiocytes. Mean age was 34,6 (23-51 years), all patients were at a reproductive age, except one. Gram stains revealed organisms in 14 (48,2%) of 29 cases. The patients had various management approaches, including surgery, steroids and antimicrobials. Nine (25.7%) patients received antibiotics, six (17.1%) patients received local and two (5.7%) patients received systemic steroids, nine (25.7%) patients underwent segmental mastectomy. Eight (22,9%) patients had recurrent disease.
Conclusion: Although there is no consensus in the treatment of CNGM, Prolonged antibiotic therapy with lipophilic antibiotics as Doxycycline, Clarithromycin, Rifampicin and Co-trimaxazole are used for mostly isolated Corynebacterium species. Collaborative communication between specialists to accurately diagnose and manage these patients is essential to decreasing potential morbidity.

OFP-02-005
Response and outcomes of invasive mucinous carcinoma of the breast after neoadjuvant chemotherapy
G. Kir, Z.C. Olgun*, H. Seneldir, S. Koca, I. Tosun, O. Alimoglu
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Background & objectives: Mucinous breast carcinoma (MBC) accounts for approximately 2% of all breast cancers. There is limited data in the literature regarding the response and outcomes of MBC after neoadjuvant chemotherapy (NAC).
Methods: Eight patients with localized non-metastatic MBC who had been treated with NAC between 2010-2019 were identified. Paraffin blocks were available for all of the patients, as were H&E and immunohistochemistry slides of both their core biopsies and mastectomy or breast-conserving surgery specimens.
Results: Seven patients had a consistent pathologic response score at both the primary tumour site and the axillary lymph nodes after the NAC. Four patients had no pathologic response at both the primary tumour site and the axillary lymph nodes. Three patients had a partial pathologic response at both the primary tumour site and the axillary lymph nodes. One patient had a partial pathologic response at the primary tumour site but she did not have axillary lymph node involvement. Two patients, who had no pathologic response, had recurrent disease after 26 and 31 months of follow-up after surgery and they both died after 65 and 66 months of follow up, respectively.
Conclusion: In our series, none of the patients achieved a complete pathological response of the primary tumour and/or the axillary LNs. We observed that the pathological responses of the primary tumour and axillary LNs of the patients were correlated.

OFP-02-006
Lineage-specific methylation profiles in phyllodes tumours of the breast and their mimics
J. Hench, T. Vlajnic, S.D. Soysal, E. Obermann, S. Frank, S. Muenst*
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Background & objectives: Phyllodes tumour (PT) poses a diagnostic challenge, as there are no generally accepted criteria to distinguish PT from fibroadenoma (FA) or to separate between benign, borderline, and malignant PT. DNA methylation analysis represents an important tool to objectively classify tumours.
Methods: We used fresh/frozen as well as formalin-fixed, paraffin-embedded patient samples to determine DNA methylation patterns of 41 PT (22 initially diagnosed as benign, 8 borderline, 10 malignant, 1 not specified) on a standard microarray. 11 FA , 6 primary breast sarcomas and 1 metaplastic carcinoma were included as reference. Identified CNV aberrations were confirmed with fluorescence in situ hybridization (FISH).
Results: In analogy to other tumour entities, PT and FA show distinct DNA methylation profiles reflecting a breast-specific signature as well as tumour-derived patterns. PT/FA form a molecular subgroup distinct from normal breast tissue and invasive breast cancer. Whereas the histologically malignant PT are enriched for complex copy number alterations, the benign PT and FA feature less prominent to no copy number variants and their methylation signature shows a higher similarity to physiological breast tissue.
Conclusion: DNA methylation profiling allows distinction of two PT categories (benign/malignant). Of note, elimination of the diagnostically problematic category of borderline PT allows optimized prognostic patient stratification. The significant molecular overlap between benign PT and FA prompts for omission of their diagnostic distinction. Moreover, methylation and subsequent FISH analysis shows recurrent genomic aberrations limited to the neoplastic stromal cells, such as 1q gains (including the MDM4 locus), as well as CDKN2A deletions and EGFR amplifications, which may be exploited therapeutically.

Funding: Domarena Foundation Parrotia Foundation

OFP-02-007
Repeatable study of tumour infiltrating lymphocytes in breast cancer after neoadjuvant therapy based on artificial intelligence
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Background & objectives: Visual quantitative assessment of tumour-infiltrating lymphocyte(TILs) in breast cancer after neoadjuvant therapy lacks accuracy and repeatability. This study compared the difference and repeatability of visual assessment (VA) and Artificial intelligence(AI) assisted interpretation of TILs of breast cancer after neoadjuvant therapy under microscope.

Methods: This study included 50 patients with invasive breast cancer in the fourth hospital of Hebei Medical University from 2014 to 2015 and underwent surgical resection after neoadjuvant therapy. Nine pathologists of different levels used evaluate TILs of breast cancer after neoadjuvant therapy by VA and AI-assisted. In this study, SPSS 26.0 and GraphPad Prism 8.0.1 were used for statistical analysis.
Results: Nine pathologists in the VA group and the AI-assisted group found that the TILs of 50 cases of breast cancer after neoadjuvant therapy. The Friedman M test further showed that the interpretation results of the 9 pathologists in the VA group were significantly different (P<0.001), the interpretation results of the 9 pathologists in the AI-assisted group were no significant difference (P=0.416). There was no significant difference only between senior pathologists in the VA group in the TILs interpretation. The ICCs of TILs interpretation for breast cancer after neoadjuvant therapy between all pathologists in AI-assisted group and the gold standard were higher than 0.9.
Conclusion: AI significantly improves the consistency and repeatability of the interpretation results of TILs by pathologists. It can be seen that AI-assisted pathologists is a good way to improve the consistency and repeatability of the TILs interpretation results of breast cancer.

OFP-02-008
A nomogram for predicting the subgroups of ER low positive breast cancer based on clinicopathological characteristics
S. Niu, Y. Liu*
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Background & objectives: The purpose is to establish a nomogram to predict the expression status of ER based on clinicopathological characteristics, and to identify patients with ER low positive whose clinicopathological characteristics are similar to ER-negative patients.
Methods: 450 invasive breast cancer patients who had surgical treatment in the Fourth Hospital of Hebei Medical University in 2012. ER-negative groups and ER-positive groups of patients were randomly divided into training cohort and verification cohort at a ratio of 7:3. The effectiveness of the nomogram is evaluated by calculating the area under the ROC curve (AUC).
Results: Tumours with obvious nuclear polymorphism, mitosis>20/10 HPF, tumour infiltrating lymphocytes>40%, and necrosis are often ER-negative. The AUC of the nomogram in the training cohort and validation cohort were 0.804 (95% CI 0.750-0.858) and 0.828 (95% CI 0.752-0.903), respectively. By calculating the Yorden index, the best cut-off value for predicting ER expression status is 0.59. The nomogram was used to predict subgroups of patients with ER low positive breast cancer. 164 (63.08%) patients had negative predicted results, and 96 (36.92%) patients had positive predicted results. Among patients with ER low positive, those with negative predicted results have lower expression of ESR1 mRNA, cannot benefit from endocrine therapy and have a poor prognosis.
Conclusion: Based on clinicopathological characteristics, we have developed and verified a nomogram that predicts the expression status of ER in patients with invasive breast cancer. It can be used to identify patients with ER low positive whose clinicopathological characteristics are similar to ER-negative patients and will help guide individualized and precise treatment of ER low positive breast cancer patients.

OFP-02-010
Molecular subtyping of invasive breast cancer using PAM50-based multigene expression testing - comparison with surrogate subtyping by immunohistochemistry and grading and influence on oncologist's decision on systemic therapy in a real world setting
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Background & objectives: In breast cancer (BC), therapy decision depends on prognostic and predictive biomarkers including surrogate subtyping by immunohistochemistry (IHC)& grading. In intermediate risk hormone receptor (HR) positive, HER2 negative BC, decision for adjuvant chemotherapy can be supported by multigene expression tests.
Methods: 142 BCs with intermediate clinico-pathological risk were investigated using Prosigna® testing in a prospective multicenter study. Prosigna® molecular subtyping was compared with local and two central (C1 and C6) surrogate subtypes [each IHC (HR, HER2, Ki-67) subtyping and von Minckwitz (IHC+grading) subtyping] utilizing inter-rater reliability (IRR) analysis. Moreover, impact of Prosigna® test results on treatment decision on chemotherapy was studied.
Results: For 119 cases, Prosigna® and surrogate subtyping were available. According to local IHC, 35.4% were Luminal A-like, 64.6% Luminal B-like (local von Minckwitz subtype: 31.9% Luminal A-like/ 68.1% Luminal B-like). In contrast to local and C1, C6 surrogate subtyping assigned >66.7% of cases to Luminal A-like. Best agreement occurred between Prosigna® (53.8% Luminal A/44.5% Luminal B) and C1 von Minckwitz subtyping (Cohen's kappa= 0.455). Chemotherapy and endocrine therapy were recommended to 44.2% and 88.6% of Prosigna® Luminal A and Luminal B cases, respectively. For local Luminal A-like cases, chemotherapy and endocrine therapy were recommended if Prosigna® testing classified them as Luminal A with high/intermediate risk or upgraded to Luminal B subtype.
Conclusion: IRR between Prosigna® subtypes and surrogate subtyping was fair to moderate depending on surrogate subtyping method and center. Cases of high Prosigna® risk group were mostly of Prosigna® Luminal B subtype. For Luminal A-like subtypes of breast cancer assessed locally using IHC/von Minckwitz subtyping, adjuvant chemotherapy and endocrine therapy were recommended if multigene expression analysis using Prosigna® assay classified those cases as Prosigna® Luminal A at high/intermediate risk or upgraded to Prosigna® Luminal B breast cancer.

OFP-02-011
Prognostic factors of luminal A and luminal B intrinsic breast cancer subtypes of Croatian patients: a 5-year experience from Osijek
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Background & objectives: Prognosis and treatment of breast cancers are associated with clinico-pathologic and biological characteristics of the tumour. The aim of this study was to assess the frequency and prognostic parameters of luminal breast cancers among Croatian breast cancer population.
Methods: A large retrospective cross-sectional study including 1248 cases of primary breast cancer treated at Osijek University Hospital was conducted during 2016–2020. The clinico-pathologic and immunohistochemical (IHC) and dual in situ hybridization (DISH) data were extracted from pathology reports to study the luminal subtypes A and B. The cross-tabulated statistics of the observed characteristics were performed between the two subtypes.
Results: Luminal cancers comprised 89% (1006/1130) of the total number of cases. Of 1006 cases of luminal cancers, 717 cases (71.3%) were luminal B, while 289 (28.7%) were luminal A. Age profile of Luminal A and B cancers were similar (62.8 vs 62.7 years). Luminal B cancers were associated with higher grade (22.9% grade III in luminal B compared to 6.6% in luminal A), micropapillary and metaplastic histology, and high

frequency of nodal metastasis (39.8% in luminal B compared to 23.3% in luminal A).
Conclusion: Luminal B is the most frequent subtype of breast cancer in Croatian patients. They were associated with adverse clinico-histologic parameters such as higher grade and nodal metastasis. Our findings suggest that, despite lack of molecular studies in routine practice, IHC/ISH-based typing are sufficient for prognostic and therapeutic stratifications in breast cancers in Croatia.

OFP-02-012
Immunohistochemical markers in breast cancer brain metastases: the role of the cancer stem cell marker CD44 in prognosis
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Background & objectives: Up to 30% of women with breast cancer develop brain metastases (BCBM), and the overall prognosis remains poor. Different markers are on trial for guiding treatment and provide prognostic information.
Methods: A retrospective transversal study was completed using archival biological material from 114 patients with BCBM, diagnosed between 2000 and 2016 at the Coimbra University Hospital. Expression of CD44, CD133, ALDH1, PD-L1, Her-2, ER, PR, CA9 marks were assessed by immunohistochemistry. Clinical and pathological data was retrieved from the hospital database. The local ethical committee (CHUC-136-20) approved this study.
Results: One hundred and one (89%) metastases were located in the brain parenchyma and 13 (11%) in the bone. The most common site was the cerebellum (34.7%). The median age of presentation was 56 years (32-80 years). After a median follow-up of 10 months (0-225months) the overall survival (OS) was of 10±1.3months. The overexpression of CD44 was associated with a worse OS (7±2.2vs 12±1.8months, p = 0.047), on univariate analysis; however multivariate analysis did not confirm this finding (HR 1,543, 95%CI 0.99-2.4, p=0.055). The remaining markers did not exhibit statistical correlation.
Conclusion: BCBM have a very poor outcome. Cancer stem cell markers, such as CD44, may have prognostic impact on survival in patients BCBM. The conjugation with other markers may help in patients' stratification and therapy.

OFP-02-013
Tumour-associated macrophages characterisation in invasive breast carcinoma
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Background & objectives: Tumour-associated macrophages (TAM) may have a significant role in carcinogenesis and could be a potential therapeutic target in breast carcinoma (BC). We evaluated the clinico-pathological features and correlated them with TAM M1(pro-inflammatory) and M2(immunosuppressive) in molecular subgroups of BC.
Methods: We evaluated 60 untreated BCs; 20 Triple-negative (TN), 20 HER2-enriched (HER2+) and 20 Luminal (ER+). Medical records and histological slides were reviewed. Immunohistochemistry for CD68, pan-macrophage; CD163, CD206, M2 and CD80, M1, was performed. Expression was determined by counting the absolute number of intratumoral macrophages in ten high-power-field "hot-spots". Fisher's exact test was used for groups comparison.
Results: Patients´ median age was 62,7 years. The median follow-up was 75,65 months (9-250). TN tumours presented with higher stages than ER+ tumours (p=0.026), were frequently bilateral (30%) and BRCA1/2 mutated (30%). TN carcinomas were larger than ER+/HER2+ carcinomas (p=0.008; p=0.041) and more necrotic than ER+ carcinomas (p<0.001). Ki67 was not significantly different among TN/HER2+ tumours but it was higher than ER+ tumours (p<0.001). The number of CD68/CD163 positive cases was higher in TN than ER+ tumours (p=0.008). No statistical difference was found between TN and HER2+ groups. CD80 and CD206 TAM were rare and neither relevant nor different among the 3 groups.
Conclusion: CD163 is more frequent in TN tumours, confirming the relationship between M2 macrophages and tumour aggressiveness in BC. CD163 allows a better estimation of M2 macrophages than CD206. CD80 was not useful in the evaluation of BC TAM.

OFP-02-014
B3 lesions diagnosed on core needle biopsy and diagnostic upgrade at excision: a single institution experience from 2002 to 2018
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Background & objectives: On core needle biopsies (CNB), B3 diagnostic category involves a spectrum of lesions with uncertain malignant potential. We aim to describe B3 lesions, diagnosed on CNB between 2002- 2018, and the final diagnosis on vacuum-assisted biopsy (VAB) and/or tumourectomy (TM).
Methods: We collected information on CNB, VAB and TM of patients diagnosed with: in-situ lobular carcinoma/atypical lobular hyperplasia (LCIS/ALH), radial scar (RS), papillary lesion with/without atypia (PAP), flat epithelial atypia (FEA), atypical ductal hyperplasia (ADH), and fibroepithelial lesion with stromal hypercellularity (FELSH). We contrasted diagnoses of CNB and excision, comparing the percentage of intraductal (IDC) and invasive carcinoma (INVC) by B3 groups.
Results: We identified 410 patients (mean age 48,4 years) diagnosed with LCIS/ALH: 30(7,3%); RS: 63(15,4%); PAP: 66(16,1%); FEA: 60(14,6%); ADH: 74(18,1%), and FELSH: 117(28,5%). 382 (85,9%) showed pure B3 lesions, and 58 (14,1%) combined. Among the 305 (74,4%) patients with excision data: 53 (12,9%) underwent to VAB-only, 238 (58,1%) TT, and 14 (3,1%) VAB+TT. None of the patients treated by VAB-only showed carcinoma. On excision (VAB/TT), diagnoses included: 57 (18,7%) benign lesions (B2), 184 (60,3%) B3 lesions, and 64 (20,9%) carcinoma: 30 (9,8%) INVC, and 34 (11,2%) IDC. Patients with LCIS/ALH showed the highest percentage of INVC (24%) at excision, and those with ADH showed the highest percentage of IDC (33,3%).
Conclusion: In our series, the most frequent B3 diagnoses on CNB were fibroepithelial lesions, and atypical ductal hyperplasia. Most of the lesions identified were pure. Overall, the percentage of upgrade, including invasive and intraductal carcinoma, among our patients with B3 diagnosis was 20,9%, being higher among those with LCIS/ALH and ADH.

OFP-02-015
The impact of COVID-19 on the practice of breast pathologists; a survey of the United Kingdom Breast Pathologists
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Background & objectives: There is little information on the impact of COVID-19 on breast pathologists. This survey assesses the effect of the COVID-19 pandemic on UK and Ireland-based breast pathologists in order to optimise working environments and ensure preparedness for potential future pandemics.
Methods: A 35-question survey on working practices during the COVID 19 first wave including redeployment, professional development, training, health and safety & wellbeing was distributed to consultant breast

pathologists on the National Coordinating Committee for Breast Pathology and the Association of Breast Pathology databases, and responses collected anonymously.
Results: There were 135 responses from breast pathologists based in the UK and Ireland. Most participants (75.6%) stated that their workload had decreased, and their productivity dropped. 86/135 were given the option of working from home and 36% of those who did reported improved efficiency. Multidisciplinary team meetings (MDTMs) largely moved to virtual platforms (77.8%) with fewer members present (41.5%). Online education including webinars and courses were popular and utilised by 92.6%. 16.3% of pathologists reported shortages of masks, visors or gowns as the commonest health and safety concern. 33.3% felt that COVID had a significant negative impact on their physical and mental health. 10.4% were redeployed/retrained.
Conclusion: Going forward, most respondents were keen to adopt flexible working hours, virtual MDTMs, remote working and digital pathology. 57% felt their pathology departments were not adequately prepared for a potential surge in activities due to patient treatment backlogs.
The COVID-19 pandemic significantly impacted on UK breast pathologists and their practice. It is important to apply flexible working patterns and environments that improve productivity and mental health. The changes suggested should be considered for long-term shaping of breast pathology services.

OFP-02-016
Leptomeningeal metastasis of breast carcinoma
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Background & objectives: Leptomeningeal carcinomatosis (LMC) is an uncommon complication of breast carcinoma (BC) associated with poor outcome. We evaluated the clinicopathological features of BC associated with LMC and correlated them with patient survival.
Methods: We performed a retrospective study of patients with LMC from BC diagnosed in cerebrospinal fluid (CSF) from 2000 to 2019 with available histology of primary BC. Clinical data (age, genetic susceptibility, neoadjuvant therapy, metastasis, and follow-up) was accessed from clinical records. CSF slides were reviewed as well as slides from primary BC and other distant metastasis.
Results: Thirty-one female patients with mean age at diagnosis of 51 years (29-81) were included. BRCA1/2 mutations were confirmed in 25% of the patients. Twelve patients had neoadjuvant chemotherapy. Besides LMC, fifteen patients had M1 disease, mostly lung (33.3%). Mean interval between BC diagnosis and LMC (MID) was 56 months (4-161). The median overall survival after LMC (OSLMC) was 3 months (0–13); six months OSLMC was 19.3%. Most tumours were invasive carcinoma of no special type (87.1%), 55.5% grade 3. The proportion of Luminal, HER2+ and TN was 74.2%, 12.9% and 16.1%, the respective MID was 60.8, 31.8 and 34.4 months and the OSLMC was 3.6, 1 and 1.2 months.
Conclusion: The percentage of patients with confirmed BRCA1/2 mutations is high in this series. As described in literature, prognosis of patients with LMC is poor, as less than 20% of the patients were alive 6 months after positive CSF. Luminal subtype represented the majority of cases, had the longest interval between BC diagnosis and LMC and the longest survival after positive CSF.

OFP-02-018
In situ-like morphology in invasive ductal carcinoma: association with HER2 gene aberrations and neuroendocrine differentiation
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Background & objectives: Invasive ductal carcinoma, NOS may exhibit a unique ductal carcinoma in-situ-like morphology characterized by lack of myoepithelial layer. Herein we described clinicopathological and immunohistochemical features, as well as hormonal and HER2 status of these tumours.
Methods: Slides of tissue microarrays constructed using 3-mm cores of 26 tumours of 15 female patients were immune-stained for SMA, synaptophysin, and c-erbB2 and subjected to dual HER-2 Gene amplification FISH Probe Kit (Health Care). All slides were scored by two pathologists and also scanned and reviewed via Olympus VS120 automated slide scanner.
Results: The mean age was 51,1(25-76). Mean tumour size was 3,2(0,1-14) cm. Fifteen tumours were grade 3; 9 were grade 2; 2 were grade 1. Seven (58%) cases showed synaptophysin expression, one of which diffuse and strong, while 6 cases had focal synaptophysin expression. All but 3 cases(2 c-erbB2+ and 1 triple-negative) were ER/PR+. Two cases(%29) revealed HER2 overexpression (Her2/Cep 17 ratio >4, group 5), while 5 cases fell into group 4 (Her2/Cep 17 ratio <2, HER2>4 and <6), and the rest were non-amplified (group 5). Nine(64%) tumours, 4 of which expressed synaptophysin, showed polyploidy in a range of 3 to 6 CEP17 copy numbers. Seven(47%) cases showed lymph node metastasis.
Conclusion: Given the fact that neuroendocrine marker expression in breast carcinoma is around 10-30%, synaptophysin expression seems to be slightly overrepresented in this group of tumours. Besides, tumours with HER2 polyploidy revealed higher neuroendocrine differentiation (44%) than the euploid ones. There are some overlapping morphological and immunophenotypical features with invasive solid papillary carcinoma. In our study group with this particular morphological appearance, synaptophysin expression and chromosome 17 polyploidy seem to be a unique-promising finding for further research.

OFP-02-019
Malignant breast papillary neoplasm: a clinico-pathological study of 27 cases
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Background & objectives: Malignant breast papillary neoplasm is a rare type of invasive breast carcinoma. It is characterized by predominant papillary architecture.
The aim of our study was to discuss the clinicopathological features of malignant breast papillary neoplasms.
Methods: In a retrospective study, we report 27 cases of malignant breast papillary neoplasm between 2001 and 2020 obtained from files of Pathology Department of Farhat Hached University Hospital (Sousse, Tunisia).
Results: The patients mean age was 57.35 years. The mean size of tumours was 3.89 cm (ranged between 2.2 and 14 cm). There were 15 cases of invasive papillary carcinoma, 8 cases of encapsulated papillary carcinoma (including 3 with adjacent invasive carcinoma of no special type), 3 cases of solid papillary carcinoma and one papilloma with ductal carcinoma in situ.
Immunostaining with myoepithelial markers, including Ck5/6 and p63 demonstrated the absence of myoepithelial cells both in the papillary fronds and at the periphery of the lesion in encapsulated papillary carcinoma.
Hormonal receptors were positive in 7 cases of invasive papillary carcinoma and 6 cases of encapsulated papillary carcinoma.
Conclusion: The diagnostic of papillary malignant tumours is challenging due to their broad spectrum of clinical, imaging, and histologic characteristics. Their prognosis is better than the invasive carcinoma of no specific type, but their evaluation remains a problematic. Although many of them can be categorized based on H&E-stained sections alone, others require immunostaining. Further studies are needed to elucidate the pathogenesis of these lesions and the potential tools to stratify them.

OFP-02-020

Upgrade rate and risk factors associated with malignancy in breast papillary lesions diagnosed on core biopsy in Greater Vancouver, Canada: a preliminary analysis

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Background & objectives: Papillary lesions of the breast are a heterogeneous group. The histologic distinction between papillary breast lesions remains challenging. The aim of this study was to determine the rate of malignancy in excised papillary lesions and associated factors in Vancouver, Canada.
Methods: This is a retrospective study of all breast papillary lesions diagnosed on core biopsy between 2017 and 2019 in Fraser Health in Greater Vancouver area, with a 1.8 million population. Cases were categorized into benign, atypical, and malignant. Patient demographics, histopathologic, and radiologic findings were analysed.
Results: This is a preliminary analysis of 57 cases of papillary lesions, including 29 (50.9%) benign, 26 (45.6%) atypical, and 2 (3.5%) ductal carcinoma in situ (DCIS). Mean age was 59.3 years. The age profile of those with benign pathology was significantly younger (53.3 years) than those with malignant (63.5 years) (p=002). The upgrade rate in benign lesions to atypia/malignancy was 17.2% (5/29). Atypia on core needle biopsy was significantly associated with a final malignancy diagnosis (p<0.001). Upgrade rate to invasive carcinoma was found in 4/28 (14.3%) lesions with atypia. Final resection diagnosis with atypia/malignancy was significantly associated with lesions >10 mm and patients older than 55 years (p<0.01).
Conclusion: The overall risk of malignancy is significantly associated with older age, larger lesion, and the presence of atypia on core needle biopsy. The indications for surgical resection can be justified as age > 55 years and mass size > 10 mm, even in benign lesions in core biopsy. We suggest that close observation without surgery is sufficient for younger women with a small papilloma without atypia.

OFP-03 | Cardiovascular Pathology

OFP-03-001

Vitamin D deficiency and its correlation with morphological changes in peripheral arteries in the patients with a critical limb ischemia

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Background & objectives: Assessment of the vitamin D deficiency and morphological changes of arterial wall may help to clarify the reasons of aggressive course of the peripheral arterial disease (PAD) in patients with diabetes mellitus (DM).
Methods: A morphological analysis performed in 44 arteries of 17 amputated lower limbs in patients with DM. Evaluated in 30 patients with CLI levels of Vitamin D, parathyroid hormone, calcium, phosphorus, and cholesterol in the blood. Patients divided into two groups: patients with CLI and DM (19) and patients with CLI by pure atherosclerotic lesion of peripheral arteries (11).
Results: In 14 out of 17 vessels, calcification of the middle layer of the tibial arteries was revealed. The level of vitamin D is 11.16 ng / ml, in patients with diabetes - 8.42 ng / ml and without diabetes - 17.10 ng / ml. In chronic renal failure, vitamin D levels were below normal. In patients with chronic renal failure and diabetes, severe vitamin D deficiency in 85.8%, and without diabetes - 33.3%. The content of calcium, phosphorus, cholesterol is within normal limits. The level of parathyroid hormone is increased in patients with diabetes - 79.17 ± 11.7, in patients without diabetes - 62.86 ± 22.11 pg / ml.
Conclusion: Thus, this allows one to suspect a direct connection between vitamin D deficiency and CLI, especially in patients with DM. Given the presence of severe medicalcinosis, apparently it is necessary to reconsider the algorithm of therapy in patients with DM with CLI, by including Vit D for long life therapy.

OFP-03-002

COVID-19-associated pathology of heart

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Background & objectives: New coronavirus infection is accompanied by the development of a wide range of cardiovascular lesions. We studied the clinical and morphological features of SARS-CoV-2-associated pathology of heart, determining the presence of viral RNA and proteins in myocardial tissue.
Methods: The study was based on 55 autopsies with a confirmed coronavirus RNA in the myocardium (paraffin blocks). The average age of the patients was 72.8±14.1 years. Men predominated (52,7%). Immunohistochemical determination of the surface markers of CD3, CD20, CD45, CD 68, perforin, TLR-4, TLR-9 and SARS-CoV-2 nucleocapsid and spike-protein were presented.
Results: Lymphocytic viral myocarditis was detected in 35 cases (63.3%), including 8 cases with lymphocytic pericarditis and 11 cases with lymphocytic endocarditis. Coronariitis was found in 37 cases (67%) and endotheliitis in 8 cases (14.5%). Lymphomacrophage infiltration of myocardium (more than 7 CD3+ T-lymphocytes, more than 14 CD45+ lymphocytes and more than 7 CD68+ macrophages per 1 mm2) were found in cases with myocarditis. Virus proteins were identified in macrophages of the inflammatory infiltrate and endothelial cells. Chronic ischemic heart disease and hypertensive cardiomyopathy were detected in 32 cases. There were also of sludge phenomenon, coronary artery thrombosis and DIC syndrome in all cases.
Conclusion: Morphological and molecular findings confirm that COVID-19-associated pathology of heart may be presented by viral myocarditis, endo- and pericarditis.

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OFP-03-003

Post-Covid syndrome with persistence of SARS-Cov-2 in the myocardium and development of chronic myoendocarditis

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Background & objectives: Possibility of the development of post-COVID-19 myoendocarditis is discussed in the literature. Purpose: to study morphological and molecular features of myoendocarditis and its possible mechanisms (including persistence of SARS-Cov-2 in the myocardium) in the long-term period after acute COVID-19.
Methods: Five males (age 45.8±14.4) diagnosed with post covid myocarditis were included in the study. The diagnosis of COVID-19 was confirmed by positive PCR in myocardial biopsy. The average time of admission after COVID-19 was 4 months. The diagnosis of myocarditis was confirmed by right ventricular endomyocardial biopsy. The PCR for cardiotropic viruses and PCR with immunohistochemical study for SARS-Cov2 were used
Results: Three patients had no evidence of heart disease prior to COVID-19; another two patients had moderate arrhythmias or heart failure in the absence of evidence of myocarditis. The symptoms started 2-9 months following COVID-19. SARS-Cov-2 RNA was detected in 5 biopsies. The longest period of virus persistence after COVID-19 was 9 months. By using antibodies to spike and nucleocapsid antigenes, coronavirus was

detected in cardiomycytes, endothelium and macrophages. Lymphocytic myocarditis was confirmed immunohistochemically; giant cell myocarditis with atrial standstill was detected in one more case. Three patients had also signs of endocarditis, one case of infective endocarditis and two cases nonbacterial lymphocytic endocarditis with parietal thrombosis.
Conclusion: COVID-19 can lead to chronic myoedocarditis of varying severity. Post covid myocarditis manifests itself as isolated arrhythmias or systolic dysfunction with heart failure and characterized by prolonged persistence of coronavirus (up to 9 months) in combination with high immune activity. Prolonged post covid endocarditis associated with myocarditis, presents as non-bacterial thromboendocarditis or meets the criteria of infective endocarditis. SARS-Cov-2 persistence and autoimmune mechanisms play a significant role.

OFP-03-004
Aortic dissection and sudden cardiac death in the young
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Background & objectives: The link between bicuspid aortic valve (BAV) and aortic dissection (AD) was raised by early autopsy studies leading to the concept of BAV-related aortopathy. To assess the burden of BAV in juvenile SD and its histopathologic features.
Methods: The juvenile SCD Registry was searched for AD. Aortic diameters were measured at 4 different levels. Histopathological analysis was performed on the ascending aorta. Histopathologic changes of the tunica media in terms of mucoid extracellular matrix accumulation (MEMA), elastic fibre fragmentation and/or loss, and smooth muscle cell (SMC) nuclei loss were assessed.
Results: Among 816 SCD cases, 27 had aortic rupture including 24 AD (29.4%). Risk factors were BAV in 9 (37.5%), hypertension in 5 (21%), isolated isthmic coarctation in 2, pregnancy in 2, Marfan syndrome in 2, Turner Syndrome in 1, familial aortic dissection in 1 and idiopathic in 2. BAV-AD had significantly larger aortic diameters than BAV-non AD ($P < 0.05$). The proximal ascending aorta was significantly larger in Marfan-AD than in BAV-AD ($p=0.03$). Among histopathological changes of the tunica media, MEMA and elastic fragmentation were higher in Marfan (0.005 and 0.004) and SMC nuclei loss was higher in BAV (0.008). SMC apoptosis was higher in BAV than in controls ($p= 0.004$).
Conclusion: Juvenile SCD due to AD mostly recognizes a congenital or genetic background, with BAV identified in 37.5% of cases. Significantly smaller aortic diameters are observed in BAV than in Marfan syndrome patients and SMC loss is the more distinctive histopathologic feature.

OFP-04 | Cytopathology

OFP-04-001
Adequacy of cytology samples for molecular alterations in lung non-small cell carcinoma
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Background & objectives: Ancillary studies are essential for therapeutic guidance in non-small cell lung carcinoma (NSCC). Cytology is frequently the only material available for mutational analysis. The aim was to evaluate the adequacy of cytological samples for mutational alteration detection in lung NSCC.
Methods: A search was performed electronically on the departmental database for cytology samples with a diagnosis of NSCC for 18 months from April 2019. The data collected from cytology reports included the amount and type of the sample, type and adequacy of tumour as well as the results of ancillary investigations including PDL1, ROS1, ALK and EGFR.
Results: 117 cytology samples with NSCC were received during this period. A total of 87 cases required mutational analysis. However, these tests were not requested by the reporting pathologist in 6/87 cases (7%) due to insufficient tumour content. 74 of the remaining 81 cases (91.4%) were fully adequate for all requested tests. 7/81 samples (8.6%) showed partial to complete inadequacy, with PDL1 having the highest inadequacy rate (100%) while EGFR showed the lowest (20%). 2 out of the 3 samples with complete inadequacy were from bronchial washings/ brushings in which 12 and 15mls of fluid was received. While the third, was 20mls from a lymph node by transbronchial fine needle aspiration.
Conclusion: Cytology is a minimally invasive approach for the diagnosis and staging of non-small cell lung carcinoma. Our results demonstrate that cytology samples can provide sufficient material for detection of mutational alterations especially when biopsy is not available.

OFP-04-002
The prevalence and age distribution of high-risk *human papillomavirus* infection from Turkish women with normal cytology
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Background & objectives: The aim of this study was to investigate the prevalence and age distribution of high-risk *human papillomavirus* (hrHPV) infection from Turkish women with normal cytology.
Methods: Our study population consisted of 6273 women with normal cytology and adequate hrHPV molecular testing.
The cases were divided into 6 groups according to their age ranges as under 25 years old, 25-29 years old, 30-45 years old, 45-54, 55-65 and over 65 years old. Groups were compared with hrHPV positivity and type 16/18 positivity.
Results: HrHPV was detected in 689 (10.98 %) of 6273 cases. The positivity of hrHPV were 26.3% in group 1 (<25 years), 16.83% in group 2 (25-29 years), 10.7% in group 3 (30-45 years), 8.46% in group 4 (45-54 years), 10.72% in group 5 (55-65 years) and 4.65% in group 6 (> 65). There was statistically significant difference in the rates of hrHPV between group1 and the other groups ($p < 0.05$). There was statistically significant difference in the rates of hrHPV of group2 and the other groups ($p < 0.05$) . There was statistically significant difference in the rates of type 16 between groups 1 and the other groups ($p < 0.05$) .
Conclusion: According to meta-analysis studies, hrHPV positivity was reported to be approximately 6.6% in women with normal cytology. This rate ranges from 1.4% to 25.6%; more frequently in societies with low-medium socioeconomic status. In our study, regardless of age groups, this rate was found to be 10.98%, and it can be found in accordance with the literature.

OFP-04-003
The results of *human papillomavirus* testing and cytology with reflex mRNA expression analysis in the practice of liquid-based cytology in postmenopausal women
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Background & objectives: The goal of this study was to determine the accuracy of liquid-based Pap test and HPV genotyping for high-grade squamous intraepithelial lesions (HSIL) or severe and opportunity of the reflex mRNA expression analysis by quantitative PCR among postmenopausal women.
Methods: Histological follow-up results of 31 postmenopausal women with Pap test CellPrep and HPV testing results with HPV QUANT-21 Quantitative Real-Time PCR Kit were analysed. All cases were tested for the expression of the 21 genes (Ki-67, STK-15, CCNB1, CCND1, MYC,

MYBL2, P16INK4A, PTEN, BIRC5, BCL2, BAG1, TERT, NDRG1, ESR1, PGR, HER2, GRB7, MGB1, MMP11, CTSL2, CD68) in a residual media.
Results: We discovered that in histologically confirmed HSIL cases (n=10) there was the highest prevalence (100%) of hrHPV types with significant load of hrHPV 16 and 33. HPV-associated were 2 (100%) squamous cell carcinomas and 1 (50%) endocervical adenocarcinomas. At the threshold of LSIL positivity for histologically confirmed HSIL +, considering false positive conclusions about the presence of HPV in the case of a benign process (n = 10), the sensitivity was 88.24% for HPV DNA testing and 87.50% for cytology. The combined evaluation of the 21- gene expression panel allows, according to the discriminant analysis, to carry out the correct differentiation for HSIL+ from LSIL or less in 100%.
Conclusion: The evaluation of Pap test CellPrep media for hrHPV genotyping with viral load and cytology among postmenopausal women complement each other and therefore increase the diagnostic sensitivity of precancerous processes and cervical cancer, mainly squamous epithelial origin. The expression analysis of 21-gene panel by quantitative PCR may introduce like a reflex testing for severe cervical lesions including endocervical adenocarcinoma without association with HPV and requires further studying.

OFP-04-004
Metastatic Merkel Cell Carcinoma presenting as a solid pancreatic mass
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Background & objectives: Merkel Cell Carcinoma (MCC) is a rare skin cancer that frequently exhibits locoregional and distant recurrence, without a clearly defined treatment. Few cases of pancreatic metastases from MCC have been reported in the literature.
Methods: We present a case of a 63-year-old man with an enlarged right inguinal lymph node. Excisional biopsy diagnosed a metastatic MCC. Additional workup did not reveal the primary lesion and he was submitted to adjuvant radiotherapy. A follow-up computed tomography(CT) scan revealed a tissue densification in the right inguinal region and a 12x9cm mass involving the pancreatic body and tail.
Results: A positron emission tomography (PET) scan showed intense pancreatic uptake. An endoscopic ultrasound (EUS) was performed, showing an 8.6x8.3cm, hypoecoic, heterogeneous, ill-circumscribed lesion with local vascular spread. EUS-elastography revealed a predominantly hard pattern. A EUS-guided fine-needle aspiration with cytoblock was performed. Morphologically, the tumour displayed neuroendocrine architecture with mostly solid formations of small to medium round cells, with a high nuclear-cytoplasm ratio. It was mitotically highly active (>10 mitoses/mm2) and contained abundant necrosis. Immunostains for chromogranin and synaptophysin showed granular cytoplasmic staining and cytokeratin 20 demonstrated a dot-like perinuclear pattern, supporting the diagnosis of metastatic MCC. The patient was evaluated for systemic therapy.
Conclusion: MCC is a rare and aggressive neuroendocrine tumour of the skin that typically affects Caucasian patients over the age of 65 years. It commonly appears as a red to violaceous, indurated dome-shaped nodule or plaque on sun-exposed areas of the head and neck, with a high incidence of local recurrence, regional lymph node, and distant metastases. Metastatic spread to the pancreas is exceptional and its impact on prognosis and surveillance is unknown.

OFP-04-005
Pleomorphic adenoma: What features accompany false-positive and false-negative cases in cytological specimens?
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Background & objectives: Fine needle aspiration (FNA) is a well-established tool for preoperative diagnosis for salivary gland lesions. Pleomorphic adenoma (PA) is the most common salivary gland tumour comprising 45-74% of all salivary gland tumours with diagnostic accuracy of FNA to be 89.5-96.2%.
Methods: Specimens from parotid gland and submandibular gland with both cytological diagnosis and histological follow-up were searched over a ten-year-period (2009–2018) from a laboratory information system of Pathology Department, Fimlab Laboratories, Tampere and PA cytological and histological diagnoses were matched to determine concordant and discordant cases.
Results: Either cytological or histological PA diagnosis was given in 189 cases with 174 concordant cases and 14 discordant cases: 4 false-positive cases and 10 false-negative cases. Cell type predominance was more often myoepithelial in true-positive cases (65%, 13/20) and epithelial both in false-negative cases (73%, 8/11, p=0.001) and in false-positive cases (75%, 3/4, p=0.013). Only 10% (2/20) of true positive cases did not show matrix in cytology whereas 64% (7/11) of false-negative cases did not show matrix in cytology (p<0.001). Nuclear changes were rare in true positive cases (10%, 2/20) and common in false-negative cases (73%, 8/11, p=0.002) and false positive cases (75%, 3/4, p=0.018).
Conclusion: Statistical analysis showed diagnostic accuracy of 96.6% for FNA cytology regarding PA diagnosis. Sensitivity and specificity were, respectively, 94.6% and 98.2%. Positive predictive value and negative predictive value were, respectively, 97.8% and 95.6%.

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OFP-04-006
Cytomorphology, immunophenotype and cytogenetic profile of leukemic serous effusions
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Background & objectives: Serous effusions in leukaemia can be due to infections, therapy, volume overload, lymphatic obstruction or malignancy having implications on treatment and mortality. The objective of the present study is to highlight the cytomorphology, immunophenotype and cytogenetics in leukemic serous effusions.
Methods: Present study is retrospective and descriptive. We reviewed all the serous effusions which were reported as suspicious or positive of leukemic infiltration from 2016 to 2019 for cytomorphological features. CSF and effusions involved by lymphomas were excluded. Cytodiagnosis was compared with primary proven diagnosis (by ancillary techniques) and disconcordant cases were analysed.
Results: Out of total 9723 effusions, only 0.4% (n=40) showed leukemic involvement and included 9 cases of AML, 3 of B-ALL, 13 T-ALL, 2 MPAL, 6 CML, 5CLL, one each of CMML and AML with myelodysplasia. The most common site of involvement was the pleural cavity (n =30), followed by the peritoneal cavity (n=7) and the pericardial cavity (n =3). T –ALL (41.9%) was the most common leukaemia involving pleural fluid followed by AML (23.3%). CML (42.8%) was the most common leukaemia involving the ascitic fluid followed by B-ALL (28.6%). Accurate diagnosis was given on cytomorphology in 72.5% (29/40) cases and 15.0% (6/40) were reported as NHL.
Conclusion: Cytology is an effective tool available to make a diagnosis of LSE. Nuclear indentations in large atypical cells and cells with eosinophilic granular cytoplasm with sparse or abundant eosinophils in the background are an important clue in favour of leukaemia over lymphoma.

OFP-04-007
Comparison of conventional and liquid-based cytology using The Paris System for reporting Urinary Cytology
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Background & objectives: This is a retrospective study conducted in the Cytopathology Department of Laiko Hospital in order to compare the conventional cytospin method and the liquid-based urinary cytology in diagnosing bladder cancer by using The Paris System of urinary cytology classification.
Methods: We have searched our laboratory files in 2020 and we have retrieved 100 cases of void urinary cytology classified according TPS and including 35 TPS2, 25 TPS3, 20 TPS4 and 20 TPS5 cases. The number of cases chosen from each category was arbitrarily decided in order to compare the two methods in a meaningful manner.
Results: In the study material risk of malignancy (ROM) was 5.7% for TPS2, 28% for TPS3, 55% for TPS4 and 95% for TPS5. Agreement rate between cytospin and the original diagnosis was 86% and between Thinprep and the original diagnosis 82%. No significant differences were observed among the two techniques and their combination regarding sensitivity and specificity, with a mild advantage for the cytospin method. Intra-observer reproducibility and repeatability for the TPS was high.
Conclusion: Our study demonstrated that no significant differences exist concerning sensitivity and specificity among the two techniques used, when applying the TPS criteria. The TPS is a reliable classification scheme for either conventional/cytospin or liquid-based cytology or even the combination of them.

OFP-04-008
Immunocytochemical expression of Galectin 3 in the thyroid fine-needle aspiration (FNA) specimens
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Background & objectives: Galectin3 is a human lectin that is related to malignant transformation in thyroid gland and its expression in thyroid carcinomas was known. The aim of this study to examine the diagnostic utility of Galectin3 in the thyroid FNA specimens.
Methods: Fifteen papillary thyroid carcinomas (PTC) and 5 benign follicular nodules that diagnosed cytolomorphologically from 19 patients were evaluated. All slides prepared by liquid based cytology (LBC) (Surepath, BD®) and there were no cell blocks.
Immunocytochemical (ICC) analysis was performed with avidin-biotin-peroxidase complex on second slides that prepared by LBC, using the antibody Galectin 3 (Ventana Medical Systems®, Clon: 9C4).
Results: The mean age of patients was 44.1 ± 14.8 (Range 22-72 years). There were 4 male 15 female patients. Fourteen (93.3%) of the 15 PTC aspirates showed strong cytoplasmic and/or nuclear immunoreactivity for Galectin 3. The all of benign aspirates were negative. Focal positivity was seen in 2 of 14 immunoreactive PTC aspirates. If we consider cytomorphology the gold standard in this restricted study group the sensitivity and the specificity for Galectin 3 immunostainig were 93.3% and 100%, respectively.
Conclusion: A positive immunostain for Galectin 3 on a thyroid FNA is a strong supporter for PTC, whereas a negative result for Galectin 3 favor a benign nodule. With LBC additional slides can be obtained for additional studies such as immunocytochemistry. The Galectin 3 can be effectively applied to LBC slides of thyroid FNAs and can be a valuable ancillary marker in the cytologic diagnosis of PTC especially in FNAs with limited material.

OFP-04-009
Cytohistological correlation of salivary gland lesions
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Background & objectives: Fine needle aspiration (FNA) is an accurate minimally invasive technique used in the management of salivary gland tumours. Our aim is to study the utility of FNA in the diagnosis of salivary glands lesions through cytohistological correlation.
Methods: A total of 124 patients (69 women and 55 men; aged 22-92 years) with salivary gland lesions underwent surgery between 2010 and 2020: 68 had previous FNA. These FNA diagnosis were categorized according to the The Milan System for Reporting Salivary Gland Cytopathology and correlated with the surgical specimen diagnosis. The risk of malignancy (ROM) for each category was determined.
Results: FNA results: 11 non-diagnostic (ND), 1 non-neoplastic (NN), 3 atypia of undetermined significance (AUS), 44 benign neoplasms (BN), 8 salivary gland of uncertain malignant potential (SUMP), 0 suspicious for malignancy (SM) and 1 malignant (M). Histopathological follow-up: 55 benign tumours (32 pleomorphic adenomas, 16 Warthin tumours, 3 basal cell adenomas, 1 canalicular adenoma, 1 papilloma, 1 myoepithelioma, 1 sialolipoma), 6 malignant tumours (2 acinic cell carcinomas, 3 mucoepidermoid carcinomas, 1 carcinoma ex adenoma pleomorphic) and 7 inflammatory conditions. Excluding the ND, AUS and SUMP, 41 out of 46 (89%) cytological diagnoses had concordant histology. ROM for each category: ND 9.1%, NN 100%; AUS 0%; BN 6.8%, SUMP 0%, M 100%.
Conclusion: The percentage of concordant cases are within the range of published data. ROM by categories were different from the ones recommended by The Milan System for Reporting Salivary Gland Cytopathology. These results can be attributed, at least in part, to the small sample size. Most of the salivary gland lesions can be accurately diagnosed via FNA. In difficult cases, FNA is a useful diagnostic tool for risk stratification of these lesions.

OFP-04-010
Secretory carcinoma of the parotid gland: a tumour with many diagnostic clues
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Background & objectives: Secretory carcinoma is a rare tumour mostly affecting the parotid gland. It remains under-reported in the literature. We present a secretory carcinoma diagnosed on a cytology to increase awareness of its unique cytological features, key diagnostic, and molecular characteristics.
Methods: An ultrasound-guided fine needle aspiration of a parotid lump was obtained from a non-smoker elderly woman with past medical history of breast cancer. She presented with a history of a unilateral progressively enlarging parotid lump over several months.
Results: The cytology sample showed clusters and papillary configuration of small to medium sized uniform cells with vacuolated cytoplasm. The lesions cells characteristically lacked zymogen granules. The cells exhibit prominent hobnailing. The cells show pale vacuolated to eosinophilic cytoplasm. Immunocytochemistry showed positive staining for S100 and CK7, and patchy positivity for Mammoglobin. The cells were negative staining for DOG-1. Molecular testing confirmed the diagnostic ETV6-NTRK3 fusion.
Conclusion: Cytological diagnosis of salivary gland tumours possess major challenge, even for head and neck specialists. Diagnosing a rare tumour like secretory carcinoma requires a high index of suspicion and awareness of its characteristic cytological and histological diagnostic features. Confirming ETV6-NTRK3 fusion remains the gold standard for diagnosis, which can be done on both cell block and tissue samples.

OFP-04-011
Simulation module for palpation of lesions suitable for fine needle aspiration cytology. Validation study
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Background & objectives: Physical examination continues to be essential in clinical diagnosis. Adequate examination is a basic prerequisite for performing the fine needle aspiration (FNA) cytology technique on palpable lesions. With the goal of contributing to medical training, a simulation module was designed.
Methods: Taking advantage of the FioNA® simulator for FNA, modifications to the model were made. Handmade simulated lesions were designed, creating different clinical scenarios (neoplasms, cysts, and adenopathies) and providing a variety of tactile sensations (shape/size/consistency/demarcation/movement). It was evaluated for face and content validity by 30 specialists. Additionally, 23 third-year medical students were assessed after receiving basic theoretical training in palpation.
Results: The external aspect (appearance, location, degree of realism, and tactile sensation) of the modified model used to acquire palpation skills received an average rating of 8.9/10 (σ 0,78); the item that received the lowest valuation was the feeling when palpating (8.4/10; σ 1.9). The educational value (use for training, variety of exercises, and preparation for real-life procedures) was validated by all of the specialists. All but one of the physicians rated the variety of exercises as adequate. Moreover, the simulator was perceived as intuitive (9.2/10).
Regarding participant assessment, average student scores were 3.6/5 (range 1.2-4.6; σ 0.97); only 4 students received an unsatisfactory result (a score less than 2.5)
Conclusion: It is possible to adapt a palpation module to the FioNA® simulator for skills assessment.
This study showed face and content validity of this prototype for exploratory purposes.
Given that FNA is a routine medical procedure, formal training to acquire palpation skills seems appropriate.

OFP-04-012
Malignancy rate of atypia of undetermined significance/follicular lesion of undetermined significance in thyroid FNA in Greater Vancouver, Canada: a preliminary analysis
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Background & objectives: Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance (AUS/FLUS) is a challenging category comprised of a heterogeneous group of lesions. This study's objective was to evaluate the malignancy rate of the AUS/FLUS in fine needle aspiration (FNA) of thyroid nodules.
Methods: This is a retrospective cross-sectional study assessing malignancy rate in thyroid nodules FNA performed in Fraser Health in Greater Vancouver area, with a 1.8 million population, during a six-year period (2014-2019). FNA results were correlated with clinical outcome in subsequent years including repeat FNA, surgery, and clinical/imaging follow-up. Clinical and radiologic factors were compared to identify malignancy-related features.
Results: This is a preliminary analysis of 61 cases of AUS/FLUS. Mean age was 60.2 years, with 50/61 (82%) being female. Repeat FNA was performed on 21 (34.4%) nodules, and 30 (49.2%) underwent surgery. Of 21 repeat FNAs, 5 were AUS/FLUS, 7 benign, and 5 suspicious for follicular neoplasm or malignancy. 7 of 30 patients who underwent immediate surgery had papillary or follicular thyroid carcinoma. The upgrade rate to malignancy was 11.5% (7/61). There were no significant differences in age, sex, and nodule size between benign and malignant cases. The rate of malignancy was 14.3% (3/21) in patients underwent surgery, while it was 10% (4/40) for patients underwent repeat FNA (P>0.05).
Conclusion: The malignancy rate of AUS/FLUS in the study is consistent with the recommended range proposed by the 2017 Bethesda System for Reporting Thyroid Cytopathology. Demographic and radiologic findings were not significantly associated with upgrade malignancy risk. No significant difference was found in malignancy risk between those who underwent immediate operation following the AUS/FLUS diagnosis versus patients with repeated FNA after the initial diagnosis.

OFP-05 | Dermatopathology

OFP-05-001
Cutaneous metastases of internal malignancies: a single institution experience
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Background & objectives: Cutaneous metastases of internal malignancies are infrequent. Therefore, the diagnosis can sometimes be challenging, especially in cases with an unknown primary cancer. This clinicopathological study aimed to review the cases of cutaneous metastases of internal malignancies in our institution.
Methods: The retrospective review included all cases of skin metastases from non-cutaneous primary neoplasms diagnosed in the Department of Pathology at the Maastricht University Medical Center+ from 2006 to 2021. The clinicopathological data were collected, and appropriate immunohistochemical or molecular procedures were performed to confirm the primary origin of the metastases.
Results: We identified 132 cases of cutaneous metastases of non-cutaneous internal malignancies (74 female; 31 male patients; median age of 68.5 years [range 29 to 90 years]). Among the female patients, the most common primary tumour was breast cancer (46.2%), followed by lung (15.0%), tumours of gynecological (7.5%) and gastrointestinal origin (5.4%). Among the male patients, the most common primary sites were gastrointestinal and lung origin (altogether 46% of the specimen). In the majority of the cases, a primary tumour was known. However, in 11 cases, the cutaneous metastasis seemed to be the first presentation of the clinically silent malignancy (8.3%), leading to the diagnosis of a primary non-cutaneous malignancy.
Conclusion: Breast and gynecological tumours are the leading origins of cutaneous metastases in female patients, which is in line with previously published data. Lung and gastrointestinal cancer are among the most common primary tumours, demonstrating skin metastases in both female and male patients. Infrequently, cutaneous manifestation could be the first sign of a clinically silent visceral malignancy; therefore, broad immunohistochemical profiling and a high level of awareness are necessary for a precise diagnosis.

OFP-05-002
Nuclear protein in testis (NUT) expression and loss of C-terminus yes-associated protein 1 (YAP1) in a subset of hidradenomas
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Background & objectives: YAP1-NUTM1 fusion transcripts were recently identified in poromas, porocarcinomas, poroid hidradenomas and poroid hidradenocarcinomas. Adnexal tumours harbouring YAP1-NUTM1 fusions display immunohistochemical loss of YAP1 C-terminus and expression of NUT. Our aim was to analyse YAP1 and NUT expression in hidradenomas.
Methods: Our cohort included sixteen hidradenomas. We performed IHC for YAP1 (using an antibody specific for C-terminus YAP1) and

NUT on formalin-fixed paraffin embedded sections. We considered as YAP1 C-terminus negative cases with total loss of YAP1 C-terminus in tumour cells and positive staining in internal control (stromal and endothelial cells). NUT1 positive cases displayed strong and diffuse nuclear NUT expression.
Results: Four hidradenomas (4/16) had abolished YAP1 C-terminus expression whereas the rest (12/16) displayed cytoplasmic and nuclear (to a lesser extent) staining of comparable intensity to internal positive control. Robust nuclear NUT expression was detected in all (4/4) YAP1-negative hidradenomas. All cases that retained YAP1 C-terminus expression were negative for NUT (0/12). In summary, 25% of hidradenomas had a YAP1 negative/ NUT positive immunohistochemical profile.
Conclusion: YAP1-NUTM1 fusions are implicated in the pathogenesis of benign and malignant adnexal tumours. Immunohistochemical expression of NUT with parallel loss of YAP1 C-terminus in these tumours is a useful diagnostic tool and represents a surrogate marker for the presence of YAP1-NUTM1 fusion. Our findings indicate that a YAP1-NUTM1 fusion may be present in hidradenomas. Combined immunohistochemical and molecular analysis facilitates the diagnosis and may shed light to the genetic events driving the development of hidradenomas.

OFP-05-004
Clinicopathologic features and overal survival relationship in metastatic melanoma
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Background & objectives: Melanoma can metastasize both hematogenous and lymphatic routes. Five-year survival for melanoma with distant metastasis was reported as 22.5%. The present study evaluates the relationship between clinicopathologic parameters and overall survival for metastatic melanoma patients.
Methods: In this study, 122 metastatic melanoma cases (45 F, 77 M) that were metastatic at the time of diagnosis or consulted for molecular pathological analysis in the Gazi University Hospital, Pathology Department, were included. Pigmentation, necrosis, perivascular pseudorosette, tumour-infiltrating lymphocytes (TILs), pleomorphism, cell type, cytoplasmic and nuclear features, mitotic count were evaluated. Survival analysis was calculated using the Kaplan-Meier method.
Results: The mean age of diagnosis at the time of metastasis was 55.95 ± 1.35 years (range 19-89). At the end of the study, 26 (21.3%) of the patients were alive, whereas 96 (78.7%) were deceased. The diagnosis age of greater than 60 years had shorter overall survival than the patients with the diagnosis age of 31-60 years (p=0.013). Lung and central nervous system metastasis had a worse overall survival than lymph node, skin, and subcutaneous soft tissue. In contrast, liver, bone marrow, and paranasal sinus metastasis had shorter overall survival than lymph node metastasis. Perivascular pseudorosette formation was noticed in 64 metastatic melanoma cases and reduced overall survival time (p=0.002).
Conclusion: Ishida et al. described the perivascular pseudorosette formation of primary melanoma as a case report. Lugassy and Barnhill reported that angiotropism is seen more frequently in metastatic melanoma than melanoma without metastasis. This difference leads to an argument that melanoma metastasis pathways could include other options besides lymphovascular invasion. The reduced overall survival in metastatic melanoma that formed perivascular pseudorosette might support the idea of melanoma extravascular metastasis pathway in which melanocytes have a perivascular arrangement and show angiotropism.

OFP-05-005
NTRK - fused spitz tumours – histopathological, immunohistochemical and molecular features
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Background & objectives: Kinase fusions have been identified in Spitz tumours with subsequent studies aiming to characterise morphological features which may correspond to these fusions. The aim of our study was to examine the immunohistochemical and histopathological features of NTRK-fused Spitz tumours.
Methods: Immunohistochemical analysis of NTRK, ALK, ROS1 and BRAF with follow up molecular analysis was performed on 153 Spitz tumours over 8 years. We examined the histopathological features of the nine Spitz lesions with an NTRK fusion and compared them with those with ALK (7 cases) or ROS1 fusions (9 cases) and those without a kinase fusion to determine discriminating features.
Results: NTRK fusions were identified in 5.8% (9/153) of our Spitz tumours. The majority of Spitz tumours with an NTRK fusion occured on the extremities (77.8%). The majority of the NTRK-fused tumours (55.6%) were compound with spindle cell morphology. Filigree-like rete ridges were noticed in 55.6% of the lesions. 71.4% of the cases demonstrated a lobulated nest while only 16.7 % of the cases shows rosette-like configuration. In all the cases, immunohistochemistry for the pan NTRK antibody showed membranous and cytoplasmic staining in all cells. In 88.9% of the cases the intensity of the staining was strong (3+). Molecular studies confirmed 8/9 of the cases to have an NTRK fusion.
Conclusion: NTRK-fused Spitz tumours have distinctive histological features including lobulated nests and filigree-like rete ridges. The pan NTRK immunohistochemical antibody showed strong membranous and cytoplasmic staining in lesional cells and thus may be a useful tool in the arsenal in the diagnosis of Spitz tumours particularly when access to molecular testing may be limited.

OFP-05-006
Retrospective study of 31 cases of pityriasis lichenoides from a Portuguese dermatopathology department and review of the literature
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Background & objectives: Pityriasis lichenoides is an infrequent dermatosis whose clinical spectrum encompasses an acute form characterized by haemorrhagic, crusted and/or necrotic papules that resolve with varioliform scars, and a chronic form presenting with scaly papules. Histopathological diagnosis can be challenging.
Methods: We describe 31 patients with histopathologically confirmed diagnosis of pityriasis lichenoides diagnosed from 2010 to 2020. Our series had a female predilection, representing 61% of total patients and a broad age distribution at the time of diagnosis, between 5 and 67 years-old. Twenty three percent of the cases were diagnosed at paediatric age.
Results: Pityriases lichenoides et varioliformis acuta (PLEVA) represents 19,4% (six cases), including a 5-year-old boy and a 67 year-old woman. Histopathology revealed a dense dermal inflammatory cell infiltrate with extension into the epidermis, showing basal vacuolar change, focal spongiosis, apoptotic keratinocytes and focal epidermal necrosis. Edema of the papillary dermis and leukocytoclastic vasculitis were also common findings.
Pytiriasis lichenoides chronica (PLC) accounts for 80,6% of cases, with characteristic macules and papules with central mica-like scale. Microscopically it showed a predominantly lymphocytic perivascular infiltrate without vasculitis and minimal exocytosis of lymphocytes. Occasional extravasated erythrocytes were present.
No cases of the ulceronecrotic variant of PLEVA were reported and no cases progressed to lymphoma.
Conclusion: The diagnosis can be difficult, because clinical correlation is essential to confirm both forms, especially PLC, that presents more subtle histopathological findings. Erythema multiforme and lymphomatoid papulosis are the main differential diagnosis in PLEVA.
Our study also reveals that the majority of cases presented exacerbations and remissions in both forms of the disease (81%) with appearance of

new lesions that were responsive to treatment, predominantly oral antibiotics and topical corticosteroids.

OFP-05-007

Primary and Metastatic Cutaneous Lymphomas: a 10-year study from a tertiary center in Coimbra

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Background & objectives: Primary cutaneous lymphomas represent a diverse group of extranodal lymphomas and should be distinguished from secondary involvement, although the histopathology might be identical in both cases. Careful assessment of histology and clinical features are the mainstay of diagnosis.
Methods: Retrospective study of 118 patients with histopathological diagnosis of primary and metastatic cutaneous lymphomas from 2010 to 2020. There was not a significant sex predilection, with 51,6% being male patients; the youngest patient had 7 years old and the oldest one had 90 years old at the time of diagnosis.
Results: Primary cutaneous lymphomas represent 68,6%, while secondary involvement represents 31,4%. Mycosis fungoides is the most common diagnosis (33%), followed by primary cutaneous CD30-positive T-cell lymphoproliferative disorders (16,9%). Primary cutaneous diffuse large B-cell lymphoma, leg type represents 5,9%, primary cutaneous follicle center lymphoma and peripheral T-cell lymphoma NOS account for 3,4% each, extranodal marginal zone lymphoma 2,5%, and intravascular large B-cell lymphoma, subcutaneous panniculitis-like T-cell lymphoma, extranodal NK/T-cell lymphoma, nasal type, and primary cutaneous gamma delta T-cell lymphoma represent 0,8% each.
Diffuse large B-cell lymphoma (11%), follicular lymphoma (7,6%), extranodal marginal zone lymphoma (3,4%) and angioimmunoblastic T-cell lymphoma (1,7%) were the most frequent cases with secondary skin involvement.
Conclusion: The majority of primary cutaneous lymphomas has a good prognosis. In our series, mortality rate was 17,3% for primary lymphomas associated to progression of disease and late stage diagnosis and 54% for secondary involvement.
Primary cutaneous or secondary diffuse large B-cell lymphoma and peripheral T-cell lymphoma NOS had the worse outcome. However, more than half of mycosis fungoides had recurrent disease, seven of each died due to other comorbidities related to immunosuppression, such as organ transplantation and other non-lymphoproliferative neoplasms.

OFP-05-008

Detection of NTRK fusions in atypical Spitz tumours

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Background & objectives: Atypical Spitz tumours (AST) are melanocytic proliferations with uncertain malignant potential. Activating NTRK1/NTRK3 fusions act as oncogenic events in Spitz lesions and are targetable with kinase inhibitors. We aimed to define the optimal approach for their detection in ASTs.
Methods: 180 FFPE AST samples were screened with pan-TRK immunohistochemistry. The positive cases were further analysed with FISH (NTRK1, NTRK2, and NTRK3 probes), two different NGS panels for solid tumours, and specific real time RT-PCR panel to confirm the presence of NTRK fusions.
Results: Overall, 26 ASTs showed pan-TRK immunostaining. NTRK1 fusions were detected in 14 of these cases showing cytoplasmic immunoreaction, whereas NTRK3 was detected in the only case showing nuclear immunoreaction. The molecular tests resulted all positive in only 2 ASTs (included the NTRK3 translocated one), whereas FISH and real time RT-PCR were concurrently positive in another 2 cases. In 6 ASTs NTRK1 fusions were detected only by FISH, in 3 cases by both NGS and real time RT-PCR, and in the remaining one only by real time RT-PCR.
Conclusion: The frequency of NTRK fusions in ASTs is 8%, with a clear prevalence of NTRK1 compared to NTRK3 alterations. Pan-TRK immunohistochemistry is a good test to screen ASTs. The confirmation of NTRK fusions may require the use of different techniques.

OFP-05-009

Reflectance confocal microscopy (RCM) features of inflammatory skin disorders overlap with horizontal histopathological sections (HHSs)

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Background & objectives: RCM shows the epidermal layers and papillary dermis with a horizontal "point of view". The aim of this study was to compare the RCM features of skin inflammatory diseases with HHSs, that reflected the same observation plane as RCM.
Methods: Two 5-mm punch biopsies were performed in 19 selected patients (7 females and 12 males) affected by psoriasis (five cases), eczema (five cases), discoid lupus erythematosus (DLE) (3 cases) and molluscum contagiosum (MC) (6 cases). One biopsy was processed for vertical histopathology for diagnostic confirmation, one underwent extra paraffin-embedding for horizontal histopathology.
Results: A strong correlation between RCM features and HHSs was seen. RCM in eczema cases showed at the level of stratum spinosum hyporefractive areas with broadband intercellular spaces, with scattered round-polygonal mildly refractive cells, reflecting the spongiotic features and the presence of scattered lymphocytes intermingled with keratinocytes, seen on HHSs. On both techniques, dermal psoriasiform papillae were superficially visible, dilated and filled with tortuous vessels. DLE RCM epidermal images showed roundish areas filled with hyperrefractive amorphous material (follicular plugging) and partial disappearance of the dermal papillae. RCM in MC cases exhibited roundish lobules filled with bright cells, corresponding to the histopathological lobulated squamous-cell hyperplasia, composed of large keratinocytes with Henderson-Paterson bodies.
Conclusion: This comparative study between horizontal histopathology and RCM imaging is useful to further validate the diagnostic use of RCM in dermatological clinical practice. The possibility to create a panel of morphological matches between these two techniques may also improve the accuracy of the dermatologists in choosing the best site for biopsy sample, or in promptly recognizing a potential relapse of disease.

OFP-05-010

Does the sampling method have any impact on the evaluation of skin biopsies?

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Background & objectives: Skin diseases are common health problems. They are evaluated with punch biopsies, especially in clinically challenging situations. There are different sampling methods for skin biopsies. The aim of this study is to compare two different techniques with the clinicopathologic findings.
Methods: 608 skin punch biopsies of 529 patients between May 2020 and March 2021 were included in the study. 339 biopsies were sampled without cutting, while 269 biopsies were cut into two equal parts. The site, diameter, preliminary diagnosis were collected from the clinical data. The histopathological findings were obtained from pathology reports. The results were statistically analysed.

Results: Of the 529 patients, 54% were female and the average age was 42,8+ 19,8 (range 0-91). The lower extremity was the most common biopsy site (229 patients, 43%). The average biopsy diameter was 1.05 cm (range 0.1-2 cm). Perivascular dermatitis was the most common histopathologic diagnosis (176 biopsies, 29%). The number of serial sections were significantly lower in the group which underwent macroscopic cutting technique (p=0.001). Clinicopathologic discordance was seen in 103 biopsies (17%). More sections were significantly requested in case of clinicopathologic incompatibility (p=0.01). When compared to interphase and psoriasiform group, more extra sections were evaluated in bullous dermatitis (p=0.01).
Conclusion: In this study, we evaluated big number of biopsies with different sampling methods. Our findings suggested that dividing biopsies into two equal parts reduced the necessity of extra sections. Besides the sampling methods, one of the reason for extra sections was clinicopathologic discordance. The other reason was some lesions tend to appear in focal areas and they can show up in extra sections. If suitable conditions are provided, applying the cutting method can reduce expenses and shorten pathology report time.

OFP-06 | Digestive Diseases Pathology - GI

OFP-06-001
MLH1/PMS2 expression could tell classical NTRKs fusion in fluorescence in situ hybridization positive colorectal carcinomas

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Background & objectives: To gain insight into the clinicopathologic profile of colorectal carcinomas harbouring oncogenic NTRK fusions based on eastern populations as well as make the best testing algorithm for the screen.
Methods: We use pan-Trk immunohistochemistry (IHC), fluorescence in situ hybridization (FISH) respectively to screen NTRK fusions in a large, unselected cohort of 819 colon cancers, either IHC or FISH positive cases were further detected by next-generation sequencing (NGS).
Results: IHC staining was observed in ten cases, FISH positive was observed in 13 cases, total of 18 cases were under both a DNA-based and an RNA-based NGS assay. For clinicopathologic characteristics, besides MMR status (p=0.001), there is no difference between NTRK fusion-positive and negative cases. Nevertheless, classical fusion cases prefer to low differentiation (p=0.001) and different pattern of growth(p<0.001). Besides, we found all five classical NTRK fusion cases and only one sub-classical case were harbouring MLH1/PMS2 deficiency. When combining FISH and MMR status, besides one sub-classical case, all five classical fusion were all detected, which means MLH1/PMS2 expression could further narrow classical fusions in FISH NTRK fusion positive cases.
Conclusion: Combine FISH and MLH1/PMS2 IHC would be a good testing algorithm for the screen effective NTRK fusions. Finally, if patients are going to undergo TRK-based targeted therapy only RNA-based NGS for detection of the specific fusion could tell the precise rearrangement information.

OFP-06-002
Human epidermal growth factor receptor 2 positivity in gallbladder carcinoma is associated with papillary structure and shows bidirectional prognostic value

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Background & objectives: Gallbladder carcinoma (GBC) is associated with poor prognosis. HER2 is a promising therapeutic targe for GBC. The objective of this study is to explore HER2 status in a cohort of patients with GBC and its correlations with clinicopathological features.
Methods: High-output tissue microarrays were constructed for 306 cases of GBCs. HER2 expression was assessed using immunohistochemistry (IHC), and HER2 gene amplification was assessed using fluorescence in situ hybridization (FISH) in accordance with the up-to-date consensus for HER2 testing in gastric cancer. Correlations between HER2 status, clinicopathological parameters, and survival data were analysed.
Results: Of 306 GBC cases, 223 (72.9%) were adenocarcinomas, of which, 62 (27.8%) cases were papillary adenocarcinomas or had partial papillary structure. HER2 positivity was observed in 16.1% (36/223) of patients with adenocarcinomas. However, HER2 positivity was higher in adenocarcinomas with papillary structures (41.9%, 26/62, P < 0.001). Survival data were available for 143 radical resected primary gallbladder adenocarcinoma cases with 24 HER2-positive tumours; the five-year survival rate was 52.9%. In stage 0-II, the HER2-positive group had a similar prognosis to that of the HER2-negative group (P = 0.354). The HER2-positive group had a lower mortality rate in stage III (P = 0.005), but higher mortality in stage IV (P =0.005).
Conclusion: HER2 positivity was significantly higher in patients with gallbladder adenocarcinoma with a papillary structure. The prognostic value of HER2 was discordant among different clinical stage in GBC, showing no predication in the early stages, better in stage III, but worse in stage IV.

OFP-06-003
BRAF mutational testing practices in metastatic colorectal cancer

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Background & objectives: The metastatic colorectal cancer (mCRC) treatment landscape is rapidly evolving. Molecular testing is critical for guiding treatment decisions according to current guidelines. Determining BRAF mutation status is of diagnostic and therapeutic relevance. Many methods exist for BRAF mutational testing.
Methods: BRAF mutation testing practices in BEACON CRC study and BRAF ring trial (Quality Assurance in Pathology, QuIP) for mCRC 2020 were reviewed. We evaluated the methods used for BRAF status determination from 510 samples in BEACON CRC study, the largest Phase III trial in BRAFV600E-mutant mCRC. We evaluated real-world BRAF diagnostic testing practices in mCRC across 53 sites in Germany.
Results: In the BEACON CRC study, 50.5% of BRAF tests were performed alongside those for other gene alterations. Single gene detection was used in 48.8% of samples; IHC employing antibodies for detecting the mutated BRAF protein was used in 0.7% of samples. Discrepancies were observed between local and central testing, with confirmation of a locally detected BRAFV600E mutation in 90.7% of samples. Most discrepancies were due to insufficient neoplastic tissue in the sample. In the BRAF ring trial for mCRC, a broad range of methods for BRAF testing were used (NGS, PCR, IHC), with varying reliability. Molecular testing was the most reliable method (100% of positive tests vs 67% for IHC).
Conclusion: BRAF mutational testing is necessary in all patients with mCRC before initiation of first-line treatment. There are a large number of methods available for determining BRAF mutational status; however, the reliability of the tests vary. The BRAF ring trial for mCRC demonstrated the need for standardization of diagnostic procedures. Other tests are preferred over IHC for testing of genetic alterations in mCRC; the BRAF antibody IHC test may be useful for screening, however, molecular testing is the gold standard.

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OFP-06-004

Ex vivo sentinel lymph node mapping and one-step nucleic acid amplification (OSNA) for ultrastaging in gastric cancer

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Background & objectives: One-step nucleic acid amplification (OSNA) is an established method for molecular lymph node (LN) staging by detecting cytokeratin 19 (CK19) mRNA. In this study, the effectiveness of OSNA with ex vivo SLN mapping is compared with conventional histology including immunohistochemistry.
Methods: LNs were retrieved from gastrectomy specimens in an unfixed state and after ex vivo SLN mapping using methylene-blue. LNs were sectioned to provide samples for histological investigation and OSNA. After fixation, further LNs were dissected to gain sufficient LN counts.
Results: In total, 334 LNs were retrieved in fresh state from 41 patients. SLN detection was successful in 29 out of 40 cases, with a correct LN status prediction in 23 cases (79%). The low ex vivo SLN detection rate resulted in an overall accuracy of only 58%. Excluding one case with failure likely caused by processing error, OSNA showed a high effectiveness with sensitivity, specificity, and accuracy rates of 85.4%, 93.5%, and 92.4%, respectively. The LN status could be predicted in all but one case, in which the single positive LN was not eligible for OSNA testing. OSNA evaluation led to upstaging from N0 to N+ in three cases (14%).
Conclusion: The ex vivo SLN protocol used resulted in a relatively poor detection rate. However, the OSNA method was not compromised by this detection rate and proved to be a safe method for LN staging in gastric cancer. The OSNA method has the potential to surpass conventional techniques.

OFP-06-005

Predictive value of NLR, TILs (CD4+/CD8+) and PD-L1 expression for prognosis and response to neoadjuvant chemotherapy (NAD-CT) in locally advanced Gastric Cancer (LAGC)

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Background & objectives: The combination of perioperative chemotherapy plus complete surgical resection is currently accounted as the first-choice strategy in patients with LAGC. Nevertheless, the partial response rate makes it necessary to search parameters to select patients who would benefit most from NAD-CT.
Methods: We performed a retrospective analysis on a cohort of 65 LAGC cases, EBV negative and without MMR defect, submitted to NAD-CT plus surgical resection. We evaluated the neutrophil-lymphocytes ratio (NLR) in peripheral blood (before and after treatment) and the TILs density (CD4/CD8 tissue ratio) and PD-L1 expression by immunohistochemistry (IHC) on bioptic tissues before the treatment.
Results: Our results were correlated with the biological features, histological response (TRG) and clinical outcome (PFS and OS). We found that NLR, TILs and PD-L1 expression showed a significant correlation with TNM stage, lymphovascular invasion and response to NAD-CT (TRG). Correlating the NLR, TILs and PD-L1 expression with PFS and OS, we found that patients with lower NLR levels (<2.5 ratio), lower TILs (<0.2 ratio) and higher PD-L1 level (CPS≥1) had a significantly better PFS and OS than those with higher NLR, higher TILs and lower PDL1 expression ($p<0.0001$). Multivariate and multiple regression analyses confirmed the predictive and prognostic role of all three parameters, especially when all three parameters are combined.
Conclusion: Our study demonstrated that pre-treatment NLR, TILs and PD-L1 expression, are predictive and prognostic parameters in NAD-CT treated LAGC suggesting a pivotal role of the systemic and tumour microenvironment (TME) immunological profile in the response to chemotherapy.

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OFP-06-006

Immunohistochemical expression of autophagy-related proteins in HER2 positive gastric carcinomas

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Background & objectives: Autophagic related proteins (ATGs) have been analysed in differentiation and cancer progression. The aim of the present study is to investigate a cohort of gastric carcinomas (GC) by five ATGs antisera evaluating their possible relationship with final outcome of patients.
Methods: 123 GCs has been studied by ATG antisera utilizing Masuda's criteria that define positive cases those in which at least two out of five protein expressions were documented. Sensitivity, specificity and efficiency (expressed as a result in percentage of what could be ideally expected, hence with 100% as ideal case) of each immunohistochemical expression of autophagy-related-proteins have been evaluated.
Results: The immunohistochemical signature for autophagy (A-IHC) was 49.59% as whole. The percentage of A-IHC ranged from 31% for poorly cohesive carcinomas to 56% for adenocarcinomas. High values for sensitivity, specificity and efficiency were recorded relatively to LC3A/B, Beclin-1 and p62. In univariate analysis of GC, grade, stage, Ki67 expression, HER2 status as well as A-IHC appeared as prognostic significant parameters with a high p-value ($p < 0.001$). Finally, in multivariate analysis HER2 status, stage and A-IHC emerged as independent prognostic variables. In the comparison of survival curves, GC cases immunoreactive for A-IHC exhibited a shorter survival with a worse outcome.
Conclusion: A-IHC could represents an additional morphological tool to provide prognostic elements in order to identify patients affected by aggressive with shorter survival and worse outcome.

OFP-06-007

Prognostic significance of the lymph node ratio in stage III colorectal adenocarcinoma

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Background & objectives: The lymph node ratio (LNR) may offer superior prognostic stratification in colorectal adenocarcinoma compared with the N stage. However, candidate cut-off ratios require validation. Our aim was to study the prognostic significance of LNR at a cut-off ratio of 0.10.
Methods: We reviewed the pathology records of all patients with stage III colorectal adenocarcinoma who were managed at the King Hussein Cancer Center between January 2014 and December 2019. We then studied the clinical characteristics of the patients, correlates of the lymph node count, prognostic significance of positive lymph nodes, and value of sampling additional lymph nodes.
Results: We included 226 patients. The number of lymph nodes sampled was < 12 in 13 cases (5.8%) and ≥ 12 in 213 (94.2%). The median number of lymph nodes sampled varied according to tumour site, neoadjuvant therapy, and the pathologist's level of training. According to the TNM system, 142 cases were N1 (62.8%) and 84 were N2 (37.2%). The LNR was < 0.10 in 98 cases (43.4%) and ≥ 0.10 in 128 (56.6%). Survival distributions differed according to LNR ($p = 0.022$) but not N stage ($p = 0.065$). In adjusted analyses, both N stage and LNR predicted overall survival ($p = 0.044$ and $p = 0.010$, respectively).

Conclusion: The LNR is a robust predictor of overall survival in patients with stage III colorectal adenocarcinoma. At a cut-off ratio of 0.10, the LNR offers better prognostic stratification compared with the N stage and is less susceptible to variation introduced by the number of lymph nodes sampled, which is influenced by both clinical characteristics and grossing technique.

OFP-06-008

Inter-laboratory variation in the assessment of lymphovascular invasion in T1 colorectal cancer in the Netherlands

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Background & objectives: Lymphovascular invasion (LVI) is a risk factor for lymph node metastasis in T1 colorectal cancer (CRC). When LVI is present in the local resection, complementary surgery needs consideration. We aimed to study the inter-laboratory variation in the assessment of LVI.
Methods: All synoptic pathology reports of locally resected T1 CRCs between 2015 and 2019 were retrieved from the Dutch Pathology Registry (PALGA). Absolute proportions of LVI per laboratory were determined and compared between the laboratories. Multivariable logistic regression was performed to adjust for case mix. Additionally, a questionnaire about assessment methods and criteria for LVI was circulated among 50 pathologists.
Results: In total, 5917 T1 CRCs from 35 laboratories were included. Of these T1 CRCs, 18.3% were reported to have LVI (range 7.1% - 43.5%). After adjustment for case mix, still 37% of laboratories (n=13) reported a proportion of LVI outside the 95% confidence interval limits of the overall national proportion. In a subgroup of 3459 patients where LVI would have been the decisive factor for additional surgery (i.e., patients without other high-risk factors), case-mix adjusted proportions of LVI varied between the laboratories by a factor of nine (range 4.6% – 41.7%). The questionnaire showed considerable differences between pathologists in definitions and methods used to assess LVI.
Conclusion: The results of this nationwide study show that substantial inter-laboratory variation in the assessment of LVI in T1 CRC exists, independent of case mix. This variation might be partly explained by differences in assessment methods and criteria, suggested by the results of our questionnaire. This underlines the importance of standardization of the assessment of LVI, because the observed variation may lead to unwanted differences in treatment of patients with T1 CRC.

OFP-06-009

Shrinkage versus fragmentation response in neoadjuvant treated oesophageal adenocarcinoma: significant prognostic relevance

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Background & objectives: No consensus exists on different tumour regression grading (TRG) systems for therapy effects of neoadjuvant chemoradiotherapy (nCRT) in oesophageal adenocarcinoma. The aim is to identify tumour regression patterns of oesophageal adenocarcinoma in response to nCRT, and their association with survival.
Methods: Patients with a potentially curable oesophageal adenocarcinoma (cT1-4N0-3M0) who achieved partial response to nCRT combined with surgery in the period 2005–2018 were included. Two representative H&E slides of the surgical specimen were selected per case for histomorphologic assessment of the regression pattern. Scoring of regression patterns was performed by two observers according to a predefined three-step flowchart.
Results: In total, 110 cases were included. Histopathology review showed two major regression patterns: fragmentation (60%) and shrinkage (40%). There was an excellent interobserver agreement using the flowchart (κ=0.87). Compared to patients with a shrinkage pattern, patients with a fragmented regression pattern had a significantly higher pathological stage (stage III/IV: 52% vs 16%; p<0.001), less downstaging (48% vs 91%; p<0.001), higher residual tumour cells in the muscularis (88% vs 32%; p<0.001) and subserosa (67% vs 16%; p<0.001), and a higher risk of disease recurrence (RR 2.83, 95% CI 1.5-5.5). Patients with a shrinkage pattern had a better overall survival compared to patients with a fragmentation pattern (5-years: 80% vs 30%, p=0.002).
Conclusion: We established a reproducible classification of tumour response that was associated with downstaging and better prediction of patient outcome.

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OFP-06-010

The prediction model for gastric cancer development based on gastritis assessment and miR-21 expression

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Background & objectives: The accuracy of gastric cancer risk evaluation can be increased by joint assessment of gastritis parameters, including corpus-predominant gastritis index (CGI), gastritis OLGA staging and miR-21 expression with gastric cancer risk stratification.
Methods: All parameters were assessed in 62 cases of chronic gastritis (CG) and 60 resected gastric samples (adenocarcinoma). Samples localization in both group corresponded to the OLGA staging protocol. miR-21 expression was evaluated by qRT-PCR, normalized to RNU6B. Multiple logistic regression was used for predictive potential assessment and nomogram construction.
Results: Predictor variables showed significant positive association with gastric cancer: OLGA stage (OR = 8.07, CI [1.52-42.85]; p= 0.013), CGI (OR = 11.77, CI [2.59-53.6]; p= 0.001) and miR-21 expression (OR= 13.56, CI [4.6-40.04]; p 0.000002). Parameters after model accuracy estimation were as follows: -2 Log likelihood - 58,3, criterion $\chi 2$ - 110,84 (p=0.00001), ROC curve AUC - 0.97, sensitivity 93%, specificity 90%. The constructed nomogram indicates gastric cancer risk by connection the value of OLGA stage (right axis) with the expression level of miR-21 (left axis) and tailored to the CGI value. Indication and stratification of gastric cancer risk based on the result value.
Conclusion: The predictive statistical model and the nomogram based on previously defined parameters allows to perform stratified assessment of gastric cancer risk with having high validity. This approach can be used in organizing strategies for secondary prevention of gastric cancer.

OFP-06-011

HER2 assessment for differential diagnosis in gastric precancerous lesions

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Background & objectives: Amplification of HER2 is suitable not only for gastric cancer, but for precancerous changes also. The aim of the study was to reveal the usefulness and patterns of HER2 protein and gene expression on the spectrum of carcinogenesis.

Methods: Gastric biopsy samples (n=111) were included in the study: atrophic gastritis (26), uncertain/indefinite dysplasia (21); intestinal type adenomas and non polipoid lesions with low-grade dysplasia (18) and high-grade dysplasia (23); early invasive adenocarcinoma (23). 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 pattern were found in 14 cases: 5 among invasive carcinoma group with SISH confirmation of all 2+/3+ positive cases, 1 in indefinite, 3 in high grade dysplasia and 2 in low grade. The presence of non-conventional staining variants of HER2 expression were revealed in 52 cases: apical label (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 ($p<0,05$).
Conclusion: We did not reveal the presence of classical significant HER2 overexpression during early precancerous changes. Non-conventional HER2-staining needs more data and additional analysis for practical interpretation and realisation of appropriate follow up strategy. These results defined the possibility of using this marker for differential diagnostics in the situations of small volume or low informative biopsy material according to its high specificity.

OFP-06-012
Identification of Epstein-Barr virus-encoded small RNAs (EBER) in gastric adenocarcinomas
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Background & objectives: Gastric adenocarcinoma associated with the Epstein-Barr virus is a separate molecular subtype of gastric cancer with a characteristic set of genetic disorders and clinical and morphological features. In this study we performed EBER identification in patients from the Russian Federation.
Methods: We used samples of surgical material from 233 patients from Russian Federation with a verified gastric cancer. EBER chromogenic hybridization in situ (EBER-CISH) was performed in each case. The results of EBER identification were compared with the main clinical and morphological characteristics of gastric cancer.
Results: A total of 18 EBER-positive gastric adenocarcinomas and 215 negative cases were identified using EBER-CISH. The frequency of occurrence (incidence) was 7.73%. As in other described patient populations the identified EBV-associated gastric adenocarcinomas were characterized by a less aggressive phenotype. EBER identification in gastric adenocarcinomas was statistically significantly associated with the absence of distant metastases ($p=0.047$). Among all 18 identified cases of EBV-associated adenocarcinomas there were no cases with distant metastases and, accordingly, IV stage tumours. There were no statistically significant differences for other TNM clinical stages. This fact can be explained by the significant dominance of 106 cases of III stage tumours in our sample.
Conclusion: It is known that the prevalence of EBV-associated gastric adenocarcinoma differs depending on the population. The results obtained showed that the incidence of EBV-associated gastric adenocarcinoma in the studied sample of cases from Russian Federation is 1.27% lower than the world average of 9%.

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OFP-06-013
Immunohistochemical markers as additional criteria for evaluation of efficacy of GERD-related therapy
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Background & objectives: Pathogenesis of gastroesophageal reflux disease (GERD) has close association with intercellular contacts and appropriate level of epithelial proliferation. The aim was to determine the potential of histopathological changes and IHC markers for assessment of 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 esophagus were taken for analysis by histopathology and claudin-1, claudin-4 and Ki-67 expression assessment by immunohistochemistry.
Results: GERD-specific alterations in the esophageal 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 and claudin-4 were statistically higher after therapy ($p < 0,05$). Migration of claudin-1 expression towards the upper layers of esophageal 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 (claudins) and Ki-67 can be used as additional criteria for evaluation of efficacy of GERD therapy.

OFP-06-014
Assessment of the density of the population of cancer-associated fibroblasts near the tumour budding in colorectal cancer
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Background & objectives: Cancer-associated fibroblasts (CAF) are cells with mesenchymal properties located in the tumour stroma. One of CAF`s marker is podoplanin (POD). Tumour budding (single cells are located in the invasive edge of the tumour) is an independent prognostic factor.
Methods: We used Double Stain IHC Kit: M&R on human tissue (ab210058) with antibodies PCK (Dako, to identify buds) and POD (Abcam, as CAF marker) in 43 colorectal cancer. POD expression was evaluated by quantitative method (by color separation and half-counting of the area in the field of view in the LAS X program) in invasive region and around buds.
Results: The aim was assessment of the density of CAF near the buds. POD around bud was negative in 30,4%, weak in 21,7%, moderate in 30,4% and significant (17,4%). A statistically significant relationship ($p<0.01$) was found between the level of POD around the tumour budding and its level in the invasive region. No significant differences in the density of CAF depending on the presence of the mucinous component, detected by the c2method($p=0.98$). In most mucinous adenocarcinomas, a significant POD reaction was observed directly around the mucinous complexes and mucus lakes ($p=0,85$). We detected a relationship ($p=0,023$) between presence of buds and depth of tumour invasion(T), and on the presence of metastases(N).
Conclusion: Using the duplex stain technology, the expression of POD around tumour budding was demonstrated for the first time, which allows

us to judge the density of CAF. It was shown that the density of the POD expression around the tumour budding significantly corresponds to the reaction in the invasive region, which indicates that there is no need to evaluate it specifically around the tumour buds. For the first time, we described a more significant reaction near mucinous complexes.

OFP-06-015

Lymph node molecular analysis of colorectal carcinoma in situ

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Background & objectives: Colorectal carcinoma in situ (pTis) is considered to have little or no risk of lymph node (LN) metastasis. However, lymphatic vessels proliferate in the lamina propria through a process of "aberrant lymphangiogenesis". We aimed at characterizing pTis LNs with OSNA.
Methods: In this observational and retrospective study, LNs from pTis CRC surgical specimens were freshly dissected. Part of the LN was used for conventional histological stage with H&E (pN) and the rest used for analysis with the OSNA (One Step Nucleic Acid Amplification) molecular assay, based on RT-LAMP PCR, for amplification of CK19 mRNA.
Results: LNs from 39 CRC pTis were analysed by H&E and OSNA. Mean age was 68.6 years-old, 59% (23) men, 41% (16) women; 56% (22) were right-sided, 23% (9) transverse, 15% (6) left-sided, and 6% (2) rectal. All carcinomas were low grade. All cases were pN0 by H&E. OSNA was positive in 11 (28%) cases, with a total tumour load (TTL), defined by the amount of CK19 mRNA copies/μL in all LN of a given case, was between 400 and 4270 copies/μL. No patient received adjuvant therapy. All patients are alive without disease at 1 to 5 years follow-up.
Conclusion: We demonstrate the presence of tumour cells in regional lymph nodes in exceedingly early stages of the disease, detected only by molecular methods. We corroborate our previous observations of the prognostic value of the amount of tumour burden in LNs, demonstrating that TTL values <6000 copies/μL are not associated to risk of recurrence.

OFP-06-016

Entire Lymph Node Molecular Analysis (ELNMA) of colorectal carcinoma. Correlation with pN staging using immunostained cytology smears. A multicentre study

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Background & objectives: All lymph node (LN) molecular staging studies using OSNA from colorectal cancer (CRC) have used half LN obtaining 15-50% overstaging. We aimed at analysing the entire LN with OSNA as well as providing the pN staging with cytological smears.
Methods: This ongoing multicenter and prospective ELNMA (Entire Lymph Node Molecular Analysis) study includes non-metastatic CRC patients without neoadjuvant treatment. LNs are freshly dissected, cut in half and cytological smears are performed. Then, the whole LN is processed with the OSNA assay. Each slide contains smears from 6 LNs, which are stained with cytokeratin 19 (CK19) immunocytochemistry for pN staging.
Results: We analysed 980 fresh LNs from 53 patients (mean 18 LN/patient); 57% (30) men, with a mean age of 71.36 years. By cytology, 81% (43) cases were pN0, 15% (8) pN1a+b, and 4% (2) pN2a+b. The concordance between OSNA and cytology was 96% (51). All OSNA negative cases (41; 77%) were negative by cytology, and two presented isolated tumour cells (ITC) on cytology smears, pN0(i+). OSNA positive cases (12; 23%) had total tumour loads (TTL, amount of CK19 mRNA in all LNs/patient) of 410 to 88.000 copies/μL, with 83% (10) concordance with the cytology. The remaining 2 cases were pN0 by cytology, with TTL of 410 and 5800 copies.
Conclusion: LN cytology smears stained with CK19 immunocytochemistry allows performing the pN stage based on the number of positive LNs and enables to use the entire LN for the OSNA assay, with 96% concordance. LN molecular analysis identifies 4% (2) of patients who were pN0 by morphological methods. Although preliminary, these results show the utility of molecular LN staging, which could be used for stage II CRC, where conventional H&E pN staging is less sensitive for the detection of micrometastasis.

OFP-06-017

pT1 CRC patients at risk of recurrence are identified with lymph node molecular analysis. A multicentre study

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Background & objectives: A high percentage of early colorectal carcinomas (pT1) undergo surgery, with no clear impact on survival. Molecular analysis of lymph nodes of pT1 surgical resections was performed in order to identify cases at risk of recurrence to optimize patient's management.
Methods: In this multicentre retrospective study we analysed the lymph nodes (LN) from pT1 CRC surgical specimens treated either primary by endoscopic resection or by surgery using the OSNA (One Step Nucleic Acid Amplification) assay, which detects mRNA from CK19. LNs were freshly dissected, using half for the OSNA assay and the other half for H&E analysis.
Results: Eighty-nine pT1 CRCs were included, 50 treated with endoscopy followed by surgery and 39 treated primarily with surgery. Mean age 62.6 years, 55% male, 49% in the left colon, 37% right, and 14% rectal. 22 cases (25%) had positive LNs with OSNA, 5 of them also with H&E. The total tumour load (amount of CK19 mRNA in all LNs of a patient) was low, but for 3 cases with ≥6000 copies. LNs were positive with H&E in 9% (n=8), two of them were negative by OSNA. At follow-up (5 months to 8 years), 82 patients are alive without disease, 3 died of other causes, and 4 were lost to follow-up.
Conclusion: We detected 25% lymph node positivity with the OSNA assay, 16% more than with H&E. The total tumour loads (TTL) were low in all patients except in 3 cases with TTL > 6000 copies/μL, which is associated with a higher risk of recurrence and worse survival according to previous studies. These patients would be candidates for closer follow-up. Molecular LN analysis from early CRC provides more information than H&E about the real nodal status and could help in patient's management.

OFP-06-018

The relationship of clinicopathological features and the Ki67 proliferation index with prognosis in colorectal carcinomas

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Background & objectives: Colorectal cancers are very common. Many histopathological and molecular features that can be used to predict the prognosis. It was aimed to investigate the prognostic significance of the histopathological features and the immunohistochemical Ki67 proliferation index in colorectal cancers.
Methods: A total of 196 patients who underwent resection for colorectal adenocarcinoma in one centre from 2006 to 2012 were included in this study. All of the cases were evaluated in terms of age, sex, localization, tumour size, growth pattern, histological grade, LVI and PNI, surgical margin positivity, pT, pN, stage, recurrence, metastasis, site of metastasis and immunohistochemical Ki67 proliferation index.

Results: In statistical analysis, female gender, polypoid growth pattern, medullary histological type, absence of lymphovascular and perineural invasion, negative surgical margin, low pN grade and no metastasis were found to be associated with long disease-free and overall survival time. Although high Ki67 proliferation index was associated with poor differentiation and surgical margin positivity, it was not associated with disease-free survival (DFS) and overall survival (OS).
Conclusion: The results of our study show that the Ki67 proliferation index is not more important in predicting DFS and OS than histological features. Our study has a feature to shed light on the literature in terms of being a study in which many histopathological features were evaluated in a large series. However, it should not be forgotten that the search for new target molecules that will predict the behaviour of tumours and prevent the progression of the tumour continues.

OFP-06-019
Incidental primary tumours of the appendix: analysis of 4047 appendectomy specimens in a 15-year retrospective study
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Background & objectives: Acute inflammation is the most frequent finding in appendectomy specimens. Nonetheless, it is well known that tumours may be incidentally found. The main goal of this study was to characterise the primary tumours diagnosed in appendectomies performed in our institution.
Methods: A retrospective review was conducted for all appendectomies received in our department between January 2006 and December 2020. Patients with clinical and radiological suspicion for neoplasm were excluded. Reports with incidental histopathological diagnosis of neoplasm were further analysed, and nomenclature was updated according to the 5th edition of WHO Classification of Tumours (Digestive System).
Results: A total of 4047 surgical specimens were retrieved. Appendiceal tumours were found in 73 cases (overall incidence of 1,80%), including appendectomies performed for acute appendicitis or at staging procedures for extra-appendiceal malignancies. The median age was 52 years (range 14-95), without age predilection (M/F ratio =1,03). Neuroendocrine tumours were the most frequent entity (n=29, comprising 39,72% of all incidental findings). Additional diagnoses include low-grade mucinous neoplasm (n=17), high-grade mucinous neoplasm (n=1), adenocarcinoma (n=8, comprising 3 goblet cell adenocarcinomas, 3 adenocarcinomas NOS and 2 mucinous adenocarcinomas), and diffuse large B-cell lymphoma (n=1, initial presentation). Sessile serrated lesions (n=15, low-grade dysplasia in 4) and hyperplastic polyps (n=2) were also described.
Conclusion: Incidental primary tumours of the appendix are rare. Our incidence correlates with that described in the literature. These neoplasms may be diagnosed in different clinical settings, isolated or in combination with additional histopathological processes. Therefore, careful macroscopic and microscopic examination should be performed in all appendectomy specimens, independently of the preoperative diagnosis.

OFP-06-020
RAS and BRAF mutational study in synchronous colorectal cancer
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Background & objectives: Colon cancer comprises molecular alterations that guide treatment in advanced stages. Regarding synchronous tumours, there is no consensus about testing all or only the advanced CRC. We aim to assess mutational concordance in synchronous CRC.
Methods: In the last two years, at our institution, eight patients, aged between 44 and 79 year-old with synchronous CRC were tested for KRAS and BRAF mutations. Clinical and pathological data was retrieved from the hospital database. The local ethical committee (CHUC 137-20) approved this study.
Results: Seven patients presented two synchronous tumours, in which three had mutational concordance: one was wild-type for KRAS/BRAF, other had the same mutation in KRAS (p.Gly12Asp) and the remaining one was wild-type for KRAS, having both neoplasms BRAF V600E mutation.
The group composed of four patients with mutation discrepancy only had KRAS mutation in one tumour: two patients with pGly13Asp mutation, one patient had p.Gly12Asp and p.Gin61Arg and the last one p.Gly12Val.
The youngest patient presented a three synchronous tumours with mutational discordancy: two had NRAS mutation and the other KRAS mutation.
Conclusion: Synchronous colorectal neoplasias seem to exhibit a different gene mutational signature. As the treatment approach is tailored according to this information, as such, it is crucial to test all tumours in synchronous cases.

OFP-06-021
Sessile serrated lesions (SSL) of the colon and their way towards malignancy - immunohistochemical features
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Background & objectives: Serrated neoplasia pathway leads to approximately 30% of all colorectal carcinomas.
The aim of this study was to evaluate MLH1, BRAF and p53 status by immunohistochemistry in sessile serrated lesions and to identify molecular alterations as steps towards malignancy.
Methods: We designated a retrospective case control study, including 11 sessile serrated lesions with dysplasia. For each patient with dysplasia we included a non-dysplasia patient matching sex and age.
Immunostaining of MLH1, BRAF and p53 was done on all 22 cases and we evaluated the percent of nuclear loss of MLH1, cytoplasmic positivity of BRAF and nuclear positivity of p53.
Results: Fourteen patients had microsatellite instability with surprisingly higher nuclear loss of MLH1 in non-dysplastic crypts (65%), comparative to the rate found in those dysplastic (55%).
p53 mutation was noticed in 9 lesions, mostly dysplastic with a double nuclear positive rate (30%) compared to only 15% in non-dysplastic crypts. One third of p53 mutated SSL are microsatellite stable (MSS), all of them with dysplasia.
Half of the SSL with intense cytoplasmic positivity of BRAF were also p53 positive, almost all cases being dysplastic.
Almost 1/3 of cases were MSS (5 non-dysplastic and 3 dysplastic) with BRAF cytoplasmic positivity in 70% of the cells in dysplastic crypts and 54% in non-dysplastic.
Conclusion: Our results suggest that loss of MLH1 expression in non-dysplastic crypts in SSL could precedes the development of MLH1-deficient dysplasia and further to adenocarcinoma. SSL with microsatellite stability, but BRAF mutated, has poor prognostic. p53 mutation is common in MSS/BRAF mutant SSL.
Including immunohistochemical evaluation of BRAF V600E and Tp53 mutation and loss of MLH1 expression may be the key to identify sessile serrated lesions with higher potential to progression into carcinoma.

OFP-06-022

Density of CD8+ infiltration in the peritumoral mucosa in gastric cancer is significantly associated with lymphovascular invasion

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Background & objectives: The immune microenvironment of peritumoral tissues is an important trend in gastric cancer research, as immune cells in peritumoral tissues probably take part in epithelial-mesenchymal transition, metastasis and other processes of tumour progression.
Methods: We used samples of surgical material from 134 patients with a verified gastric cancer. Immunostaining for CD8 (clone C8/144B) were performed in each case. The immunostaining results were evaluated using an automatic LASX morphometric analysis system. The results of the morphometric analysis are presented as the average area of the selected colour range objects in three fields of view.
Results: By conducting morphometric analysis it was found that the average area of CD8+ cells in the peritumoral mucosa in tumours with lymphovascular invasion is 6598.01 sq. microns, and in tumours without areas of lymphovascular invasion the average area of CD8+ cells is 4012.45 sq. microns. This difference is characterized by a high statistical significance p=0.0085. But when we assessed the density of CD8+ cell infiltration in the centre of the tumour tissue there were no significant differences in lymphovascular invasion.
Conclusion: Our results indicate that the presence of a high density of CD8+ infiltration of the peritumoral mucosa in gastric cancer may be an indirect sign of the presence of lymphovascular invasion. This fact also indicates a possible significant role of inflammatory infiltrate cells in the peritumoral mucosa for accelerating the processes of invasion and metastasis.

OFP-06-023

SOX9 mutation correlates with good prognosis and immune infiltration in stage II colon cancer

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Background & objectives: The identification of molecular biomarkers is essential for a better therapeutic management of early-stage colon cancer (CC) patients. This study aims to characterize SOX9 mutational status, immunohistochemical (IHC) expression and its association with recurrence in stage II CC.
Methods: 84 chemotherapy-naive stage II CC were included. Tissue microarrays comprising normal mucosa, bulk of the tumour and invasive front were constructed for 71 cases and stained with SOX9 and CD8 antibodies. The remaining cases were whole-sectioned and stained with CD8. DNA-sequencing was performed in 44 cases using a panel of 48 CC-related genes that included SOX9.
Results: SOX9 was overexpressed by IHC in both SOX9 mutated and wild-type CC when compared to colonic mucosa (P<0.001), being higher when SOX9 was mutated (P<0.001). Recurrent cases showed higher SOX9 IHC expression in the bulk of the tumour (P=0.023) but not in the invasive front. DNA-sequencing revealed SOX9 mutation in 8 cases, of whom only 1 showed disease recurrence (P=0.046). Consistently, SOX9 mutations were associated with longer overall survival (P=0.029) in a validation cohort of 1095 colorectal cancers from the MSK-IMPACT. SOX9 mutated tumours showed higher CD8 lymphocytic infiltration analysed by IHC. Likewise, colorectal tumours from the TCGA (N=449) harbouring SOX9 mutations exhibited increased expression-based ImmunophenoScores compared to wild-types (P=0.016)
Conclusion: SOX9 is overexpressed by IHC in stage II CC and it is associated with the presence of gene mutation. SOX9 mutated tumours exhibit higher levels of cytotoxic lymphocytes and less frequency of recurrence, which highlights the potential value of SOX9 as a biomarker of relapse-free in early-stage CC.

OFP-06-024

"The imitation game" in mucosal prolapse syndrome: many faces of one clinical entity

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Background & objectives: Mucosal prolapse syndrome (MPS) is an umbrella term for rectal mucosal disorders comprising solitary rectal ulcer syndrome (SRUS), proctitis cystica profunda, inflammatory cloacogenic polyp, and inflammatory cap polyposis. Histopathological features of MPS causing resemblance with other disorders including neoplasias were reviewed.
Methods: In this study, the medical records of 100 patients based on endoscopic, clinical and histological findings were reviewed retrospectively between 2015-2020. Histopathological features including fibromuscular obliteration, angulated crypts, serrated epithelial change (SEC), surface ulceration, muscularis mucosa thickening, mucin lakes and vascular changes were evaluated by an experienced team, while resemblance with other disorders was determined by a junior pathologist.
Results: Gender distribution was approximately equal (48% males, 52% females) with a median age of 54 years. The most common symptom was abdominal pain and constipation (61%), followed by rectal bleeding (16%) and weight loss (%6). Endoscopically only 40% of cases showed ulceration which correlated with histopathology (41%). Fibromuscular obliteration and crypt distortion were seen in almost all cases (%99 and %98%, respectively) while angulated crypts were noted in 92%, and SEC in 93% of cases. Majority of the cases (57%) showed resemblance with serrated polyps (43% hyperplastic polyps, 14% SSL) while 43% had the potential to be mistaken for an adenoma (27%) or dysplasia and/or neoplasia (15%).
Conclusion: The results of the study suggest that not all MPS cases have an ulcerated or polypoid appearance endoscopically. However, histopathologic features including complex crypt architecture, SEC, regeneration, acellular mucin may imitate polyps and/or neoplasia. Therefore, pathologists should be aware of the "imitation game" this entity likes to play before making an erroneous diagnosis. This is particularly true for untrained eyes who are likely to have difficulties at recognizing this benign entity.

OFP-06-025

Congenital enteropathies: a multidisciplinary approach for diagnosis

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Background & objectives: Congenital enteropathies constitute a heterogeneous cluster of disorders that are rare, typically presenting with severe diarrhea in infancy. A detailed clinicopathologic documentation of rare congenital enteropathies with special emphasis on the role of pathologist in the diagnostic team is presented.
Methods: Clinical, histopathological, and genetic characteristics of 27 cases of congenital enteropathy comprising microvillus inclusion disease, abetalipoproteinemia, chylomicron retention disease, primary immunodeficiency, early onset IBD, DGAT1 deficiency, prolidase deficiency, RIPK1 gene defect were documented. All patients had duodenal and/or colonic biopsies which were evaluated for villus morphology, brush border, endocrine cells, epithelial changes, type and degree of inflammation, granulomas, lipid accumulation.
Results: Mean age of admission was 1.19 decimal years. Diarrhea was watery in 74%, fatty in 18.5%, bloody in 11.1% and started within two months of birth in %59,2. Consanguinity and sibling death due to diarrhea was present in 74% and 25.9%. Endoscopically, 88% showed duodenal,

51,8% had colonic mucosal abnormalities with 20% requiring repeat biopsies for diagnosis. Genetic diagnosis (SAR1B, STX, MTP, CYBB, MYO5B, dGAT, RIPK1, PEPD mutations, IL-10 R, IL-21 deficiencies) was possible in 55.5%. Histopathologically, villous and brush border abnormalities were observed in 14.8% and in 18.5%, respectively while 40.7% showed active colitis. Electron microscopy revealing microvillous inclusions and lipid vacuolization was diagnostic in 14.8% of the cases.
Conclusion: Diagnosis of congenital enteropathies is difficult and requires close collaboration between the members of an experienced multidisciplinary team comprising paediatric gastroenterologists, immunologists, geneticists, and pathologists. In the present series, pathologic diagnosis was possible in 37% of the cases suggesting that overlaps in the histopathology of these entities are common and full picture may not be present in initial biopsies. Therefore, the pathologist should be aware of such pitfalls and should employ sophisticated techniques for an accurate diagnosis, as necessary.

OFP-06-026
Mesenchymal tumours of the digestive system: not all are GISTs!
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Background & objectives: Mesenchymal tumours of the digestive system among which GISTs are the most common, show great diversity similar to their soft tissue counterparts. We share our sixteen years' experience by presenting a large cohort of mesenchymal tumours of digestive system.
Methods: A total of 851 mesenchymal tumours was diagnosed in our institution between 2005-2021. We encountered 19 out of 26 types of mesenchymal tumours included in WHO blue book of GI tract. Five additional sarcomas (dedifferentied, well-differentiated liposarcomas, myxoid, pleomorphic liposarcomas and undifferentiated pleomorphic sarcoma) were identified as well. Retroperitoneum-only tumours were excluded. Tumours were analysed for age, gender, and localization.
Results: Among 851 cases, mean age was 62.91 (Range:5-98) and 54.8% were women. Top five localizations were stomach (27.3%), colon (25.7%), liver (20.3%), small intestine (14.5%), esophagus (9.8%) while pancreas (0.6%), anal canal (0.5%), appendix (0.4%) and biliary tract (0.3%) were rare. Five most common diagnoses were GISTs (%24.7), hemangiomas (18.2%), leiomyomas (16.3%), lipomas (15.7%) and inflammatory fibroid polyps (IFP) (8.5%). Stomach was the most common site for GIST (65.2%), followed by small intestine (20.5%) and colon (5.2%). Hemangiomas preferred liver (96.1%). Esophageal leiomyomas (50.4%) outnumbered colonic (28.1%) and gastric ones (16.5%). Colon was the predominant site for submucosal lipomas (78.4%). IFPs were mostly encountered in stomach (68.1%).
Conclusion: The present series contains a whole spectrum of mesenchymal lesions ranging from benign lesions like angiomyolipomas or perineuromas to malignant ones like angiosarcomas or even rhabdomyosarcomas. The majority was benign mesenchymal tumours with fewer sarcomas similar to the literature. As expected, GISTs were the most common mesenchymal tumours of digestive system in our series. Except for leiomyomas which had a higher incidence in the esophagus, site distribution of tumours was similar to published data.

OFP-06-027
Clinical-demographical characteristics and incidence of young-onset colorectal carcinoma
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Background & objectives: While the overall incidence of colorectal carcinoma (CRC) tends to decrease by the help of screening methods, the incidence under the age of 50 is gradually increasing. Young-onset CRCs tend to present at advanced stages and generally follow poor prognosis.
Methods: All patients aged under 50 years who were diagnosed with CRC in resection specimens between 2006-2019 were included in the study. Data were obtained from the hospital database. The cases were reviewed according to clinicopathological characteristics.
Results: A total of 188 young-onset CRCs were identified which constituted 15.8% of all CRCs. The ratio of young onset cases from 2006-2019 per year was as follows: 15.9%, 13.6%, 11.6%, 12.5%, 11.7%, 23.7%, 17.9%, 16.9%, 27%, 12.5%, 8.7%, 15.8%, 13.7%, 20.8% respectively. The most common histological type was adenocarcinoma (84%), followed by mucinous (13.3%) and signet-ring cell carcinoma (2.7%). Male to female ratio was 51.6 vs 48.4%. According to the stage, the distribution was as follows; stage 1(8%), stage 2(36.7%), stage 3(41%) and stage 4(14.4%). Mismatch repair gene (MMR) immunohistochemical status information was available for 44 patients performed after 2017. MMR-deficiency was detected in 12/44 (27%) of them.
Conclusion: According to our single centre data, in contrast to the literature, the incidence of young onset CRCs is variable and does not seem to follow an increasing trend. Also, presentation at early stage vs advanced stage seem to be similar. These variations could be due to epidemiological differences. The rate of microsatellite instability is in keeping with the literature and it is approximately 2 times higher in comparison to reported ratios in adult population.

OFP-07 | Digestive Diseases Pathology - Liver/Pancreas

OFP-07-001
Pancreatobiliary adenocarcinomas: an immunomarker panel proposal
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Background & objectives: Pancreatobiliary adenocarcinomas comprise various entities that largely share an inconspicuous evolution leading to abrupt disease in metastatic setting, posing particular challenges to the histopathological differential diagnosis. Herein, we propose a panel of immunomarkers for a reliable approach to such tumours.
Methods: Tissue microarrays (TMAs) of 3mm diameter cores were prepared from surgical specimens of 45 primary pancreatobiliary adenocarcinomas of the liver, extrahepatic bile ducts, gallbladder, ampulla of Vater and pancreas, along with 5 colorectal and 5 gastric adenocarcinomas, included as controls. A panel of CK7, CK20, CK19, CDX-2, SATB2, Villin, CEAp, IMP3, S100p and Ca19.9 was evaluated.
Results: All TMAs were independently assessed by two observers: undisputable staining (whether focal or diffuse) was considered positive, whereas complete or near total absence of expression was deemed negative; instances with equivocal staining were disregarded. The majority of markers displayed high positive predictive values, when compared to both proximal and distal gastrointestinal tract tumours (CK7: 100%, CK19: 91%, villin: 71%, CEAp: 83%, IMP3: 83%, S100p: 88% and Ca19.9: 92%) as well as when plotted only against gastric carcinomas (CK7: 100%, CK19: 98%, villin: 83%, CEAp: 92%, IMP3: 83%, S100p: 95%, Ca19.9: 94%). The remaining markers also presented robust overall negative predictive values (CK20: 98%, CDX-2: 92%, SATB2: 97%).
Conclusion: A panel comprising the aforementioned antibodies may provide compelling evidence for a definite diagnosis of pancreatobiliary adenocarcinomas in metastatic setting, both through the presence and absence of immunoexpression. However, we are aware our data stems from a restricted series and limited framework, particularly regarding the imbalanced number of gastrointestinal controls, and does not reflect the heterogeneity inherent to distinct grades and entities, namely pertaining to different organs and tumoral microenvironment.

OFP-07-002

Clinicopathological characterization of steatohepatitic variant of hepatocellular carcinoma (SH-HCC)

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Background & objectives: Steatohepatitic hepatocellular carcinoma (SH-HCC) is a recently described variant of HCC with no consensus definition and unclear prognosis. The objectives of this study were (1) to evaluate the frequency of SH-HCC and its prognosis, (2) to describe their histological characteristics.
Methods: We conducted a retrospective study including 298 patients surgically treated for HCC between 2012 and 2019. Histological features of tumours were reassessed by two pathologists. The diagnosis of SH-HCC was retained if at least 4 of the 5 described criteria were present (steatosis, ballooning, Mallory-denk bodies, fibrosis, inflammation) and if the SH contingent was >50% of the tumour area.
Results: Of the 298 HCCs, 39 (13%) were classified as SH-HCC. SH-HCCs were observed more frequently in a context of metabolic syndrome and chronic alcohol intake compared to other HCCs (56% vs 26%, p<0.001 and 28% vs 15%, p=0.039, respectively). Ballooning, fibrosis and inflammatory were observed in all SH-HCCs whereas steatosis and Mallory-denk bodies were observed in 92% and 74% of SH-HCCs. No significant difference was observed with other HCCs in terms of histoprognostic factors such as tumour differentiation (well-differentiated tumour, 41% vs 31%, p=0.239). SH-HCCs had similar recurrence-free and overall survival compared to other HCCs (14 months vs 13 months, p=0.985 and 23 months vs 24 months, p=0.894, respectively).
Conclusion: SH-HCC is a relatively frequent variant (13% of HCCs in our cohort) with specific macroscopic and microscopic features that distinguishing it from other HCCs. It occurs mainly in a context of metabolic syndrome or chronic alcohol intake. SH-HCC seems to have a similar prognosis compared to other HCCs, particularly in terms of histoprognostic factors and survival.

OFP-07-003

Ferroptosis in intrahepatic cholangiocarcinoma: an immunohistochemical study

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Background & objectives: Ferroptosis is a regulated, iron-mediated, cell death, induced by glutathione peroxidase4 (GPX4) inhibition. GPX4 is overexpressed in aggressive cancers and directly inhibited by ferroptosis-inducer drugs. We investigated ferroptosis markers in intrahepatic cholangiocarcinoma (iCCA), since no data are reported so far.
Methods: Sixty-two consecutive patients, who underwent hepatic resection for iCCA, were retrospectively enrolled. Immunostaining for transferrin-receptor 1 (TFR1) and GPX4, and Pearls histochemical stain for iron deposition were performed to evaluate ferroptosis. Immunostaining for STAT3 was performed to investigate the well-known anti-apoptotic background of iCCA, which justifies its chemotherapy resistance.
Results: STAT3 was expressed in the majority of cases (88.7%), confirming the anti-apoptotic milieu in iCCA. A high STAT3 expression was associated with a worse prognosis (OS p = 0.006; DFS p = 0.001). None of the cases showed iron deposition, and a complete negativity for TFR1 was observed in 93.5% of cases. GPX4 was overexpressed in 72.6% of cases, and its overexpression correlated with poor histological prognostic parameters, such as vascular and perineural invasion and high grade (p <0.005 for all) and a worse prognosis (OS p = 0.005; DFS p = 0.0002).
Conclusion: Our study firstly demonstrated that ferroptosis is not an activated form of regulated cell death in iCCA. GPX4 overexpression is observed in most cases and correlates with poor outcome. These promising results pave the way to the possible therapeutic use of ferroptosis inducers in iCCA to overcome cancer cell drug resistance.

OFP-07-004

EUSFNB of pancreatic lesions: a prolific outcome

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Background & objectives: Endoscopic ultrasound (EUS)-guided fine-needle biopsy (FNB) is replacing conventional EUSFNA in the diagnosis and management of pancreatic mass. The aim is to document the diagnostic precision, accuracy and IHC studies of EUS-FNB of pancreatic lesions when compared to EUSFNA.
Methods: This is a cross sectional study of EUSFNB samples of pancreas received in Clinipath laboratory in the year 2020, with clinical, CT scan and endoscopy correlation. A total number of 131 EUSFNB samples of pancreatic lesions were documented for histological features and IHC outcome, the latter performed, wherever it was deemed necessary.
Results: A wide range of pancreatic lesions, mostly well to poorly differentiated primary adenocarcinomas of the pancreas, along with a small number of neuroendocrine tumours were documented. Spindle cell tumours, mucinous cystic neoplasms, serous papillary lesions, lymphomas, and cases of chronic pancreatitis were also seen. Metastatic lesions from the lung and kidney were also noted. IHC helped to differentiate the primary and metastatic lesions with precision. Correlation with clinical picture, tumour markers and CT scan findings were undertaken in all cases.
Conclusion: EUSFNB has emerged to be the most safe, reliable diagnostic procedure replacing the conventional EUSFNA and cell block of pancreatic lesions in Malaysia. The precision of the procedure and accuracy of the results of EUSFNB samples have considerably increased in the year 2020. This initial study carried out for the first time in Malaysia in a private laboratory set up is to document the increasing diagnostic capability of EUSFNB in the management of pancreatic lesions.

OFP-07-005

Integrated signature of tumour budding and immunoarchitectural features significantly improves prognostic stratification of patients with pancreatic cancer

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Background & objectives: Tumour budding and the immune cell infiltrates are known to be important prognostic factors in pancreatic ductal adenocarcinoma (PDAC). However, they are assessed independently. Here we combine their assessment in order to achieve a more precise risk stratification for PDAC-patients.
Methods: We evaluated the cell-cell interactions and spatial relationship between tumour budding cells and immune cells at the tumour centre (TC) and invasive front (IF) of two PDAC-cohorts (n=112:training and n=30:validation) by using multiplex immunofluorescence for CD3, CD4, CD8, FOXP3, CD68, CD206, PD-1, PD-L1 and pancytokeratin, followed by automated image analysis for quantification, proximity analysis and a Random-Forest variable selection approach.
Results: High numbers of tumour buds (HR=4.678; 95% confidence interval (CI) 1.204-17.644), low numbers of CD3+CD8+PD-1-T cells within a radius of 50 μm from the budding cells at the TC (HR=5.010; 95% CI 1.315-19.585) and high CD68+CD206+ tumour associated macrophages (TAMs) (HR=5.563; 95% CI 1.544-23.742) within a radius of 50 μm from the budding cells at the IF area, were associated with reduced disease specific survival. A prognostic signature integrating all the above three parameters achieved a more significant cohort stratification (HR=11.585; 95% CI 3.649-46.813). This was confirmed in the validation cohort (HR=10.333; 95% CI 2.742-38.563).

Conclusion: An Integrated Budding Immune Signature (IBIS) stratified PDAC-patients into prognostic subgroups more efficiently than each biomarker alone, improving the prognostic power and risk stratification independently of other known prognostic factors, including tumour grade or tumour stage.

OFP-07-006

High tumour mutational burden identifies a subset of pancreatic cancer patients with prolonged survival and improved anti-tumour immunity

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Background & objectives: Imunotherapy in pancreatic cancer (PC) has focused on microsatellite-instable (MSI-high) cases, representing <2% of patients. Identifying microsatellite-stable (MSS) PCs with high tumour mutational burden (TMB-H) and exploring their microenvironment might expand the number of PC-patients that could benefit from immunotherapy.
Methods: We evaluated TMB in 110 MSS PC-specimens using the Oncomine Tumour Mutation Load Assay (ThermoFisher) and the Comprehensive Cancer Panel. Moreover, whole tissue sections of 12 TMB-H cases (i.e. TMB≥10; TMB-H) and 15 cases with low TMB (TMB<10, TMB-L) were immunoprofiled by multiplex immunofluorescence for CD3, CD4, CD8, FOXP3, CD20, CD68, PD-1, PD-L1 and DC-LAMP, followed by automated image analysis.
Results: Twelve TMB-H cases (10.9%; median TMB: 14.87, range: 10.21-34.96) were detected. TMB-H cases exhibited significantly increased CD3+CD4+FOXP3- T cells (P=0.0398), CD20+ B cells (P=0.0296) and DC-LAMP+ dendritic cells (DC; P=0.0093) when compared with TMB-L cases. No significant differences were observed regarding all other immune cell infiltrates or their subsets. No correlation was found between TMB and the PD1/PD-L1 staining pattern. TMB-H cases exhibited an improved overall survival (median OS:27 months, range:5-171) and progression free survival (median PFS:21.5 months, range:3-165) compared with the TMB-L cases (median OS:13 months, range:3-161; median PFS:6.5 months, range:3-157), each P<0.001.
Conclusion: TMB-H PCs display improved anti-tumour immunity mediated by increased DC numbers, which have the capacity to initiate and regulate T cell responses, and increased counts of CD3+ CD4+FOXP3-T cells, known to exhibit direct cytotoxicity against tumour cells as well as potentiate the DC. Moreover, CD20+ B cells and DC can prime T cells to target tumour cells due to antigen presentation. These results partially explain the improved survival of TMB-H patients and suggest that they might be good candidates for immunotherapy.

OFP-07-007

Intra and extra-hepatic cholangiocarcinoma distinction – useful ancillary markers

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Background & objectives: Cholangiocarcinoma originates anywhere in the biliary tract epithelium. Frequently the pathologist is questioned if the tumour sample is from a primary liver tumour or a metastasis. This study assessed the value of ancillary techniques in that distinction.
Methods: A retrospective transversal study was completed using archival biological material from 32 patients with cholangiocarcinomas, 16 intra-hepatic (IHC) and 16 extra-hepatic (EHC), 25 male and 7 female, diagnosed between 2009 and 2014 at the Coimbra University Hospital.
Expression PAS/D, EMA, Gamma-GT markers were assessed by histo- and immunohistochemistry. Clinical and pathological data was retrieved from the hospital database.
Results: The median age of presentation was 69.7±9.7years. After a median follow-up of 12±29.4months, the overall survival (OS) was 12 ±3.7months. There was no difference in survival between the IHC and EHC (p=0.168).
EMA expression was associated with the site of origin: apical EMA expression in 56.3% of IHC and complete EMA expression in 87.5% of the EHC (p=0.012). The complete EMA expression was also associated with a worse OS (5 vs. 66months, p=0.008) on univariate and multivariate analysis (HR=3.2, 95% CI 1,21-8.09, p=0.013).
Expression of Gamma-GT was present in 43,8% of IHC and 6,3% of EHC (p=0.019).
PAS/D did not disclose statistical correlation with either OS or tumour location.
Conclusion: The expression of Gamma-GT and EMA were helpful in determining the origin of cholangiocarcinoma, and EMA complete expression was predictor of worse OS. These markers should be tested in any cholangiocarcinoma biopsy.

OFP-07-008

Solid pseudopapillary neoplasm of the pancreas – a 21-year long experience in a tertiary Portuguese institution

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Background & objectives: Solid pseudopapillary neoplasm (SPN) of the pancreas is a rare low-grade malignant tumour which accounts for 0,9-2,7% of all exocrine pancreatic neoplasms, with higher incidence in women of young age. Herein, we present our expertise through a 21-year long series.
Methods: Data of all cases of SPN diagnosed in our institution pertaining to the period of 2000-2020 were retrieved. The clinicopathological, gross and histopathological features along with performed immunomarkers (beta-catenin, CD56, CD10, progesterone receptors (PR), chromogranin and synaptophysin) were reviewed and summarized; additionally, the expression of galectin-3, AMACR and TFE-3 was also retrospectively evaluated in different tumour areas.
Results: A total of 9 cases were assessed: 6 patients were female (mean:30years; range:12-58years) and 3 were male (mean:50years; range:31-75years). The tumours were large (sized 3-8cm; mean:5cm), unifocal, well-demarcated and cystic-solid, with no preferential topography. Histologically, the classical features were present; most had perineural invasion and focal pancreatic infiltration, along with singular findings: areas of oncocytic differentiation, strands of neoplastic cells within a myxoid/edematous stroma, extracellular iron deposits and infrequent mitoses (range:0-4 high-power-fields). Beta-catenin, CD56, CD10, PR, AMACR and TFE-3 were diffusely positive, whereas focal expression for synaptophysin and negativity for galectin-3 and chromogranin were observed. Noteworthy, nodal, and hepatic metastases were reported in two cases.
Conclusion: Histological features of SPN are quite specific, although diverse. The differential diagnosis becomes intricate in the presence of small-solid lesions or large-unilocular cysts, especially in male patients. Beta-catenin, AMACR and TFE-3 can aid pathologists to differentiate this entity from other pancreatic circumscribed tumours, namely neuroendocrine tumours; interestingly, galectin-3 was negative in all cases, unlike reported in the literature. SPN may uncommonly behave aggressively with no well-established malignant criteria; however our case with hepatic metastization showed a higher mitoses count.

OFP-08 | Electron Microscopy

OFP-08-001
Diagnostic challenges in ichthyosiform dermatoses

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Background & objectives: Neonatal and infantile erythroderma is a rare skin disorder, frequently associated with ichthyoses or immunodeficiency syndromes. This study emphasizes the ultrastructural features found in ichthyosiform conditions in order to establish a relationship between electron microscopy findings and genetic mutations.
Methods: Two infants with clinical ichthyosiform dermatoses, one with erythroderma, were biopsied for diagnostic purpose. Skin biopsy specimens were processed at "Victor Babeş" National Institute of Pathology for both light microscopy and electron microscopy (EM) studies. Clinical data were gathered from patients' medical record. The cases were evaluated according to age, sex, clinical diagnosis, genetic profile, and histopathologic and ultrastructural findings.
Results: Case 1: A 7-day-old boy with erythroderma was ultimately diagnosed with Omenn syndrome (RAG-1 gene mutation). Light microscopy revealed acanthosis, parakeratosis, and perivascular lymphocytic infiltrate in the dermis. EM showed an increased number of lamellar bodies in stratum granulosum (SG). Lipid vacuoles were found in stratum corneum (SC), both intercellular and intracellular.
Case 2: Skin biopsy from a 2-month-old boy presents microscopically orthohyperkeratosis with lipid droplets in SC and a reduced SG. Ultrastructural study of SG revealed a decreased number of keratohyalin granules and keratinocytes with cytoplasmic vacuoles and angulated, electron-lucent structures. Cholesterol clefts, aggregates of membranous structures and lipid vacuoles were found in corneocytes.
Conclusion: This study highlights the significant overlap between ultrastructural features found in Omenn syndrome and autosomal recessive congenital ichthyosis (ARCI) type I.
The second case presents particular EM findings, consistent with ARCI type II/III. Even if the initial presentation pointed towards ichthyosis vulgaris, the diagnosis of ARCI was genetically confirmed by NIPAL-4 gene mutation. At follow-up, the patient developed erythroderma.
As etiologic diagnosis of ichthyosiform conditions is often difficult, EM examination may point out some genetic defects before becoming clinically apparent.

OFP-09 | Endocrine Pathology

OFP-09-001
TROP2: a potential new marker in diagnosis of thyroid neoplasms

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Background & objectives: The human trophoblast cell surface antigen (TROP-2) which is a transmembrane glycoprotein, has recently been investigated as a useful marker of thyroid epithelial neoplasms. In this study, we aimed to show the diagnostic utility of TROP2 in thyroid neoplasms.
Methods: A total of 306 cases, including 170 cases of different PTC variants, 50 cases of benign and non-neoplastic lesions, and 86 cases of other neoplasms (NIFT-P, follicular carcinoma, Hürthle cell carcinoma, poorly differentiated carcinoma, anaplastic carcinoma, and medullary thyroid carcinoma), were included in this study. Only membranous staining with TROP2 was considered positive.
Results: In PTC, classical(n=35), tall cell(n=41), follicular(n=39), solid(n=19), hobnail(n=10), Warthin-like(n=10), columnar(n=7) and oncocytic variant(n=9), respectively, 100%, 97.6%, 5.1%, 42.1%, 90%, 90%, 28.6% and 33.3% positivity were seen. A negative reaction was observed in all 50 cases of benign and non-neoplastic lesions (follicular adenoma(n=10), Hürthle cell adenoma(n=10), hyperfunction(n=10) and multinodular goiter(n=20)). Negative reactions were observed in 83 (n=86) of other thyroid neoplasms which consist of NIFT-P(n=20), follicular carcinoma(n=18), Hürthle cell carcinoma(n=18), poorly differentiated carcinoma(n=10), anaplastic carcinoma(n=10) and medullary thyroid carcinoma(n=10). Only focal positivity were seen in 3 Hürthle cell carcinoma cases. The sensitivity for tall cell and classical variant was 97.5% and 100%, respectively, and specificity was 100% for both.
Conclusion: TROP2 was seen to be a very useful marker in differentiating PTC, especially in particular variants (classic, tall cell, hobnail and Warthin-like variant), from benign and non-neoplastic lesions and other neoplasms of the thyroid.

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OFP-09-002
Poor prognostic factors of papillary thyroid microcarcinomas

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Background & objectives: Papillary thyroid microcarcinomas (PMC), by definition, are tumours 1 cm or less and are considered to have a good prognosis. However, PMCs may sometimes cause lymph node metastasis, distant metastasis, and even disease-related death.
Methods: Pathology reports of patients who underwent thyroidectomy were analysed. 1194(44.9%) of 2660 papillary thyroid carcinoma cases were PMC. 58 cases (4.85%) who had lymph node metastasis and/or received multiple doses of radioactive iodine (RAI) and/or tumour-related death, were re-examined in detail, and were assigned as the study group. The remaining 1136 cases were included in the study as control group.
Results: In the study group, 44 had lymph node metastases, 4 had distant metastases, 14 had disease-related death. The remaining 14 patients received multiple doses of RAI therapy for recurrences or other causes. The tumour was bilateral in 29 patients (50%) and multifocal in 36 patients (62%). Microscopic extrathyroidal extension (ETE) was detected in 32 patients (55.2%). 32 patients (55.2%), whether focal or diffuse, had a tall cell histological variant component. Tumour diameter was >0.5 cm in 35 patients (60.3%).
We found that aggressive course of the tumour was associated with; age at diagnosis (≥ 55 age), bilaterality, male gender, tumour diameter (>0.5 cm), microscopic ETE, lymph node metastasis, distant metastasis, tumour-thyroid capsule relationship, and aggressive histological variants.
Conclusion: Although a very good prognosis is mostly observed in papillary microcarcinoma, it should be kept in mind that some clinical and histomorphological features may cause poor clinical course.

OFP-09-003
Extra-adrenal paraganglioma clinical and histopathological features: a 16-year period institutional case review series

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Background & objectives: Extra-adrenal paragangliomas are non-epithelial tumours originating from paraganglion cells of the autonomic nervous system, with a biological behaviour ranging from indolent to metastasizing. Herein, we reviewed and evaluated 36 paraganglioma cases received by our institution during a 16-year period (2000-2015).

Methods: The clinical history and slides of all cases were reviewed by an anatomic pathology resident and a senior pathologist and assessed for: tumour size, location, multifocality, microscopic characteristics, catecholamine secretion profile, Grading of Adrenal Pheochromocytoma and Paraganglioma (GAPP) score, hereditary conditions, metastasis and cancer-related death.
Results: Eighteen cases were from the head and neck (13 from the carotid body, 3 jugulotympanic, 1 laryngeal and 1 non-specified), 3 were thoracic and 15 were abdominal/pelvic. Two and one patients had a Succinate dehydrogenase complex subunit D (SDHD) and subunit B (SDHB) gene mutations, respectively, and 1 had Von Hippel Lindau disease; save for the later, they had multiple tumours and a mean age of 38 years. GAPP score grading was feasible on 14 cases: 6 were well-differentiated and 8 were moderately differentiated type. All three patients that showed metastasis were moderately differentiated type and sporadic, of which only one died due to disease progression.
Conclusion: In our study, the factors that were possibly related to a worse prognosis were the GAPP score grade, size, and location. While these tumours are biologically unpredictable, multivariable prognostic tools, such as the GAPP score, can aid in outlining an appropriate patient's management. Despite its small sample size, our case series' findings are consistent with current reported data.

OFP-09-004
Immunological landscape of medullary thyroid carcinoma: PD-1 and PD-L1 expression analysis.
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Background & objectives: Medullary thyroid carcinoma (MTC) is an indolent neoplasm with lymph-node and distant metastases and there is no effective therapy to achieve a remission in advanced stages. Our study paid attention on the role of the immunoregulatory PD1 / PD-L1 axis.
Methods: The study considered 130 patients with histological diagnosis of MTC (104 sporadic and 26 hereditary MTC) with a follow-up time of 39 months. All patients were characterized for clinical-pathological variable and disease progression at the end of follow-up. Immunohistochemical analysis were performed for CD8, PD-1 and PD-L1. PD1 and PD-L1 staining was evaluated according to the Combined Positive Score system.
Results: The immunoreaction for PD-L1 was positive in 32.3% of MTC. PD-L1 was more expressed in patients with sporadic disease ($p = 0.01$) and in patients with aggressive disease characterized by the presence of lymph node metastases ($p < 0.0001$) and elevated Calcitonin values at diagnosis ($p = 0.003$). The expression of PD-L1 correlated with the expression of PD1 ($p < 0.0001$) and the presence of positive CD8 T lymphocytes ($p < 0.0001$). At the end of follow-up, PD-L1 positivity correlated with the progression of disease. At the multivariate analysis, the loss for PD-L1 expression, together with a lower stage at diagnosis, were the only prognostic markers associated with biochemical cure.
Conclusion: This study confirms the importance of the PD-L1 / PD1 interaction also in MTC. The correlation between PD-L1 expression and disease progression opens the way to the possibility of using immunomodulatory drugs with PD-L1 as target in MTC, which could significantly modify the clinical course of the disease, especially in those patients who cannot be already cured.

OFP-09-005
The functional activity of thyroid nodules during aging
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Background & objectives: The study of age-related changes in the thyroid tissue is important for understanding the essence of the processes occurring in the organ. Is there a relationship between background changes and nodal pathology?
Methods: The material was 73 thyroid glands, autopsy material without clinical and laboratory signs of endocrine pathology. Follicle diameter, epithelial height, colloid accumulation index, follicular epithelium volume and stromal volume were studied in histological preparations. Age-related changes were analysed both in the background tissue and in nodular pathology, taking into account age groups.
Results: In the age group over 60 years old, there was increased the volume of stroma, decreased of the epithelium volume, a decreasing the height of the epithelium and increasing the diameter of the follicles compared with the group under 60 years old. Characteristics of the nodes: the same morphological indicators demonstrated that the decreasing functional activity in the tissue of the nodes does not occur with age, as in the background tissue. There is no pronounced process of sclerosis. Decreasing the size of follicles, the index of colloid accumulation, increasing volume of the epithelium speaks of a higher functional activity of the nodules in the group over 60 years old.
Conclusion: Age-related changes in the background tissue of the organ indicate a natural decrease in the functional abilities of the thyroid gland. The data obtained may be a manifestation of adaptive intraorgan restructuring, which allows the thyroid gland to maintain a high level of functional activity, despite the natural processes of extinction.

OFP-09-006
Clinicopathological and biological features of well-differentiated Grade 3 neuroendocrine neoplasms of various primary origins
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Background & objectives: Grade 3 neuroendocrine tumours (G3 NETs) represent a group of well-differentiated neuroendocrine neoplasms that demonstrate a Ki-67 index higher than 20%. Little is known regarding clinicopathological differences between G3 NETs from different primary sites, most commonly gastroenteropancreatic (GEP) and lung.
Methods: The study included 71 resected G3 NET cases, which were reviewed for morphology and immunohistochemistry and graded according to the WHO 2019 criterions. Median age at the diagnosis was 50 ± 12 (range 20 – 73) years and 48 (65.8%) were females. The results were correlated with clinicopathologic data, Ki-67 index, somatostatin receptor 2A expression and disease-free survival (DFS).
Results: Of the 71 well-differentiated G3 NET cases, 40 (56.3%) were GEP, 17 (23.9%) lung, 12 (16.9%) other (ovary, thymus, unknown primary). The most common primary site was pancreas, followed by gastric. The mean Ki-67 index was 35.4% (min. 23.0% - max. 65.0%). Metastatic disease was present in 45 (67.4%) patients. We found that tumours arising from GEP site, compared to lung, had significantly worse survival ($p<0.05$). Median DFS in GEP, lung and all other sites of G3 NETs was 9.7, 16.6 and 2.5 months, respectively. The most of G3 NET patients (56, 78.8%) had SSTR 2A-positive immunohistochemical status. SSTR 2A expression did not correlate to clinical parameters, Ki-67 index, DFS survival.
Conclusion: Well-differentiated G3 NENs with elevated proliferation may develop anywhere in the digestive tract, lung, and rare sites. G3 NENs of different primary origins are a heterogeneous group of neoplasms regarding clinicopathological and biological characteristics, behaviour and survival outcomes. Among G3 NEN cohort, tumours which originate from a GEP site have a worse survival compared to lung. The most of G3 NETs have SSTR 2A-positive status which provides additional important information and can help guide management of these group of patients.

OFP-09-007

Diagnostic concordance study in non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) and bordering entities

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Background & objectives: The diagnosis of Non-Invasive Follicular Thyroid Neoplasia with Papillary Nuclear Features (NIFTP) is based on morphological criteria that may be subjective. The aim of our study was to assess the concordance between pathologists regarding this entity and its diagnostic criteria.
Methods: After a previous multicentre study about NIFTP incidence, slides considered representative of typical NIFTP (8), doubtful for NIFTP (8) or without NIFTP criteria (6) were selected and reviewed by 8 pathologists with special dedication to endocrine pathology, assessing nuclear criteria, presence of papillae, psammoma bodies, capsule, capsular invasion, vascular invasion and diagnosis. Brennan-Prediger kappa coefficient was established to assess agreement.
Results: The overall agreement reached a kappa value of 0.60. For the different variables, kappa values were: nuclear shape: 0.33; nuclear membrane: 0.39; chromatin: 0.25; nuclear score: 0.16; papillae: 0.48; psammoma bodies: 0.77; capsule: 0.50; capsular invasion: 0.60; vascular invasion: 0.86 and diagnosis: 0.25. When grouping the cases according to initial diagnosis, kappa values improved in the typical and non-NIFPT groups in terms of overall agreement (0.63 and 0.62), presence of papillae (0.67 and 0.65), capsular invasion (0.66 and 0.67) and vascular invasion (0.93 and 1) respectively, and only in the typical group in terms of diagnosis (0.33), being 0.17 in the doubtful group and 0.24 in the non-NIFTP group.
Conclusion: The degree of agreement regarding NIFTP and bordering entities (hyperplastic nodule, follicular adenoma, follicular or well differentiated tumour of uncertain malignant potential, subtypes of papillary carcinoma, follicular carcinoma) among pathologists with special dedication to endocrine pathology was moderate, with the lowest values being observed in the nuclear characteristics and the highest values in the presence of psammoma bodies, capsular invasion and vascular invasion. Fortunately, the two latter criteria are the most significant to determine a diagnosis of carcinoma.

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OFP-10 | Gynaecological Pathology

OFP-10-001

Clear cell carcinoma (CCC) of the cervix is a Human Papillomavirus (HPV)-independent tumour associated with poor outcome

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Background & objectives: Cervical clear cell carcinoma is an HPV-independent adenocarcinoma. While recent studies have focused on gastric type endocervical adenocarcinomas (GTA), little is known about CCCs. We analysed clinico-pathologic parameters and outcomes of CCCs compared to GTA and HPV-associated endocervical adenocarcinoma (HPVA).
Methods: 58 CCCs were collected from 14 international institutions. Correlation between various parameters to overall (OS) and recurrence free survival (RFS) was retrospectively analysed using univariable and multivariable methods. OS and RFS were also compared to those of 36 GTA and 173 HPVA.
Results: Most cases were treated with radical surgery (84.5%), 55.2% adjuvant therapy, were FIGO stage I (70.7%), Silva C pattern (75.9%), and histologic grade 3 (96.6%). Lympho-vascular invasion was present in 31% and lymph node metastases in 22.4%; 10.3% had pelvic metastases, 32.8% had recurrences and 18.96% died of disease. There were no statistically significant differences in OS and RFS between CCC and GTA at 5 and 10 years (p=0.313 and p=0.508 respectively), but there were significant differences in OS and RFS between CCC and HPVA (p=0.003 and p=0.032 respectively). Multivariate analysis showed that OS in influenced by recurrence (p=0.009), while RFS is influenced by FIGO stage (p=0.025).
Conclusion: CCCs have poorer outcomes than HPVA but similar outcomes to GTA. Oncologic treatment significantly influences RFS in univariate analysis but is not an independent prognostic factor in multivariate analysis. Since current therapies do not improve outcome in patients with CCCs, new oncologic strategies are needed.

OFP-10-002

Horizontal tumour extend (HZTE) has limited prognostic significance in endocervical adenocarcinoma (ECA): a retrospective study of 2019 FIGO low-stage 416 cases

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Background & objectives: FIGO2019 update on cervical cancer staging removed horizontal tumour extent (HZTE) as a staging variable in microscopic disease (stage IA) due to its poor reproducibility. We aimed to investigate the association of HZTE with survival outcomes in patients with ECAs.
Methods: We retrospectively analysed 416 cases of stage I ECAs from 16 international institutions. Clinico-pathologic parameters and HZTE were retrieved from pathology reports and stage was assigned using 2019 FIGO criteria. Correlation between HZTE, prognostic parameters, overall survival (OS) and recurrence free survival (RFS) were performed using univariable and multivariable analyses.
Results: 71 (56.3%) stage IA cases had HZTE <7 mm and 55 (43.7%) ≥7 mm, while 23 stage IB cases (7.9%) had HZTE <7 mm and 267 (92.1%) ≥7 mm (p=0.0001). 4 (3.2%) stage IA patients developed recurrence compared to 41 (14.1%) stage IB patients (p=0.002). Of the 4 stage IA patients with recurrences (1 IA1, 3 IA2), 3 had tumours with HZTE <7 mm, one of which was IA1. One stage IA2 case had tumour with HZTE ≥7mm. 14 stage IB patients died of disease, all with HZTE ≥7 mm, while no stage IA patients died of disease. In multivariate analysis OS and RFS were not influenced by HZTE.
Conclusion: HZTE does not improve the prognostication of patients with stage IA cancer as per the 2019 FIGO staging system and does not add meaningful prognostic information in early-stage microscopic lesions. Consequently, the FIGO rationale to remove this variable from the staging exercise is justified for ECAs.

OFP-10-003

Primary versus metastatic uterine leiomyosarcoma: differences in hormonal receptors' expression

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Background & objectives: Uterine leiomyosarcomas (uLMS) have variable expression of hormonal receptors. High tumour expression is associated with good response to hormonal therapy. In this study we aimed to

evaluate the concordance of hormonal receptors' expression between primary uLMS and matched recurrences/metastases.
Methods: Retrospective cohort study (1980-2019), including 29 uLMS patients with recurrent/metastatic disease confirmed by histology; 24 with available primary uLMS. Clinical files and histological slides were reviewed. Immunohistochemistry study with antibodies for oestrogen(ER) and progesterone(PR) receptors was performed. ER/PR were evaluated in primary uLMS and all recurrence/metastatic samples, both using a binary classification (positive/negative) and categories of % positive tumour cells.
Results: Most primary tumours were ER/PR positive (ER: n=21, 87.5%; PR: n=17, 70.8%), with a variable proportion of expression (ER/PR: median=30-40%, range: 0 to 90-100% tumour cells). Thirteen (44.8%) patients had biopsies from more than one metastasis. ER/PR positivity was observed in 19 (65.5%) of first metastases. Most primary tumours had concordant expression with first metastasis (n=16, 66.7%), but 8 had discordant results: 7 changed from positive to negative and 1 from negative to positive. Within those that lost ER/PR expression in metastases, 5 had less than 30-40% of positive tumour cells in primary uLMS. Three showed discordant expression between different metastases of the same patient.
Conclusion: Our results demonstrated that concordance between primary uLMS and metastasis is moderate. This variation most likely is due to biological subclonal selection or changes in metastatic tumour cells, but pre-analytical sample conditions may also influence results. If hormonal therapy guided by hormonal receptors' expression is considered for patient management in metastatic uLMS, ER/PR evaluation in metastasis may be useful.

OFP-10-004
Macroscopic and histological sentinel lymph node processing in endometrium carcinoma - pathological routine aspects of ultra-staging
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Background & objectives: Molecular characterization of endometrial carcinoma should be balanced by complete conventional histopathological parameter of the TNM-system. Sentinel lymphadenectomy represents a safe and informative compromise for pN evaluation. The various ultrastaging options enclose macroscopic preparation, frozen section, step-sectioning and pan-cytokeratin immunohistochemistry.
Methods: 834 sentinel lymph nodes from 206 patients treated at the University Hospital Inselspital Bern between 2012-2020 were processed. Macroscopic treatment allowed for complete (26.9%), bi-valved (37.6%) or lamellated (35.5%) lymph nodes. Histologically, specimen were treated with frozen section (5.8%), with step sectioning in 3 steps with 200 microns distance (95.1%) and pan-cytokeratin immunohistochemistry (93.4%), referenced to the first HE (100%).
Results: In total 73 positive lymph nodes were found (8.8%), which could be split to 42 macroscopic, 6 micro metastasis and 25 lymph nodes with isolated tumour cells. In comparison of macroscopy, significantly higher detection rates were found in lamellated sentinel lymphnodes ($p<0.004$). In the small part of frozen section no macro metastasis were missed and even 2 micro metastasis detected. Pan-cytokeratin immunohistochemistry mainly contributed to the detection of isolated tumour cells and some micrometastasis, but also highlighted relevant pitfalls like endosalpingiosis, mesothelial inclusions etc. An added value to macrometastasis detection by immunohistochemistry was not found, which in 92.9% of cases were detected with the first HE before step sectioning.
Conclusion: Prior to considerations of ultra-staging in terms of immunohistochemistry, routine workup of sentinel lymphadenectomy starts with appropriate grossing with lamellation. Frozen section is a robust technique in terms of macro-metastasis detection. The roles of micrometastasis and isolated tumour cells have yet to be clarified in terms of prognostication.

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OFP-10-005
BRCA1/2 mutation status in neoplastic ascites of serous carcinoma of the ovary by Next Generation Sequencing: a reliable method
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Background & objectives: BRCA1/2 test on ovarian cancer tissue is recommend at the time of diagnosis to predict response to PARP-inihibitors. As malignat ascites is a rich souce to characterized cancer cells, we aim to investigate BRCA1/2 status on this material.
Methods: 24 cases of high-grade serous carcinoma with neoplastic ascites were selected for the study. 5/24 of ascites were neoplastich rich (neoplastic cells >50% x 4), 16/24 had an intermediate cellularity (20-50%) and 3/24 had a poor neoplastic cellularity (< 20%). NGS techniques were used and BRCA1/2 variants were compared with data previously obtained from peripheral blood/tumour tissue.
Results: 21/24 cases were informative for BRCA1/2 status: 10 were BRCA1/2 positive and 11 were BRCA1/2 negative. The concordance of BRCA1/2 between malignant ascites and tumour tissue/blood was 100%. Among the BRCA1/2 positive cases, 9 had germline mutation and 1 had somatic mutation. Of the 3/24 non informative cases 2/3 had poor neoplastic cellularity and 1/3 was neoplastic rich.
Conclusion: Malignant ascites is a good source of neoplastic cells to characterize BRCA1/2 status. As the paracentesis is quick, easy to perform, the NGS analysis on cytologic material can be considered comparable to that obtained in conventional neoplastic materials. This open new prospective to study BRCA1/2 status at the time of diagnosis and follow the evolution of BRCA1/2 mutation during therapy in ovarian cancer as well as in other neoplasia eligible to PARP-inhibitors therapy.

OFP-10-006
Next Generation Sequencing somatic BRCA1/2 mutation in 64 endometrial serous carcinoma
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Background & objectives: Endometrial serous carcinoma (ESC) shares with ovarian serous carcinoma morphology, p53 mutation and behaviour but few data are available on somatic-BRCA 1/2 status. We evaluated BRCA 1/2 status by Next Generation Sequencing technique (NGS) in a cohort of ESC.
Methods: From a cohort of 104 cases of high-grade endometrial carcinoma, 80 cases fitted the morphological criteria of serous carcinoma or mixed carcinoma with a serous component. 64 cases were eligible for molecular studies: 48 serous carcinoma, 12 carcinosarcoma and 4 mixed tumour serous-endometrioid. DNA was extracted from paraffin tissue and BRCA 1/2 genes were sequenced using NGS techniques.
Results: 62/64 (96.8%) cases were informative for BRCA 1/2 status: 5/62 (8%) had a pathogenetic variant, 2/5 in BRCA1 and 3/5 in BRCA2. 5/5 (100%) BRCA1/2 positive had a pure serous histology; 5/62 (8%) had a variant of uncertain significance (VUS) (3 cases with a pure serous histology and 2 cases were carcinosarcomas). 8/48 (16%) of serous carcinoma were BRCA 1/2 positive/VUS. 52 cases (84%) were BRCA 1/2 negative.
Conclusion: Somatic-BRCA 1/2 mutation is present in 16% of the cases and in 8% as a pathogenetic variant. If we consider endometrial

carcinoma with pure serous histology 10.4% harbour a pathogenetic variant of BRCA1/2 which is the same incidence reported in the literature for high grade serous tubo-ovarian carcinoma. Those data open the scenario of a possible predictive value for target therapy with PARP-inhibitors.

OFP-10-007

Placental pathologic findings of women with SARS-CoV-2 infection during pregnancy and early neonatal follow-up

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Background & objectives: Transplacental transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been suggested in very rare cases reported. Our aim is to evaluate the histopathologic findings in the placentas of women with prenatal SARS-CoV-2 infection and its repercussions on foetuses.
Methods: The study included placentas received for one year in our hospital. Clinical data, histopathologic placental findings, immunostaining for the SARS-CoV-2 N-protein and foetal infection rates were collected. SARS-CoV-2 RT-PCR was performed in all live births. Nucleocapsid protein and spike protein antibodies, and SARS-CoV-2 RT-PCR in some samples from the placenta, foetus blood or foetus fluids were also tested.
Results: Eighteen patients with SARS-CoV-2-positive tests at most 10 days before labour were included. The placentas were divided in two groups depending on the immunohistochemical result for SARS-CoV-2: negative (n=16) and positive group (n=2). One patient experienced minor symptoms, fourteen were asymptomatic and the remaining are unknown. The placentas were subsequently subdivided based on medical history or maternal complications usually associated with placental pathological findings. There were 10 placentas cases with maternal malperfusion (8 in the negative and 2 in the positive group), 3 had foetal malperfusion (all in the negative group), 10 had inflammatory alterations (8 in the negative and 2 in the positive group) and 7 had other findings.
Conclusion: Although the placental/foetal transmission seems to be rare, probably due to the physical and immunological barrier of the placenta, our data suggests the increased presence of maternal/foetal vascular malperfusion and histiocytic intervillositis in placentas delivered from SARS-CoV-2-positive women. All live foetuses had negative nasopharyngeal swabs despite five positive cases to nucleocapsid antibodies (totals=4, IgG=1) due to maternal immunization. At the date of the abstract, we still don't have the results from placenta, foetus blood or foetus fluids for SARS-CoV-2 RT-PCR.

OFP-10-008

Claudin-18 as a surrogate marker for endocervical gastric-type carcinoma

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Background & objectives: Claudin-18 has been shown to be frequently expressed in gastric and pancreatobiliary carcinoma. This study was carried out to investigate whether Claudin-18 could be a surrogate marker to separate endocervical gastric-type carcinoma (GAS) from other types of endocervical adenocarcinoma (ECA).
Methods: ECAs from 7 international institutions were reviewed by a panel of pathologists for consensus histotype based on recently developed International Endocervical Criteria and Classification (IECC). Tissue microarrays were constructed to analyse Claudin-18 expression using immunohistochemistry to simulate assessment in small biopsies. The staining was scored and any staining in >5% of tumour cells considered as positive.
Results: Of 174 ECAs, 125 were of usual-type, 23 GAS, 7 clear cell and 19 other types. Claudin-18 expression was significantly frequent in GASs (15/23, 65.2%) than in non-GASs (3/151, 2.0%; all usual-type) ($p<0.01$). Positive and negative predictive values of Claudin-18 for GAS were 83.3% and 94.9%, respectively. All Claudin-18 positive GASs showed strong and diffuse staining pattern with staining in more than 75% of tumour cells. None of clear cell type showed positivity for Claudin-18.
Conclusion: Our results suggest that Claudin-18 is a promising surrogate marker to separate GAS from other types of ECA, including clear cell-type.

OFP-10-009

High-risk Human Papillomavirus detection in formalin-fixed paraffin-embedded cervical tissues: performances of Aptima HPV assay and Beckton Dickinson (BD) onclarity assay

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Background & objectives: There are many scenarios where high-risk HPV (hrHPV) detection in formalin fixed paraffin embedded (FFPE) specimens are important. However, there is no Food and Drug Administration (FDA)-approved and clinically validated technique for detecting hrHPV in FFPE tissues.
Methods: We evaluated two commercially available HPV assays which are FDA approved for use on cytology specimens, the Aptima HPV assay and the BD Onclarity assay, to detect hrHPV in FFPE tissues of cervical HSIL and SCC. A total of 189 cases were tested for hrHPV with the Aptima HPV assay and a subset of cases(n=97) with the BD Onclarity assay.
Results: The sensitivities of the Aptima and BD Onclarity HPV assays were 99.4% (95%CI:96.46%–99.98%) and 75.9% (95%CI:65.27%–84.62%), respectively; the specificity and positive predictive value of the two assays were 100%. Negative predictive values of the Aptima and BD Onclarity HPV assays were 97.3% (95%CI:83.61%–99.61%) and 67.7% (95%CI:58.91%–75.47%), respectively. The kappa value for comparison of the distribution of hrHPV types between the two assays was high(κ:0.96). HPV16 was the most common hrHPV type for HSIL and SCC cases. However, SCC cases had higher percentages of HPV16 and HPV18/45 and lower percentages of other hrHPV types compared to HSIL cases.
Conclusion: Both assays are reliable methods for high-risk HPV detection and genotype determination in FFPE specimens, with high PPV and specificity. The Aptima HPV assay has the advantage of higher sensitivity. As far as we are aware, this is the first study comparing the Aptima HPV assay and the BD Onclarity assay in FFPE tissues. Our study results should be tested and confirmed in larger cohorts.

OFP-10-010

Clinicopathological analysis of 41 pole-mutated endometrial carcinomas

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Background & objectives: Endometrial carcinomas (ECs) harbouring POLE mutations have been associated with an excellent prognosis, although recurrent and metastatic cases have been described.
Methods: 41 POLE- mutated ECs were selected from our archives (2000-2021). The following clinicopathologic criteria were evaluated: histotype, grade, intratumoral heterogeneity (IH), serous-like (SA) and clear cell-like areas (CCA), the presence of bizarre nuclei (BN), tumour infiltrating-lymphocytes (TILs), peritumoral lymphocytes, MELF-type invasion (MELF), lymphovascular invasion (LVI), MMR protein and p53 expression, FIGO stage, adjuvant treatment, recurrence and status.

Results: Median age was 60.4 years. 31 patients were FIGO I-II and 10 FIGO III-IV stage. Median follow-up was 64 months. 36 patients are alive (35 without disease, 1 with disease), 2 died from disease (DFD) and 3 from unrelated causes.
35 cases were endometrioid carcinomas (EECs): 28 G3, 5 G1, 2 G2; 2 mixed carcinomas and 4 carcinosarcomas. 20 tumours showed IH, 4 CCA, 9 SA, 20 BN. 22 had LVI and 3 MELF. TILs were frequent.
8 cases were MMR-deficient, 7 p53-abnormal and 1 a multiple-classifier. The most frequent pathogenic POLE mutations were: 26 V411L, 16 P286R and 4 A456P. The 2 patients who DFD showed non-pathogenic mutations.
Conclusion: POLE-mutated ECs are typically high grade EECs in which IH, increased TILs and BN are frequently observed. Abnormal p53 expression and/or loss of MMR protein expression in high grade tumours, does not exclude POLE mutations. Patients with pathogenic POLE mutations have a favourable prognosis, despite presenting advanced stage at diagnosis.

OFP-10-011

The morphological heterogeneity of fumarate hydratase-deficient leiomyoma: a single institutional experience

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Background & objectives: Fumarate hydratase (FH)-deficient leiomyoma is a distinct subtype of uterine leiomyoma occurring in sporadic and syndromic settings. Published studies reported a characteristic morphology although its sensitivity remains questionable.
Methods: 1298 uterine samples (biopsy and surgical specimens) were retrospectively found from a single academic institution's pathology database between January 2018 and December 2020 identifying sixteen FH-deficient leiomyomas in 14 women (1.08% of all samples; 1.2% of surgical specimens). We evaluated clinical and histological characteristics (evaluated from 1 to 8 slides per tumour, median=3), collecting data on cytological and architectural features.
Results: Median age was 43 years (from 29 to 54), most nulliparous(8/14). The average tumour size was 8 cm(from 0.7 to 12). In 9 patients, conventional leiomyomas were associated. None reported a family or personal history of hereditary leiomyomatosis and renal cell carcinoma syndrome. All patients were alive without disease. Grossly, 13 tumours were white whorled (two tumours were yellowish, one was spongy). Morphologically, the tumours were cellular(2), epithelioid(1), with remarkable bizarre nuclei(1), micro-macrocystic(2). Staghorn-shaped vessels were seen in 10, thick-wall vessels in 5, multiple microvessels in 6 tumours, frequently in combination. Only one tumour displayed an unremarkable vascular pattern. Prominent nucleoli were easily encountered in 5 tumours, in the remaining cases were pinpoint. Other focal features observed were palisading arrangement(3), inflammatory infiltrate(5), nuclear pseudo-inclusions(5), scattered eosinophilic cytoplasmic globules(10). Necrosis was absent in all cases.
Conclusion: Morphological distinct features of FH-deficient were observed in 6 tumours (37%). Most of the tumours resemble conventional leiomyomas at low magnification with focal and subtle histological features of FH-deficiency. The vascular pattern (staghorn-shaped, thick-wall, and micro-vessels) is the most reliable finding.

OFP-10-012

Investigation of progestin-induced changes in the endometrial transcriptome: Implications for personalized medicine in low-grade endometrial neoplastic lesions

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Background & objectives: Mechanisms underlying resistance to progestin therapy in endometrial carcinoma (EC) are poorly understood. In this study, we characterized progestin-induced transcriptomic changes in neoplastic and non-neoplastic endometrium to distinguish physiological effects of progestin from predictive biomarkers unique to lesional treatment response.
Methods: We have previously examined the transcriptomic profile of low-grade endometrial neoplastic lesions (LGENLs) – atypical hyperplasias and FIGO grade1 ECs - that exhibited complete response (CR) to progestin therapy. In this study, Pre- and post- progestin treated biopsy samples of 4 patients with disordered proliferative and 4 with proliferative phase endometrium underwent whole transcriptome RNA sequencing of >20,000 human genes.
Results: Unsupervised analysis separated pre- and post-treatment non-neoplastic endometrium into 2 distinct clusters. Supervised analyses identified 2572 differentially expressed genes ($P \leq 0.05$, fold change≥ 2), which represent a molecular signature of progestin effect. Of these, 391 (15%) also exhibited progestin-induced changes in expression in CR LGENLs. Next, our analysis focused on 73 progesterone-related pathway genes. Interestingly, comparing the expression of these genes between non-neoplastic endometrium and LGENLs post-treatment identified only 1 common gene, *FOXO1*, a known marker of progestin response. Further, we found progestin-induced changes in expression of *PTN* were unique to CR LGENLs while changes in *FOS, ADM, PIK3R3, PGR, PTGER2, CD38, TYMS, TLR2* and *DSG2* expression were unique to non-neoplastic lesions.
Conclusion: Non-neoplastic endometrium exhibits a much wider spectrum of DEGs than CR LGENLs, both globally and when focusing on progesterone pathway genes, suggesting progestin response may be already impaired in LGENLs. Next, comparative analysis of transcriptomic features that would differentiate non-neoplastic endometrium, CR and non-responder LGENLs sampled prior to progestin therapy will be performed to search for predictive biomarkers.

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OFP-10-013

PD-L1 expression and mismatch repair status in endocervical clear cell carcinomas

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Background & objectives: Endocervical clear cell carcinoma (cCCC) is a rare tumour and resistant to conventional chemotherapy. PD-L1-expression is used as a predictive biomarker for immunotherapy. Mismatch-repair-deficiency is associated with the immunotherapy response. We evaluated PD-L1 expression and mismatch repair status in cCCCs.
Methods: Immunohistochemical staining for PD-L1 (SP263 clone) expression was performed on a tissue microarray of 14 cCCC cases (6 mm diameter two tissue cores from each case). Expression was scored in both the tumour and tumour-infiltrating immune cells as follows; negative (<1%), low (1-4%), intermediate (5-50%), and extensive (>50%) staining. Furthermore, tumoral mismatch repair status (MLH1, MSH2, MSH6, PMS1) was evaluated.
Results: PD-L1 expression, either tumoral or tumour-infiltrating immune cells, was present in 71.4% (10/14) of cCCCs. Most of the positive cases showed PD-L1 expression in ≤50% (8/10) of the tumoral cells. Almost all cases were accompanied by intermediate or low-level immune cell infiltration. PD-L1 expression in immune cells was present in 61.5% (8/13) of the cases. Extensive PD-L1 expression was seen in 2 cases. They also had mismatch repair deficiency (MSH2 loss, MLH1-PMS2 loss). Overall mismatch repair deficiency was seen in 35.7% (5/14) of the cases. PD-L1 expression was observed at all mismatch repair deficient cases except one (4/5). However, 60% of the PD-L1 positive cases were remained mismatch repair intact.

Conclusion: The prevalence in endocervical CCC is still underinvestigated. We evaluated PD-L1 expression in 14 endocervical CCCs and correlated with the mismatch repair status. We herein demonstrate that some degree of tumoral and peritumoral immune cell PD-L1 expression is present in endocervical CCCs. This finding suggests a role for further investigation of anti-PD-L1/PD-1 immunotherapies in the treatment of PD-L1-positive cCCCs. Moreover, mismatch repair deficiency may support this finding. Further studies in larger series are needed to confirm our findings.

OFP-10-014

Lynch Syndrome screening algorithm in endometrial carcinoma can be improved

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Background & objectives: Lynch syndrome(LS) screening in endometrial carcinoma(EC) starts with mismatch repair protein(MMR) immunoexpression, followed by MLH1 methylation in ECs showing MLH1/PMS2 expression loss. We aim to identify points of improvement in LS screening algorithm, focusing on MMR immunoexpression patterns and second allele MLH1 methylation.
Methods: All consecutive patients diagnosed with EC showing altered MLH1 protein expression were selected (2009-2020, n=55). Clinical files and immunohistochemistry slides were reviewed. DNA was extracted from FFPE samples, and subjected both to bisulfite modification followed by amplification by quantitative methylation-specific PCR (qMSP), and to Methylation-Specific Multiplex Ligation-Dependent Probe Amplification (MS-MLPA).
Results: We were able to distinguish three MLH1 methylation groups: the first, with patients whose tumours do not have methylation in any alleles (n=20), the second with patients whose tumours had partial methylation (n=14), most probably in only one allele, and lastly, patients whose tumour had methylation in both alleles (n=21). The vast majority of patients that proceeded to germline testing belong to the first group, and patients on the other groups were rarely tested. Immunohistochemistry study showed that MLH1 expression can be completely lost (n=44) but also presented as subclonal loss (n=6) and decreased immunoexpression (n=5). All these patterns of immunoexpression can be associated with LS.
Conclusion: LS screening in EC patients is highly dependent of immunohistochemistry and MLH1 methylation results. All altered immunohistochemistry patterns should be taken into account. Patients with partial MLH1 methylation, most probably have only one methylated allele, as a putative second hit, and thus may be considered for LS germline testing. By including these patients in LS screening, we expect a small increase in the number of patients diagnosed with LS; but importantly, identifying a patient with LS, means identifying a family with LS.

OFP-10-015

Cytology-histology correlation in HPV-related patients based on the recent American Society of Cytopathology guidelines (2017)

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Background & objectives: The aim of the study was to conduct a retrospective comparative analysis of the cytological and histological diagnoses in women with cervical pathology associated with the human papillomavirus (HPV).
Methods: A retrospective review was conducted for cervical biopsies with their corresponding liquid-based cervical smears (SurePath) over a 2-year period (2018-2019). According to ASC guidelines, a discrepancy assessment grid was prepared. Major cytology-histology discordance was defined as a diagnosis of high-grade squamous intraepithelial lesion (HSIL) or CIN2+ in one of the tests with negative result in the other.
Results: We analysed 3 groups based on the results of studies: the 1st group included patients with complete coincidence of cytological and histological diagnoses. The 2nd group - minor discrepancies, the 3rd group - significant discrepancies. Of the 415 cervical biopsies with corresponding Papanicolaou liquid-based smear, cytology-histology agreement was noted in 194 (46.74%). Major discordance was observed in 29 cases (6.9%), while 4.8% cases of cytological result "NILM" corresponded to the histological diagnosis of HSIL, and 2.1% of cases with a cytological findings of HSIL, a histological findings was diagnosed with "benign" (chronic cervicitis). The minor discrepancies was 192 (46%).
Conclusion: We suppose that ASC guideline helps to standardise the conduct of cervical cytology-histology correlation internationally. Our comparative analysis showed that in all groups there were cases of underdiagnosis and overdiagnosis in cytological examination, however, there were few observations in which management of the treatment changed significantly due to different cytological and histological diagnoses (6.9%).

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OFP-10-016

Malignant mixed ovarian germ cell tumours: a 9 years' experience from a tertiary referral centre

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Background & objectives: Malignant mixed germ cell tumours (MMGCT) of the ovary are relatively rare neoplasms accounting for less than 5% of all ovarian cancers. We evaluated the incidence, clinicopathological characteristics, clinical outcome of MMGCT at our centre and reviewed the existing literature.
Methods: Twenty-three cases of MMGCT were identified among 996 cases of germ cell tumours (GCT) treated at our institute from 2012 -2020. Clinical data including demographics, stage, type of surgery, chemotherapy regimens, tumour marker levels, menstrual functions, fertility, and outcome were collected for each patient from medical records and pathology reports.
Results: Ovarian MMGCT accounted for 2.3% of all GCT. Median age was 27 years (range, 17-42). Most common presenting symptoms were abdominal mass and pain (81%). Average tumour size was 16 cm (range, 6.8-30). Majority were stage I-II tumours (81%). Most frequent histological combination was yolk sac tumour and immature teratoma seen in 12 patients (52%). Seventeen (74%) patients underwent complete surgical staging. Fifteen (65%) received post-operative chemotherapy. Only one patient received neo-adjuvant chemotherapy. During a median follow-up period of 32.4 months, 2 patients had recurrence. Eleven patients (61%) developed chemotherapy complications. Median overall survival was 28.2 months. No adverse prognostic variables were identified, and 90% patients had good overall survival.
Conclusion: MMGCT are rare tumours affecting adolescent females of reproductive age, therefore fertility preservation and long-term survival is extremely important. Majority of these tumours are diagnosed at an early stage, have a good response to the standard treatment regimens and a good clinical outcome. However, due to the rarity of the disease, there is a clear need for more studies to better identify prognostic factors that will further improve the clinical outcome of patients with advanced/relapsed disease.

OFP-10-017

Association between immunohistochemistry in endometrial hysteroscopic biopsies and pregnancy within six months

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Background & objectives: Chronic endometritis is a common disease associated with infertility. Although the histopathological and immunohistochemical evaluation are considered essential for its diagnosis, the diagnostic criteria or sampling recommendations are not yet defined.
Methods: This was a retrospective cohort evaluating women with infertility submitted to hysteroscopy with endometrial biopsy in the Fleury Group, in Brazil, from 2012-2020. Variables of interest included: size of the biopsy specimen, presence, and quantification of CD56- and CD138-positive cells in the endometrial stroma, and evidence of pregnancy within six months from the biopsy (assessed either by β-HCG or pelvic ultrasound).
Results: We included 696 patients, with median age of 37-years and median biopsy size of 5mm. CD56-positive and CD138-positive cells were detected in 97.7% and 26.7% of the samples, respectively. Samples with CD138-positive cells presented a higher quantification of CD56-positive cells in the stroma (median[25th-75th percentiles]: 20%[14.25-25%] vs. 15%[10-25%]; p:0.013). Pregnancy testing was performed in 202 patients, with positive results in 112. Patients with positive testing presented more frequently CD138-positive cells in the endometrial stroma (32.1% vs. 17.8%, p:0.020). Finally, a multivariate analysis demonstrated that the presence of CD138-positive cells was an independent predictive factor for pregnancy (p:0.018), controlled by the phases of the endometrial cycle, CD56-positivity, or size of the biopsy.
Conclusion: We found that the presence of CD138-positive cells was associated with pregnancy within six months, regardless of the biopsy size, indicating the impact of endometritis assessment even in hysteroscopic biopsies.

OFP-10-018
PD-L1 expression in endometrial carcinomas: which tumours are more likely to be PD-L1–positive?
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Background & objectives: Many promising clinical trials of anti–PD-1/PD-L1 monoclonal antibodies for endometrial cancer are ongoing. Patients with endometrial carcinomas that express PD-L1 may respond better to immunotherapy. Our aim was to investigate the differential characteristics of PD-L1–positive endometrial carcinomas.
Methods: We reviewed records of patients with endometrial carcinomas who were managed at the King Hussein Cancer Center (2007–2016) and performed immunohistochemistry for MLH1, PMS2, MSH2, MSH6, p53, and PD-L1. We stratified patients according to tumoral PD-L1 expression (< 1% or ≥ 1%), described the clinical and tumoral characteristics of the strata, and tested associations using Pearson's χ^2 test.
Results: We included 231 women. According to Bokhman's classification, 156 tumours (67.5%) were type I and 75 (32.5%) were type II. Of 156 endometrioid carcinomas, 52 (33.3%) were FIGO grade I, 83 (53.2%) were grade II, and 21 (13.5%) were grade III. Overall, 89 cases (38.5%) were MMR-deficient. PD-L1 was expressed in 49 cases (21.2%) and was associated with MLH1/PMS2 deficiency ($p = 0.044$) but not MSH2/MSH6 deficiency ($p = 0.59$). p53 was mutant in 106 cases (46.5%) and mutation was associated with MMR proficiency ($p < 0.001$) but not PD-L1 expression ($p = 0.78$). In patients with endometrioid carcinomas, PD-L1 expression was associated with FIGO grade ($p = 0.008$).
Conclusion: In conclusion, tumours with MLH1/PMS2 loss and high-grade endometrial carcinomas were more likely to express PD-L1 in tumour cells. The presence of either characteristic may signal a higher likelihood of a favourable response should immunotherapy be administered.

OFP-11 | Haematopathology

OFP-11-001
Clinicopathological implications of RHOA mutations in angioimmunoblastic T-cell lymphoma: a meta-analysis
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Background & objectives: Studies have shown that RHOA mutations play a crucial role in angioimmunoblastic T-cell lymphoma (AITL) pathogenesis. We aimed to pool data from these studies to compare clinicopathological features between the RHOA mutant and RHOA wild-type groups in the AITL population.
Methods: We searched PubMed and Web of Science for the keywords "RHOA AND lymphoma" and selected only studies reporting the clinical significance of RHOA mutations in AITL. We calculated the odds ratios (OR) or the mean difference with 95% confidence intervals (CI), using a random-effect model.
Results: Our pooled results showed a significant association between RHOA mutations and a T-follicular helper cell (TFH) phenotype, especially CD10 (OR=5.16; 95% CI: 2.32-11.46), IDH2 mutations (OR=10.70; 95% CI: 4.22 - 27.15), and TET2 mutations (OR=7.03; 95% CI: 2.14 - 23.12). Although DNMT3A together with TET2 and IDH2 mutations are epigenetic gene alterations, we found an insignificant association between RHOA and DNMT3A mutations (OR=1.72; 95% CI: 0.73 - 4.05). No significant associations of RHOA mutations with other clinicopathological features and overall survival were found.
Conclusion: RHOA mutations are strongly correlated with a TFH phenotype and epigenetic mutations such as TET2 and IDH2. Further studies with large AITL samples should be conducted to validate the relationship of TET2, DNMT3A, and RHOA co-mutations.

OFP-11-002
Clinicopathologic study of mantle cell lymphoma with EBV infection
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Background & objectives: Mantle cell lymphoma (MCL) with EB virus (EBV) infectionare rarely reported. Herein, we report the largest series of analyses of the prevalence and clinicopathological features of mantle cell lymphoma with EBV infection.
Methods: 138cases of MCL diagnosed in the first affiliated Hospital of Chongqing Medical University and Chongqing University Cancer Hospital from January 2014 to November 2019 were collected retrospectively. Cases with EBV infection were screened by EBER ISH, then double labelling of EBER(ISH) and CD79α(IHC) was performed, clinical and pathological data were analysed.
Results: EBER ISH showed that there were 8 cases of MCL with EBV infection (the infection rate was 5.8%), and all of them were non-neoplastic bystander cells with positive EBV and there was no expression of LMP1 and EBNA2. All MCL with EBV infection have no abnormal immune function and without other lymphomas, and their histopathological morphology showed classic MCL. MCL with EBV infection and MCL without EBV infection have statistically significant differences in LDH, anaemia status, and MIPI grouping (P=0.008; P=0.02; P=0.001; P=0.011). The differences were not statistically significant between two groups in age, sex ratio, clinical manifestations and immunohistochemical phenotypes.
Conclusion: The incidence of MCL with EBV infection is low, and its clinicopathological features are similar to those of MCL without EBV infection. This study shows that the cells infected by EBV in MCL are background cells rather than tumour cells, which is different from previous studies, indicating that tumour cells in MCL may not prone to EBV infection.

OFP-11-003

Lymph node biopsies of primary immunodeficiency disorders: our experience in a tertiary hospital

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Background & objectives: There are more than 100 primary immunodeficiency disorders, our aim was to review the lymph node biopsies diagnosed since 2016. We collected all the clinical information from our database, molecular, immunohistochemistry studies and reviewed all the slides from each case.
Methods: We found nine patients, 6 women and 3 men. Five cases had variable common immunodeficiency (VCI), with a mean age of 43 (37-60 years-old). The other 4 cases were a Chediak-Higashi syndrome (CH); an autoimmune lymphoproliferative syndrome (ALPS), a PI3K primary immunodeficiency and a humoral immunodeficiency not yet defined. These cases were all children with ages from 2 to 12.
Results: At the lymph node biopsy the VCI cases had two type of patterns, 3 cases had non-necrotizing granulomas and 2 cases follicular hyperplasia with ill-defined germinal centres. 1 patient had a TCR clone with no histology of lymphoma.
The patient with CH had a T cell atypical population with a TCR clone. She had a bone marrow transplant to treat her immunodeficiency. The case of ALPS had an increase of doble negative T cell lymphocytes, the PI3K had a follicular hyperplasia positive for Epstein-Barr virus (EBV) and cytomegalovirus. The last case was diagnosed of lymphoproliferative disorder EBV associated, clonal for IgH and was treated with Rituximab.
Conclusion: We present a series of cases of primary immunodeficiency disorders, with a variable and complex histology. Of the nine patients only 1 patient was diagnosed as a B cell lymphoma. To diagnose, treat and follow up these patients it´s necessary to have a multidisciplinary group of physicians like at our centre.

OFP-11-004

Idiopathic multicentric Castleman disease - differential diagnosis based on histopathological features

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Background & objectives: International Consensus Diagnostic Criteria for iMCD include lymph node Castleman Disease histopathological features as major criteria. Our aim was apply those criteria in a series of 27 cases with a previous pathological diagnosis of Plasma Cell type Castleman Disease (CD).
Methods: A retrospective series of 7 cases was analysed. Clinical and laboratory criteria were collected and histopathological features (germinal centre hyperplasia/regression, plasmacytosis, hypervascularity and follicular dendritic cell prominence) were graded in the available lymph node samples. Immunohistochemistry with antibodies against CD20, CD3, CD138, HHV-8, Ig isotype (IgG, IgG4, IgA, IgM, IgD), kappa, lambda was performed in all cases.
Results: 15 out of 27 (55%) cases were HHV-8+, 7 /26%) plasma cell neoplasia (PCN)/POEMS-related CD and 5 (19%) were iMCD. The iMCD cases showed more frequently reactive germinal centres whereas the HHV-8+ showed higher degree of hypervascularization. Clusters of IgM+lambda+ cells were identified in all HHV-8+ cases. Lambda plasma cells were identified in 3 out of 7 cases (43%) of PCN/POEMS-related CD. All 5 cases of iMCD were IgG+ and polytypic. The median number of IgG4+ cells was 14. 5 out of 23 cases (22%) had 30 or more IgG4 positive cells but none had >100 IgG4+ cells. The IgG4/IgG ratio was below 0.4 in all cases.
Conclusion: HHV-8 CD and PCN/POEMS-related CD are the major mimickers of iMCD in lymph node biopsies with plasma cell type CD features. High grade of plasmocytosis is a common feature but the presence of reactive germinal centres may support a diagnosis of iMCD. Monotypic plasma cells are found in only 43% of PCN/POEMS related cases. A dim increase in IgG4+ plasma cells is found occasionally in CD but neither the histopathology nor the IgG4/IgG ratio fit with IgG4 related disease criteria.

OFP-12 | Head & Neck Pathology

OFP-12-001

Mandibular invasion in OSCC is associated with osteoclast count and expression of its regulating proteins

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Background & objectives: Oral squamous cell carcinoma(OSCC) frequently invades the mandible. Osteoclast activation via RANKL/OPG/RANK plays an important role in bone-invasion. The exact mechanism of bone-invasion remains unclear. We elucidate the role of osteoclasts and RANKL/OPG/RANK in the development of bone-invasion in OSCC.
Methods: OSCC-patients treated with resection were included and divided in three groups; Non-invasion (NI-group), erosion (E-group) and bone-invasion (I-group). Tissue sections were stained with CathepsineK (for counting osteoclasts), RANKL, OPG and RANK. Staining intensity was scored in tumour-front, tumour-center, backside of tumour and normal mucosa. A qPCR was executed for RANKL, OPG and RANK in five head and neck SCC organoids.
Results: The mean number of osteoclasts in CathepsinK stained sections was 3.09 in the NI-group, 6.15 in the E-group and 10.58 in the I-group. Compared to normal mucosa, the expression in all tumour regions was higher for RANKL, in most of tumour regions for OPG and not higher for RANK.
RANKL-expression in the tumour-front was higher than expression in the backside of the tumour in the I-group. RANK-expression in the tumour-front and the tumour-center was higher than expression in the backside of the tumour in all groups.
qPCR showed a 20-35x higher RANKL expression in 3 out of 5 tumour organoid samples compared to a normal squamous cell organoid line.
Conclusion: The number of osteoclasts and their regulating proteins (RANK, RANKL and OPG) differ between OSCC patients with and without bone-invasion. Our data suggest that tumour cells induce bone-invasion in OSCC patients by stimulating osteoclast activation by regulating the production of RANK, RANKL, and OPG proteins.

OFP-12-002

The clinical impact of PROX-1 expression in salivary gland tumours

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Background & objectives: Salivary gland tumours (SGTs) encompass benign to highly malignant entities. The human PROX-1 gene belonging to the homeobox transcription factor family, exerts lymphangiogenic, angiogenic and possibly carcinogenic properties. The clinical significance of PROX-1 expression was examined in SGTs.
Methods: PROX-1 protein expression was assessed immunohistochemically in 48 formalin fixed, paraffin embedded SGT tissue specimens (30 benign and 18 malignant). PROX-1 positivity was correlated with benign and malignant state, other clinicopathological parameters and patients' survival in malignant SGTs.

Results: PROX-1 positive immunohistochemical expression (nuclear, cytoplasmic or nuclear and cytoplasmic) was noted in 27 out of 30 (90%) benign and 11 out of 18 (61%) malignant SGT cases, respectively. PROX-1 positivity and cytoplasmic pattern of staining was more frequently noted in benign versus malignant SGT cases (p=0.017 and 0.05, respectively). On the other hand, PROX-1 positivity in malignant SGT cases was correlated with low grade of differentiation (p=0.048). The cytoplasmic pattern of PROX-1 immunostaining was also linked to high histological grade, although non-significantly (p=0.056). In malignant SGT cases, a correlation between PROX-1 positivity and poor overall patients' survival, at a non-significant level though, was noted (p=0.084).
Conclusion: Our results suggest a link between PROX-1 expression and carcinogenesis in the salivary glands, designating it as a possible diagnostic and prognostic biomarker. In addition, suppression of lymph- and angiogenesis through PROX-1 targeting should be of great importance as a potential future therapeutic strategy in malignant SGTs.

OFP-12-003
Clinicopathological characterisation of salivary duct carcinoma with rhabdoid features (SDCRF): Immunohistochemical and genetic analyses of 19 cases
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Background & objectives: Salivary duct carcinoma (SDC) has several histological subtypes. We established "SDC with rhabdoid features (SDCRF)" as a new entity, and it showed no or aberrant expression of cell-cell adhesion molecules. We aim to elucidate the clinicopathological features of SDCRF.
Methods: We collected 417 cases of SDC as Japanese cohort, and extracted the cases with rhabdoid features(RF). We immunostained sections for AR, HER2, EGFR, CK5/6, Ki-67, E-cadherin and beta-catenin, and also examined *CDH1* gene, genetically. According to Takase classification, we subclassified into apocrine A, apocrine B, apocrine-HER2, HER2-enriched, and double-negative subtypes. We analysed the outcomes of SDCRF, compared with conventional SDC.
Results: Nineteen cases of SDCRF (4.6%) were extracted from our cohort. The mean age was 67-year-old (range; 36~86-year-old) with male predilection. The primary site was mainly parotid gland (14 cases). pStage 0-I, II, III, and IV were 3, 1, 2, and 11 cases, respectively. Eight cases died of disease, whereas 8 cases harboured distant metastases relapse. One, 11, 5, and 2 case belonged to apocrine A, apocrine B, apocrine-HER2, and HER2-enriched subtype, respectively. No or aberrant expression of E-cadherin//beta-catenin were observed in 12//9 cases or 4//7 cases, respectively. All cases never showed co-expression of cytokeratin and vimentin. One nonsense mutation, six missense mutations and one insertion were detected in *CDH1* gene.
Conclusion: SDCRF was previously diagnosed as "poorly differentiated" SDC, but all cases showed the common histology with RF. From no co-expression for cytokeratin and vimentin, they were not "true" rhabdoid cells. SDCRF harboured non-/less-cohesive cell-cell adhesion. Therefore, SDCRF indicated distant metastases relapse (8/19) rather than loco-regional relapse (2/19). Although the proportion of the molecular subtypes of SDCRF were not so different from that of conventional SDC, SDCRF indicated worse outcomes than the latter, due to frequently distant metastases relapse.

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OFP-12-004
Clinicopathological and genetic analyses of sinonasal glomangiopericytoma (SN-GAP): multi-institutional retrospective study on beta-catenin and *CTNNB1* gene
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Background & objectives: Sinonasal glomangiopericytoma (SN-GAP) was previously called "hemangiopericytoma (HPC)", "solitary fibrous tumour (SFT)", or "glomus tumour (GT)" of the sinonasal cavity. This tumour is very rare but an independent entity. We aim to elucidate the clinicopathological and genetic features of SN-GAP.
Methods: We collected "GAP", "HPC", "SFT" and "GT" cases from a pathology file of our institutions during 2000-2020 and from a set of consultation files (K.K.), and re-estimated them, histologically and immunohistochemically. Some cases were examined genetically for *CTNNB1* gene, using PCR-direct sequencing method. We compared SN-GAP with other sinonasal spindle cell neoplasms, such as SFT or GT.
Results: Four cases were re-diagnosed as "SN-GAP", with female predilection. Histologically, the tumours consisted of compactly fascicular proliferation of short spindle-shaped myoid cells with mild atypia and often showed perivascular growth pattern with staghorn-like blood vessels. There was no evidence of necrosis nor anaplasia. Immunohistochemically, the tumour cells were positive for vimentin, alpha-smooth muscle actin, BCL-2, factor XIIIa and cyclin D1, but negative for cytokeratin, desmin, CD34, STAT6, and S-100 protein. Ki-67 labelling index was approximately 2-13%. The nuclear localization of beta-catenin was observed in all cases. All cases, which could be examined, indicated the missense mutations [codon110C>G(p.Ser37Cys); codon121A>G(p.Thr41Ala)] in exon 3 of *CTNNB1*gene. The outcome was good in SN-GAP cases.
Conclusion: SN-GAP indicated the nuclear localization of beta-catenin, and it was induced from the missense mutation in exon 3 of *CTNNB1* gene, which codes beta-catenin. The combination of the immunostaining for beta-catenin and the molecular examination for *CTNNB1* gene mutation are very specific and useful for differential diagnosis of SN-GAP from other spindle cell neoplasms of sinonasal cavity; especially, monophasic fibrous synovial sarcoma, GT, SFT, low-grade myofibroblastic sarcoma and biphenotypic sinonasal sarcoma.

OFP-12-005
Dyshormonogenetic goiter: a study of 4 cases
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Background & objectives: Dyshormonogenetic goiter (DG) is a rare inherited disease. It is a thyroid enlargement due to defects in thyroid hormones synthesis. The aim of our study is to highlight the clinicopathological characteristics of dyshormonogenetic goiter.
Methods: We describe 4 patients with dyshormonogenetic goiter. Data were obtained from the files of Ear Nose Throat Department and Pathology Department of Farhat Hached Hospital of Sousse, Tunisia.
Results: There were 2 male and 2 female patients. The average age was 16 years. Consanguinity and congenital hypothyroidism has been reported in all patients. Neck swelling was the complaining symptom in all cases. On macroscopic examination, the mean size was 7 cm. Histologically; it was a multinodular goiter without any normal thyroid tissue. Nodules were hypercellular with a solid or microfollicular patterns. Colloid is minimal to absent. The follicular cells exhibit marked nuclear atypia with bizarre nuclei. These nuclear atypia is more common in internodular tissue. The nodules are entrapped with extensive fibrosis which can simulate malignancy. 2 patients underwent total thyroidectomy and the 2 others had partial thyroidectomy.
Conclusion: Dyshormonogenetic goiter is an autosomal recessive disease. It is a benign thyroid hyperplasia due to hereditary defects in hormone synthesis. It is the second cause of congenital hypothyroidism after

thyroid dysgenesis. This disease affects more female than male. The mean age of patients is 16 years. Histologically, this tumour is a multinodular goiterwith markedly cellular parenchyma and extensive internodular fibrosis. Rare cases of thyroid cancers related to DG have been reported. Treatment is based on surgery and L-thyroxin.

OFP-12-006

Warthin-like mucoepidermoid carcinoma - a morphologic spectrum: report of 3 cases with histological and cytological findings and review of the literature

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Background & objectives: Mucoepidermoid carcinoma (MEC) showing Warthin's Tumour (WT) like features is a low-grade malignancy which should be differentiated from WT. Morphological features may be distinctly different in each case causing diagnostic difficulties. Three cases are discussed in this presentation.
Methods: One case was a 16 year-old female, the other two cases were 27 and 53 year-old males. All presented with a mass in the parotid gland which went to parotidectomy and all had pre-operative fine needle aspirations. On histopathological examination first case was initially interpreted as WT, the other two were morphologically consistent with low grade MEC with WT-like features.
Results: Prominent lymphoid stroma and cystic pattern was the character of these tumours. One case had the classical WT appearance with some mucinous and squamous metaplasia which could only be interpreted as MEC after the detection of MAML2 rearrangement by FISH. The other two showed either focal or relatively diffuse usual low-grade MEC findings, one of these cases was also confirmed by MAML2 rearrangement. Cytologically one case was interpreted as non-informative due to presence of cyst fluid only, one case was suggestive of WT, only one case was found to be suspicious for MEC which contained squamous and goblet cells on a mucoid background. Cytological and histopathological features revealed a spectrum.
Conclusion: Differentiating WT-like MECs from ordinary WTs may be challenging. On one end of the spectrum they may look very much like WT, on the other end, even though usual MEC features are present, still WT-like appearance may pose diagnostic difficulty. Showing MAML2 rearrangement in these cases is very helpful. Presence of mucinous and squamous cells in an otherwise WT-like looking tumour should be alarming for MEC and if possible, each case should be analysed for MAML2 rearrangement.

OFP-12-007

Deep proteomic profiling reveals two major subgroups in the extracellular matrix of salivary gland carcinomas

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Background & objectives: The extracellular matrix (ECM) is an integral component of the tumour microenvironment. As the ECM composition of salivary gland adenocarcinomas (SGC) has not yet been addressed, we set out to discover ECM profiles and putative therapeutic targets.
Methods: Using liquid chromatography–mass spectrometry (LC-MS), we quantitatively analysed the ECM proteins of 25 normal tissue samples and 89 primary SGC, encompassing the eight most prevalent tumour types. Among a total of 6478 unique proteins, we identified 329 ECM components which were subsequently analysed.
Results: All tumours exhibited a highly dysregulated ECM with a mean of 166.5 differentially expressed proteins per entity. PCA and hierarchical clustering revealed two clusters of carcinomas, either with (MYO) or without myoepithelial differentiation (non-MYO; purity: 100%, 93.75%). To asses whether a machine learning algorithm could detect MYO and non-MYO based on ECM expression, we trained an elastic net model which predicted tumour differentiation with an error rate of 3% (area-under-the-curve: 0.996). While MYO exhibited a higher fraction of upregulated collagens and glycoproteins, non-MYO displayed a higher fraction of upregulated secreted factors. We identified several ECM components known to promote tumour invasion, progression and chemoresistance, thus representing putative therapeutic targets.
Conclusion: Using machine learning tools, we demonstrate for the first time that SGC can be categorised in two classes based on their ECM expression. Tumours with and without myoepithelial differentiation exhibit dramatic differences regarding the ECM composition. Also, using highly sensitive proteomic profiling we identify several putative therapeutic targets in the ECM of SGC. Thus, our work contributes to the final goal of a personalised therapy for SGC.

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OFP-12-008

Clinicopathological correlation of transoral robotic head and neck cancer surgery

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Background & objectives: Transoral robotic surgery (TORS) has revolutionised head and neck cancer surgery including both diagnostic and therapeutic work. In this study we access the correlation between the depth of resection, volume of resection, post-operative pain level and length of stay (LOS).
Methods: A retrospective cohort study in a Head and Neck Cancer hub. All 26 patients included had either diagnostic or therapeutic TORS at our unit. The procedures were performed using the Da Vinci Si Surgical System. Histological data included: specimen dimensions and volume, presence of malignancy, depth of tumour, depth of resection. Patient-reported pain score was recorded.
Results: The depth of muscle resection had a positive correlation (r=0.264) with the LOS, this was not statistically significant (p=0.224). Similarly, the volume of resection was positively correlated to the LOS (r=0.129), this was not significant (p=0.529). Multivariate analysis using types of procedure, depth of resection and volume of resection as independent variables showed these variables not to have significant effect on the LOS.
Conclusion: The current study's hypothesis was that the extent (depth and volume and resection) of oropharyngeal resection is directly proportional to the level of post-operative pain. Interestingly however, our study showed that the depth of muscle resection did not affect the post-operative pain level. Another interesting point was a weak positive correlation between the volume of resection and pain, patient who had who had both tonsillectomy and Tongue Base Mucosectomy (largest resection volume) reported the least pain in our cohort.

OFP-13 | History of Pathology

OFP-13-001

Who was Arthur Carleton Crooke? A historical research after diagnosing a rare tumour

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Background & objectives: 36-year-old man admitted to Emergency Department with acute heart faillure. The MRI revealed a selar mass

and the histopathological diagnosis of Crooke cell adenoma. The main objective of this research is to find out who first described this entity.
Methods: Bibliographic research was performed at PubMed using the terms "Crooke cell" and "Crooke cell adenoma". Articles that most emphasized the original description were selected.
Results: According to Bettendorf G, it was Herbert Evans, Harvey Cushing and Dorothy Russel who encouraged Arthur C. Crooke (1905-1990) to study pituitary histology at the beginning of his career. Crooke's hyaline change, first described in 1936, represents an accumulation of microfilaments around the nucleus in corticotrophs in response to an excess of glucocorticoids. These cells are basophilic or amphophilic, PAS positive and show strong imunoreactivity for ACTH and CK CAM 5.2 in a juxtanuclear pattern. Despite Crooke's scientific work in the field of pituitary pathology, his obituary highlights an even bigger contribution to Medicine: the treatment of infertility with human gonadotrophins.
Conclusion: It was A.C. Crooke, a famous British endocrinologist, who first described 85 years ago a group of characteristic cellular alterations in the hypophysis of patients dying of Cushing's disease. According to the 4th edition of the WHO Blue Book, Crooke cell adenoma is the official terminology for these rare corticotrophic adenomas with these cellular alterations (largest case series of 36).

OFP-13-002
Evolution of gastric metaplasia definition and a meaning of the phenomenon in a historical perspective
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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 submissions about metaplasia (intestinal metaplasia) was accompanied by a significant meaning modification.
Methods: Content analysis through systematic review of publications (Embase) by using key words "stomach/gastric" AND "metaplasia" was carried out. Marked evolutionary modification of these terms was revealed to the present time. A comparative method and a substantial analysis of sources were used to clarify the meaning of this phenomenon.
Results: Basic aspects 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. Expanding on earlier discussion that metaplasias can develop when mature cells dedifferentiate and proliferate the modern aspects of this process is discussed about contribution of huge number of associated factors and conditions such as UACL, pseudopyloric metaplasia, TFF3-associates metaplasia etc. 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 - epithelial-mesenchimal transition). It means changing not only the terminology itself, but significantly affects the assessment of the pathological process via modern definitions and ideas.

OFP-13-003
Tortuous vessels in a historical university museum
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Background & objectives: Varicose Veins of the limbs, already referred to in Ebers papyrus (1550 B.C.), remain a major vascular nosologic problem. The authors intend to draw attention to the issue, using the resources of the "Museu de Anatomia Patológica" in Coimbra.
Methods: A retrospective study of the specimens - human liquid-fixed and dehydrated (dried), as well as wax and clay artificial models or other type - kept in the Pathology Museum was performed, concerning varices. Photographs of the specimens were taken and the literature was reviewed.
Results: Nine (n=9) specimens were represented: eight as liquid-fixed in glass containers and one case corresponding to a set of black-and-white pictures showing varices and varicose ulcers with pre-surgery and post-saphenectomy limbs representation.
Conclusion: Venous disease with multiple risk factors (from genetic predisposition to professional long-standing position), presents diverse macro and microscopic abnormalities and may complicate (ulcers, haemorrhage, thrombosis). Throughout centuries, various therapeutic measures were applied (from Wiseman boot, passing by saphenectomy, to modern non-surgical approaches). Yet, it remains a serious Public Health issue, worldwide. Historical XIXth century Museum of Anatomical Pathology (Faculty of Medicine-University of Coimbra) fulfil pedagogic mission, as internationally, by displaying such specimens, also included in pre-graduated and graduated teaching programs.

OFP-14 | Infectious Diseases Pathology

OFP-14-001
Lymphoid cells with Russell's bodies in the spleen of patients died from COVID-19
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Background & objectives: Lymphoid cells containing aggregated immunoglobulins in the form of Roussel's bodies have been described in a wide variety of diseases. With COVID-19 infection, this cellular response in the spleen is poorly understood, which makes this study relevant.
Methods: Autopsy material of 34 spleens from persons who died from COVID-19 in 2020 was examined. The material was obtained from 20 men and 14 women who died between the ages of 30 and 91. The duration of the illness ranged from 3 to 23 days. The material was stained with hematoxylin-eosin. Part of the material was stained with PAS.
Results: In the red pulp of the spleen, among the relatively rare cells of the lymphoid series, there are few lymphoid cells with Russell's bodies. Sometimes, with significant emptying of the red pulp, large cells with abundant cytoplasm of the "plasmablast" type and single large lymphoblastic cells with a bright pink cytoplasm of the "flaming" type of cells appear in the reticular stroma. According to our data, a comparatively similar morphological picture of changes in the spleen does not depend on gender, age of the deceased, duration of illness, background and concomitant diseases (such as type 2 diabetes mellitus, hepatosis, diffuse and macrofocal postinfarction cardiosclerosis).
Conclusion: The detection of lymphoid cells with Russell's bodies in the spleen of patients who died from COVID-19 indicates their participation in the pathogenesis of this infection as a morphological sign of progressive suppression of the immune system in an unfavorable course of the disease.

OFP-15 | IT in Pathology

OFP-15-001
Digital analysis of intratumoural heterogeneity reveals higher leucocytic infiltrate in VETC (Vessels Encapsulating Tumour Clusters) areas

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Background & objectives: VETC is metastatic mechanism that involves vessel remodeling and invasion; endothelial covering might also act as an immune-modulator. To investigate this possibility, we studied the VETC related intratumoural heterogeneity of the immune infiltrate.
Methods: We identified several VETC prevalent sarcomas (n=3 alveolar_soft-part_sarcomas(ASPS), n=2 de-differentiated_liposarcomas(DDLPS), n=2 other high-grade), to regularize the inference we included n=5 renal-cell_carcinomas(RCC). We trained an artificial-neural-network(ANN) to recognize VETC with CD34 immunohistochemistry. With a transformation matrix we assessed leucocytes density (automatically with CD45). We then compared VETC_positive and negative areas using a multilevel-hierarchical probabilistic model controlling for histology and case.
Results: Within the same tumour, the areas with VETC tend to have a higher density of leucocytes with a mean z-score of 0.07 Vs -0.24 in the VETC_negative_areas [with a 89% Compatibility Interval (CI) from -0.47 to 0.67 Vs -0.73 to 0.28 respectively]. This was also true across all the different histotypes: mean z-score in ASPS of VETC_positive_areas was 0.15 compared to -0.14 of VETC_negative_areas [CI (-0.45_0.73) Vs (-0.70_0.39)], in DDLPS VETC_positive_areas was 0.23 compared to -0.37 of VETC_negative_areas [CI (-0.42_0.92) Vs (-1.19_0.18)], and in RCC VETC_positive_areas was 0.17 compared to -0.04 of VETC_negative_areas [CI (-0.32_0.71) Vs (-0.59_0.49)].
Conclusion: VETC_positive_areas had –within the same tumour, the same host-response (patient) and also across different histologies– consistently an higher immune infiltrate. This finding will prompt an accurate characterization that might unravel potential sensitivity to drugs targeting the VETC and modulating the immune infiltrate. More generally, we dissected the tumour microenvironment heterogeneity automating the tasks of image annotation and positive cell detection, an approach that we anticipate to be easily scalable.

OFP-15-002
The impact of level 6 synoptic reporting system on turn-around-times in a surgical pathology laboratory of a tertiary cancer centre
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Background & objectives: TAT, a critical quality parameter in clinical laboratories, is affected by several pre-analytical, analytical and post-analytical processes. In this work, we highlight the importance and impact of data-driven IT systems, automation of data-recording, report generation processes on TAT.
Methods: We compared the TAT of reports generated in a level-6 synoptic reporting system (SRS) with that of a free-text platform (FTS). In SRS, organ and cancer specific forms were used with entries being made in customised forms with selections entered by pathologists. FTS entries were primarily by typists from paper records made by pathologists.
Results: TAT was calculated as days from sample receiving to report finalization. The median TAT for the FTS and SRS was 11 & 8 days respectively. The proportion of reports finalized within the defined TAT increased from 87% for the FTS to 93% in SRS. The most significant impact was noted in the proportion of reports finalized in 5 days (4% vs 20%), in 8 days (28% vs 50%) and 11 days (50% vs 75%) in FTS vs SRS respectively. Cases requiring decalcification also showed similar results. There was also reduction in number of supplementary reports issued for errors in main reports
Conclusion: The current benefit demonstrated in our work is primarily due to the change in the data-entry processes, automated report generation, reduction in the errors and subsequent time spent in verification and correction of reports. Our work shows the benefit of segregation of data entry processes from report generation processes in addition to reduction of paper-trail due to introduction of an elaborate data-driven reporting platform, enhancing the quality of services provided by a clinical diagnostic laboratory.

OFP-15-003
AP Macroscopy mobile app for female genital macroscopy
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Background & objectives: Due to the high demand, importance, and complexity of services in pathological anatomy, digital technologies have become fundamental for improving quality. According to the present, the objective was to develop an application for macroscopy of the female genital system.
Methods: The study applied in the technological production modality. Contextualized Instructional Design was chosen. The stages of development were: Analysis: literature review in PubMed / MEDLINE, SciELO and LILACS, Brazilian Society of Pathology and College of American Pathologists; Design: content production; Development: selection of tools; Implementation: configuration of tools and construction of download environment; Transition: performance of functionality tests.
Results: AP Macroscopy application presents 54 screens and 55 images, general information related to the macroscopy sector, and information about 11 types of macroscopic procedures of the female genital system. All of these 11 features: a brief introduction. Then, the procedures performed, on the piece/fabric (sections, handling, paintings), and macroscopic descriptions with options (Radio-Buttin) to issue text of the complete macroscopy. Subsequently, information about which sections to be represented will appear and make available two galleries: one with illustrations illustrating the anatomy of the organ and the sections to be performed and the other with photos of the organs and sections from the beginning to the end of the procedure.
Conclusion: The AP Macroscopy application was built and consisted of technological innovation in the macroscopic practice of pathological anatomy laboratories that aims to improve exams and optimize the service, open-collaborative online and shareable, contributing to an accurate microscopic diagnosis and ideal treatment for the patient.

OFP-15-004
Development of CNN-based algorithm for automatic recognition of the layers of the wall of the stomach and colon
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Background & objectives: Determination of foci of microinvasion of adenocarcinoma in polyps with low and high grade dysplasia is a rather difficult task, which can be tried to solve with the help of deep learning based methods.
Methods: We use two datasets that are developed for the purpose of whole-slide images (WSI) segmentation and tissue type recognition: NCT-CRC-HE-100K and PATH-DT-MSU. Our PATH-DT-MSU dataset contains 20 H&E WSI of digestive tract tumours with pixel-level annotation of 6 tissue types. We solve the segmentation problem via classification approach, with a simple AlexNet-based CNN trained for patch classification.
Results: The main goal for developing these algorithms is to automatically recognize the layers of the wall of the stomach and colon on WSI, namely the lamina propria, muscularis mucosa, submucosa, own muscle

layer, subserous layer, serous membrane and adjacent areas adipose tissue. Since pixel-wise annotation of typical WSI is too time-consuming, we developed the patch classification model, applying which to overlapping patches results in getting coarse segmentation with reasonable accuracy. To adopt the model trained on NCT-CRC-HE-100K to PATH-DT-MSU we replace the last fully-connected layer and perform fine-tuning. The overall test accuracy of WSI classification is 0.93 on NCT-CRC-HE-100K and 0.8 on PATH-DT-MSU.
Conclusion: Thus, we managed to develop an algorithm that detects layers of gastric mucosa and depth of invasion of intestinal-type gastric tumours with acceptable accuracy. The use of developed post-processing methods of segmentation contour analysis allows to detect depth of invasion in some cases of diffuse-type tumours. Also the next step is to train deep learning algorithms to segment tubular and papillary structures, low and high grade dysplasia, foci of invasive adenocarcinoma.

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OFP-15-005
The impact of different mounting methods in the quality of whole slide images used for digital diagnosis in pathology
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Background & objectives: The quality of digital images depends on the quality of glass slide preparations, namely of the mounting. This study compares glass coverslip, film coverslip, and liquid coverslip methods, to evaluate which is better for diagnosis in a digital pathology workflow.
Methods: Eighteen tissue samples of paraffin-fixed embed tissue processed paraffin blocks were prepared. From each block, three consecutive 3um sections were made and mounted using the three mounting methods. The slides were scanned in 3DHISTECH P1000 scanner, originally calibrated for film coverslip, and evaluated by two experienced pathologists on digital pathology.
Results: The film and liquid coverslip methods have similar results concerning the presence of air bubbles, air drying artifacts, tissue exposed and staining alterations. The glass coverslip method was the one with more air bubbles. The liquid coverslip showed more often alterations on the digital images, but like the other two methods, was found suitable for diagnosis. The liquid coverslip was the one that produced whole-slide images with the lower size.
Conclusion: The tested mounting methods generated glass slide preparations suitable to produce diagnostic quality digital images. The scanner calibration according to the mounting method may interfere with the quality of the digital image. Mounting methodology must be considered when adopting a digital workflow.

OFP-15-006
Implementation of a digital pathology workflow based on WaidX for rapid remote cytology diagnostics
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Background & objectives: The ability to provide early diagnosis of female tumours has a strong impact on survival. Telemedicine is of great utility allowing for worldwide diffusion of good level healthcare practices. WorldConnex developed an integrated model for rapid accurate PAPtest remote diagnostics.
Methods: Women book the PAPtest on a web portal that assigns the collection center. The sample is taken and prepared using CYTOfast+ that produces high quality low-cost thin layer preparations. Slide are digitized, virtual slides are collected providing an AI-assissted pre-diagnostic support. A team of remote cytologists connected via WaidX carry out the diagnosis and send the digital report to patients.
Results: We are validating the platform under a wide range of conditions, including prohibitive settings of resource. The ongoing trial is highlighting the full satisfaction of the involved healthcare professionals. The integrated management chain of biological, digital and remote diagnostics components allows to manage a high quality diagnostic process with a time-to-response of 24 hours.
Conclusion: WaidX is a versatile telemedicine platform born from WorldConnex experience in Digital Health, devoted to provide answers to the huge need of telemedicine diffusion. Our project is characterized by a high level of innovation which increases efficiency and efficacy of healthcare practices and can boost the use of telepathology both in developed and developing countries. Innovative solutions are integrated into each element of the system to improve and optimize diagnostic processes.

OFP-15-007
Mapping the evidence for the WHO Classification of Tumours: a living evidence gap map by tumour type (WCT-EVI-MAP).
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Background & objectives: Decisions for the WHO-Classification-of-Tumours (WCT) as global reference tool should be informed by best available evidence, minimising risk of incorporating misinformation into clinical decision's pathway. We aim to map the evidence-base of the WCT, identifying gaps and pockets of low-level-evidence.
Methods: The WCT-EVI-MAP project will apply a mixed-method, stepwise approach to adapt Evidence-Gap-Map (EGM) methodology to the WCT. Steps include -development of a framework through expert consultation (e-Delphi study), -retrieving of evidence applying a living approach (continuous search for new evidence), -mapping of evidence in Mega-maps of group of tumour types using EPPIReviewer®, and descriptive analysis of WCT pre-post WCT-EVI-MAP.
Results: The resulting EGMs will describe the body of evidence for single tumour types, by research field and evidence-level in an easy-to-read visual representation. Mega-maps will be combined to provide an open-access online tool with living EGMs of the WCT. Dimensions of the map defined through the first phase of expert consensus will include evidence on epidemiology, molecular pathology, prognosis, as defined in the 5th edition of the WCT and three levels of evidence (low, medium and high) as defined by the current evidence pyramid. A strict multidisciplinary approach will be applied, and the results will be integrated into the strategic planning of the WCT 6th edition.
Conclusion: The WCT-EVI-MAP will represent a ground-breaking advance for the WCT and research in the field, positively impacting cancer diagnosis and management. The online tool will increase the discoverability and use of studies by the WCT decision-makers, research commissioners and stakeholders. Such long-term, positive impact has been already observed in other specialised fields with and constitutes an additional step towards evidence-based pathology.

OFP-15-008
SimInPath: mobile application to assess skills in pathology
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Background & objectives: As an academic subject, Pathology is eminently theory based, and is routinely assessed in this fashion. The objective of this project was to design a non-profit application for mobile devices to assess competencies/practical skills in the field of Pathology.
Methods: There was an initial phase of development for the application and a second phase for testing.

A template for evaluation was created, including the descriptors for each stage for the following skills: macroscopic dissection, palpation of suitable lesions for fine needle aspiration (FNA), FNA, ultrasound-guided FNA, punch biopsy, and microscopic diagnosis. Each item could be evaluated using a Likert scale.
Results: A private company was hired to develop the SimInPath® (Simulation in Pathology) application, which took 6 weeks to complete. The Android system for mobile devices (both smartphones and tablets) was chosen as the platform for the application and it was made available for download through the GooglePlay platform. It was determined that the application would be free to download, avoiding advertising content. In order to test the application, it was used to assess a group of students by an evaluator scoring the different tasks. The students' scores, in the form of checklists, were available for analysis after each assessment.
Conclusion: The SimInPath® application for mobile devices to assess practical skills in Anatomic Pathology was designed and launched.
This non-profit tool could be used to implement simulation-based medical education in medical schools or during residency, and, indeed, it could be used in the objective structured clinical examination (OSCE) assessment format.
In addition, it could provide greater visibility for the practical side of Pathology with an increase in student interest in the field.

OFP-16 | Molecular Pathology

OFP-16-001
Comparative pan-tumour analysis of a PD-L1 22C3 antibody laboratory-developed test protocol on the BenchMark XT and PD-L1 IHC 22C3 pharmDx
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Background & objectives: In the current analysis, we compared our PD-L1 22C3 antibody–based laboratory-developed test (LDT) on the Ventana BenchMark XT platform with PD-L1 IHC 22C3 pharmDx, an FDA-approved companion diagnostic for pembrolizumab across multiple tumour types.
Methods: Tumour specimens from multiple tumour types were stained with the 22C3 antibody, scored per the previously described LDT (Neuman T. J Thorac Oncol. 2016), and compared with PD-L1 IHC 22C3 pharmDx by a trained pathologist. PD-L1 was measured by combined positive score (CPS). Assay agreement was measured after determination of PD-L1 status per the LDT and PD-L1 IHC 22C3 pharmDx.
Results: Samples from 404 patients with cervical cancer (CC) (n=77), esophageal squamous cell carcinoma (n=80), head and neck squamous cell carcinoma (n=126), and urothelial carcinoma (n=121) were evaluated. Pan-tumour intraclass correlation coefficient (ICC) of PD-L1 as a continuous variable was 0.95 (95% CI, 0.94%-0.96%); Spearman correlation was 0.95. Among patients with CC, ICC was 0.92 (95% CI, 0.88%-0.95%); Spearman correlation was 0.93. The clinical interpretation of PD-L1 status (CPS ≥10) for CC samples using the LDT and PD-L1 IHC 22C3 pharmDx resulted in a negative percentage agreement of 91% (95% CI, 72%-97%), a positive percentage agreement of 100% (95% CI, 93%-100%), and an overall percentage agreement of 97% (95% CI, 91%-99%).
Conclusion: We demonstrated that our 22C3 antibody–based LDT on the Ventana BenchMark XT platform yielded high concordance with the FDA-approved PD-L1 IHC 22C3 pharmDx in a pan-tumour analysis and in patients with CC alone. These findings suggest the comparability of PD-L1 IHC 22C3 pharmDx with an LDT based on the 22C3 antibody across several tumour types. This analysis will be expanded to include additional indications for inclusion in the presentation pending data availability.

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OFP-16-002
Exploratory biomarker analyses from a phase 2 trial evaluating sotorasib in patients with pre-treated KRASG12C-mutated non-small cell lung cancer (CodeBreaK 100)
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Background & objectives: In a phase 2 study (CodeBreaK 100/NCT03600883), sotorasib demonstrated a 37.1% objective response rate (ORR) and median progression-free survival of 6.8 months for pretreated patients with KRASG12C-mutated non-small cell lung cancer (NSCLC). We report efficacy by baseline biomarker subgroups.
Methods: Eligible patients (advanced KRASG12C-mutated NSCLC; prior therapies) received oral sotorasib (once-daily 960 mg). KRASG12C mutant allele frequency (MAF), tumour mutational burden (TMB), and gene mutations were analysed by next-generation sequencing. PD-L1 was assessed by PD-L1 IHC 22C3 pharmDx. Correlations between response and PD-L1, MAF, TMB or co-mutations were analysed. Association between MAF and response was analysed by logistic regression.
Results: ORR (95% CI) by subgroup was as follows. TP53 co-mutation status: mutant (n=84 evaluable patients) 39.3% (28.8–50.5); wild-type (n=20) 40.0% (19.1–63.9). STK11/KEAP1 co-occurring mutation status: mutant/mutant (n=13) 23.1% (5.0–53.8); mutant/wild-type (n=22) 50.0% (28.2–71.8); wild-type/mutant (n=7) 14.3% (0.4–57.9); wild-type/wild-type (n=62) 41.9% (29.5–55.2). TMB level: <10 mutations/Mb (n=69) 42.0% (30.2–54.5); ≥10 mutations/Mb (n=15) 40.0% (16.3–67.7). PD-L1 level: tumour proportion score (TPS) <1% (n=44) 47.7% (32.5–63.3); TPS 1–49% (n=33) 39.4% (22.9–57.9); TPS ≥50% (n=9) 22.2% (2.8–60.0). Response was independent of KRASG12C MAF: odds ratio for each 0.10 increase in MAF was 1.11 (95% CI 0.88–1.39). OS remained immature.
Conclusion: In these exploratory analyses of the registrational phase 2 CodeBreaK 100 trial, the clinical benefit of sotorasib in KRASG12C-mutated NSCLC was observed across a range of patient subgroups including patients with low PD-L1 expression level and those with co-occurring STK11 mutation. A signal of interaction between response rate and KEAP-1 mutations merits further study in larger populations.

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OFP-16-003
Clinicopathological features of four cases of BCOR-CCNB3-positive sarcomas
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Background & objectives: Sarcomas with BCOR genetic alterations are included in the recent WHO classification of soft tissue and bone tumours. Currently, there is a single reported study from our country on BCOR-CCNB3-positive sarcomas. We present clinicopathological features of 4 additional such cases.
Methods: Nine cases of undifferentiated round to spindle sarcomas were tested for BCOR-CCNB3 fusion by reverse transcriptase-polymerase chain reaction. All these tumours were negative for EWSR1 gene rearrangement and a single case, also for SS18 rearrangement, by fluorescence in-situ hybridization.
Results: Four tumours occurred in 3 males(13-year-old, 7-year-old, and 16-year-old) and a single female(37-year-old), in tibia, femur, temporal

region, and thigh, respectively. Histopathologically, tumours were composed of round(n=4), polygonal(n=2), to spindly cells(n=2) in a myxoid matrix(n=3) with interspersed thin-walled vessels(n=4) and focal necrosis(n=2). Immunohistochemically, tumour cells displayed dot-like reactivity for MIC2/CD99 (4/4), positivity for SATB2 (3/4), BCOR (2/2), focal positivity for EMA (1/3), and negativity for desmin (0/4) and WT1(0/3). Therapeutically, 2 patients underwent neoadjuvant chemotherapy (99% response and 78% response), followed by surgical resection. Two patients were offered palliative radiotherapy, in view of metastasis at presentation and unresectability. Three patients developed lung metastasis and a single patient developed local recurrence.
Conclusion: Certain morphological features, such as spindle and polygonal cells, in addition to round cells, along with myxoid stroma, intervening vessels; dot-like immunoreactivity for MIC2, lack of EWSR1 rearrangement, and intraosseous location constitute as diagnostic clues for BCOR-CCNB3-positive sarcomas. SATB2 and BCOR are useful immunostains for triaging such cases for BCOR-CCNB3-fusion testing.

OFP-16-004
Development of an optimised diagnostic algorithm using multiplex immunochemistry (IHC) for excluding diagnosis of carcinoma-of-unknown-primary-origin, based on experience from the Phase II CUPISCO trial
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Background & objectives: High screening failure rates observed in CUPISCO (PMID: 33687747; NCT03498521) highlight the need to improve carcinoma-of-unknown-primary-origin (CUP) diagnosis (improved accuracy; shorter time to diagnosis; reduced tissue consumption). Therefore, we intended to optimise pathology work-ups via use of brightfield multiplexed IHC.
Methods: A panel of experts evaluated over 800 pathology work-ups from CUPISCO according to ESMO guidelines, in order to improve the efficiency of establishing an appropriate diagnosis of non-CUP versus real CUP cases. On this basis we developed a systematic diagnostic algorithm utilising automated brightfield multiplexed chromogen-based IHC assays to screen a broad spectrum of markers.
Results: We defined an algorithmic system featuring up to five sequential multiplex IHC-testing panels, each analysing five markers, that would be suitable for routine clinical use. A general panel including cytokeratin 7, cytokeratin 20, vimentin, synaptophysin and thyroid transcription factor 1 enables an initial broad screening approach, subsequent to haematoxylin–eosin stain interpretation and assessments of the patient's clinical characteristics. Then, more specific panels featuring markers for gastrointestinal/pancreatic, lung/kidney or breast/gynaecological cancers can be selected for further, more focused analyses. The results of our feasibility testing, as well as the potential implications for patient management and improving CUP diagnosis, will be presented.
Conclusion: The proposed methodology may improve the detection of primary cancers in complex cases: avoiding the incorrect diagnosis of CUP. The exclusionary diagnosis of CUP can be optimised and accelerated by the use of an algorithmic progression via the application of sequential multiplex IHC panels. Such a system reduces the amount of tumour tissue needed for preliminary assessment and preserves material for further genomic testing. This will help to optimise the patient care strategy; allowing access to molecular-guided therapies.

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OFP-16-005
The emerging relevance of RNA modifications in tumour biology: VIRMA contributes to testicular germ cell tumours aggressive phenotype and chemotherapy resistance
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Background & objectives: Testicular germ cell tumours(TGCTs) are developmental cancers, reflecting embryogenesis. The recent field of RNA modifications is being increasingly implicated in such events. We previously demonstrated the relevance of VIRMA in TGCT patient samples, and now investigate this in vitro/in vivo.
Methods: We study the role of N6-methyladenosine (m6A) and related writers, readers and erasers in 4 cell lines representative of TGCTs, including after treatment with ATRA and in isogenic clones made resistant to cisplatin. Also, we investigate the immunoexpression of METTL3 in a TGCT tissue cohort.
Results: We show differential expression of m6A players in cell lines representative of seminoma/non-seminoma. We demonstrate shifts in expression during differentiation with ATRA treatment and also among cells sensitive and resistant to cisplatin treatment, implicating m6A modification in the acquisition of therapy resistance. METTL3 immunoexpression was significantly higher in non-seminomas ($p<0.0001$), but did not significantly impact relapse-free survival. CRISPR/Cas9-mediated knockdown of VIRMA, a component of the writer complex, resulted in disruption of the complex, decreased m6A deposition, reduced tumour aggressiveness (decreasing viability and proliferation) and potentiated response to cisplatin treatment (eliciting higher DNA damage). We are currently further validating these findings in vivo, using the chick chorioallantoic membrane assay model.
Conclusion: RNA modifications are a current hot topic in research, being implicated in tumour genesis, biology and resistance to therapy, with VIRMA being the major representative player in TGCTs. This is interesting given the recent development of targeted drug compounds directed at elements of the m6A methyltransferase complex, which can be envisioned as clinically useful in this particular tumour model.

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OFP-16-006
Genomic testing approaches used to identify neurotrophic tyrosine receptor kinase (NTRK) gene fusions for patient enrollment in clinical trials of larotrectinib
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Background & objectives: NTRK fusions are oncogenic drivers and are predominantly detected by NGS, PCR, or FISH. Larotrectinib, a first-in-class, highly selective, CNS-active TRK inhibitor, demonstrated a 78% objective response rate and a 36.8-month median PFS across multiple solid cancers (July 2019 data-cut).
Methods: Details of the testing methods used to diagnose patients with TRK fusion cancer enrolled in three larotrectinib clinical trials (NCT02122913, NCT02576431, NCT02637687) are reported. NTRK status was determined by local molecular testing. ETV6-NTRK3 fusions were considered inferred based on FISH break-apart results for tumour types in which NTRK fusions are pathognomonic. Data cut-off: 20 July 2020.
Results: The analysis included 225 patients (129 adults [57%]) with 19 different tumour types. Most common gene fusions were ETV6-NTRK3 (41%), TPM3-NTRK1 (16%) and LMNA-NTRK1 (8%); 54 different fusion partners were identified, 39 (72%) of which were unique occurrences. Testing methodologies/incidence of fusion partners varied by

tumour type. Most common method was NGS (196/225, 87%: DNA in 53/196 [27%], RNA in 96/196 [49%], DNA/RNA in 46/196 [23%], unknown in 1 [1%]) followed by FISH (14/225, 6%) and PCR (12/225, 5%). NanoString, Sanger sequencing and chromosome microarray were each utilized once. ETV6 and/or NTRK3 FISH were employed for specific tumour types (eg. secretory breast, IFS, salivary gland), detecting 14% of ETV6-NTRK3 fusions.
Conclusion: NTRK gene fusions occur with many partners with the majority occurring at a low frequency across multiple tumour types, supporting the need for validated and appropriate testing methodologies that work agnostic of 5' partners.

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OFP-16-007
The EGFR, ALK and ROS1 mutation profile of non-small cell lung carcinomas in the Turkish population: a single-centre analysis
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Background & objectives: The management of non-small cell lungcarcinomas(NSCLC) has changed with the identification of the molecular pathways which are now used in targeted-therapies. We aimed to reveal the 2-year epidermal growth factor(EGFR),anaplastic lymphoma kinase(ALK) and ROS proto-oncogene1(ROS1) mutation profile in the Turkish population.
Methods: The histopathological and molecular data of all NSCLC cases that were evaluated in our department between May 2019 and April 2021 were retrieved from the archives. The demographic data of the patients, type (cell block, biopsy, resection) and the localization (primary/metastatic) of the specimen in which the molecular testing was done, the histopathological diagnosis, and the mutation rates were noted.
Results: A total of 129 NSCLC (95 adenocarcinomas, 20 squamous cell carcinomas [SCC], 14 NSCLC,NOS), cases underwent molecular testing(M/F:121/28, aged 40-87). The molecular testing was performed on cell blocks obtained from cytological specimens in 46, biopsies in 69, and resections in 14 cases. EGFR mutation was seen in 15 (11,6%) cases (three exon 18[allcodon 719],five exon 19,two exon 20 [1 T790M, 1 codon 768] and five exon 21[4 L858R, 1 L861Q]). The mean age of EGFR-mutant patients was 60 (45-76) with 25% of all females(n=7) and 6.6% of all males(n=8). ALK mutation was detected in 5 (3,8%) patients (M/F:2/3,mean 65,6years) whereas ROS1 mutation was detected in 2 (1,5%) (1 male, 1 female).
Conclusion: It is well-established in the literature that EGFR-activating mutation rates vary depending on the country/race. We concluded that the EGFR-activating mutation rates of the Turkish population are similar to the European molecular data instead of the Asian. The majority of the cases with EGFR, ALK and ROS1 mutations were adenocarcinomas in our series, however exon 20 - T790M mutation in one case with SCC was seen. ALK and ROS1 mutation rates also seem consistent with the literature.

OFP-16-008
Putative germline variants from tumour-only genel panel sequencing: results of a single-centre study
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Background & objectives: Multi-gene panel NGS from tumour tissues has become the mainstay personalized oncology. However, when suggestive VAF around 50% or higher are found it remains unclear whether variants in cancer genes identified by tumour-only sequencing might potentially be of germline origin.
Methods: A total of 2057 gene panel tumour-only NGS analyses from adult and paediatric patients with solid tumours who were diagnosed between 2018 and 2020 were reviewed. NGS of 83 cancer related genes was performed. Results were reviewed for potential PGVs using following criteria: Pathogenic variants with an allele frequency ≥ 40% and a VAF to tumour purity ratio ≥ 50%.
Results: Putative PGVs with a VAF ≥ 40% and a VAF/tumour purity ratio ≥ 50% were detected in 408 patients. The list of filtered putative PGVs included those in cancers of high rates of susceptibility and with a high proportion of patients with known inherited PGVs (breast, colorectal, ovary). Further filtering by exclusion of genes with high prevalence and strong association with syndromic phenotypes resulted in 250 PGVs in 46 genes. The identified variants included those associated with genes with high germline conversion rate (BRCA, PALB2) and to a lower degree those with lower reported germline prevalence (EGFR, IDH1). In selected cases, the suspicious PGVs were successfully verified by germline analysis.
Conclusion: Although tumour-only sequencing provides a cost-effective approach to identifying somatic variants present in the tumour, it will also detect any germline variants present. These findings may influence patient care by impacting on systemic therapy choices, surgical decisions, additional cancer screening, and genetic counseling in families. The findings of this study suggest that the application of systematic filter steps combined with automated flagging and concise manual review as proposed by current guidelines can provide an opportunity to detect PGVs.

OFP-16-009
Laboratory variation of molecular testing in a Dutch cohort of metastatic non-small cell lung cancer patients from 2017
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Background & objectives: Adequate and timely testing for genetic alterations in non-small cell lung cancer (NSCLC) is necessary to consider targeted therapy. Currently, within a 2017 cohort we assessed whether molecular testing improved after 2015.
Methods: All stage IV non-squamous NSCLC with incidence year 2017 from the Netherlands Cancer Registry were matched to the Dutch pathology registry (PALGA). Using information extracted from pathology excerpts, proportions of tumours tested for EGFR/KRAS, BRAF, and HER2 mutation, ALK, ROS1, and RET rearrangement <3 months after diagnosis were determined and variation between 42 laboratories was assessed.
Results: Of 3746 identified patients, we have currently analysed 3647 (97%). Ninety-two patients were non-eligible after matching, leaving 3555 (94%) patients. EGFR/KRAS testing was performed in 2992 patients (84%) (laboratory variation 68-100%). Of the EGFR/KRAS wildtype tumours (n=1516), 1392 (92%) were tested for BRAF (14-100%), 1309 (86%) for HER2 (18-100%), 1231 (81%) for ALK (50-100%), 952 (63%) for ROS1(3-100%), and 663 (44%) for RET (0-100%). The reason for not testing was not reported for the majority of patients. Insufficient tumour tissue and inappropriate specimen were the most stated reasons for not testing within the reported group.
Conclusion: These data show significantly higher EGFR/KRAS, ALK and ROS1 testing proportions compared to 2015. Further improvement remains possible, in some laboratories more than in others, and especially for ROS-1 and RET testing, to identify candidates for targeted therapy. Initiatives for improvement will involve starting a dialogue with professionals on a regional level, where these findings and recommendations of a best practice session will be discussed.

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OFP-16-010

Prevalence of KRAS p.(G12C) in stage IV non-squamous NSCLC patients in the Netherlands; a retrospective cohort study

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Background & objectives: KRAS is the most frequent mutation in cancer, especially KRAS p.(G12C) (39%-42% KRAS-mutant NSCLC). Recently, clinical trials with drugs specifically targeting KRAS p.(G12C) showed promising responses. We aim to investigate the prevalence of KRAS p.(G12C) mutations within a NSCLC cohort.
Methods: Patients diagnosed with stage IV non-squamous NSCLC in 2013, 2015, and 2017 in the Netherlands were retrieved from the Netherlands Cancer Registry (NCR) and the Dutch Pathology Registry (PALGA). After matching of the databases pertinent clinical and pathological variables were extracted. Testing rates and prevalence of KRAS p.(G12C) were calculated from the collected data.
Results: A total of 10,851 tumours were selected from the NCR and matched with PALGA. After exclusion of 596 non-eligible patients due to exclusion criteria, 10,255 patients were included, of whom 7,908 (77%) were tested for KRAS mutations within 3 months after diagnosis. Testing rate increased from 71.8% in 2013, to 80.9% and 83.3% in 2015 and 2017, respectively. An increase in the ≥65-year-old population (50.2% (2013) to 57.5% (2017), $p<0.01$) and an increase in histological/cytological specimen ratio (65.6% (2015) to 71.4% (2017), $p<0.01$) was observed. In the total population the prevalence for KRAS p.(G12C) was 15.5%.
Conclusion: Using data systematically collected in Dutch national cancer and pathology registries, the prevalence of KRAS p.(G12C) mutations in the entire population of patients with stage IV-NSCLC in the Netherlands is 15.5%. Although the testing rate increased from 2013 to 2017, there seems to be room for improvement although reasons why a test was not requested was not systematically captured.

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OFP-16-011

Molecular profiling of BRCA1/2 genes by NGS in tumoral samples from ovarian cancer patients

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Background & objectives: Analysis of BRCA1/2 genes in ovarian cancer patients was historically assessed in the germ line and is now moving to tumoral tissue. Our aim was to evaluate the sensitivity of mutation detection by NGS approaches in FFPE tumoral samples.
Methods: Specimens from 81 previously characterized germline ovarian cancer patients from three centers were included. Each center studied their cases with the available NGS technique: customized hybrid capture based panel (VHIO), BRCAplus amplicon panel, Qiagen (Hospital del Mar) and Oncomine BRCA Research Assay, ThermoFisher (Virgen del Rocio). Sequencing was performed on Illumina (capture panel and Qiagen panel) or GeneStudio S5 systems.
Results: Of the 81 samples initially selected, 10 samples were not evaluable due to insufficient quality of the DNA obtained from the sample. Of the remaining 71 samples (30 cases with BRCA1 germline mutations, 17 cases with BRCA2 germline mutations, and 24 cases without BRCA1 / 2 germline mutations), the previously identified germline mutations were detected in 47/47 cases (100%). In addition, somatic mutations were identified in 9 cases with no germline mutations, 5 in BRCA1 and 4 in BRCA2 with allelic frequencies between 20-47%. In addition, in 2 cases that presented germline mutations, a somatic mutation was also detected (1 in BRCA1 and 1 in BRCA2)
Conclusion: These results indicate that the analysis in tumoral tissue has adequate sensitivity for the detection of germline mutations in the BRCA1/2 genes if the quality of the tissue DNA is sufficient. Furthermore, the tumoral biopsy study allows us to identify somatic alterations in these genes.

OFP-16-012

Multiparametric (2+3) assessment of PD-L1 expression in tumour tissue: a novel, rapid and easy-to-use algorithm to capture more of the biological complexity and minimise inter- and intra-observer variability

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Background & objectives: PD-L1 counting of positive TC and/or IC is difficult and time-consuming near the positivity thresholds, correlation between small biopsy and excision can be poor and morphological data are not captured. We describe a novel algorithm to address these issues.
Methods: We assessed %TC, %IC, extent, clustering and distribution (2+3) by eyeballing using 7 bins for each parameter. Matched diagnostic and excision biopsies were stained with on-label SP263 CDx and digitised (3DHistech). An initial set of 20 cases were scored by all pathologists. Non-concordant cases were reviewed and given a score by consensus. Each pathologist then assessed 25 additional cases.
Results: Six consultant pathologists, two trainee pathologists and one clinical scientist participated in the study. Training consisted of self-learning using a short presentation; this suggests that the 2+3 system [SW1]would be easy to introduce in the diagnostic routine. The 2+3 scoring algorithm was used on TNBC and NSCLC and showed excellent inter- and intra-observer concordance when compared to established CPS, TPS and IC/TC algorithms[SW2]. It also improved correlation between small biopsies and excision of the same tumour when compared to established PD-L1 algorithms used in oncology.
Conclusion: The 2+3 algorithm is easy to use, reproducible, captures more of the biological diversity and is less sensitive to tissue sampling. It reduces the influence on the overall score of imprecisions in single parameters. The 7 bins scale facilitates observer concordance. Morphological parameters such as IC distribution, important in identifying responders to immune checkpoint therapy, are part of the assessment and may improve prediction. Clinical trials will provide the correct weight to each parameter for best patient selection.

OFP-17 | Nephropathology

OFP-17-001

Diagnosis of membranous nephropathy and differentiation between primary and secondary forms applying immunohistochemistry using C4d and PLA2r antibodies

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Background & objectives: Appreciating a huge effort to clearly separate primary from secondary membranous nephropathy (MN), due to direct influence on patients' treatments, several biomarkers have been suggested, including C4d and PLA2r.

Methods: Insufficient studies concerning the aforementioned pathohistological approach have led us to explore the sensitivity and specificity of recently proposed biomarkers in distinguishing primary and secondary MN. We applied immunohistochemistry (C4d, 1:50, ab167093, Abcam; PLA2r, 1:1000, ab188028, Abcam) using 21 kidney biopsies (13 primaries, 8 secondary), as well as 40 renal samples of various non-MN diagnosis.
Results: C4d and PLA2r were expressed in glomeruli in all MNs (21/21), both primary and secondary. Furthermore, C4d was not observed among non-MN cases, while PLA2r was detected in the majority of them (39/40 non-MN diagnoses: focal segmental glomerulosclerosis (n=5), minimal change disease (n=3), mesangioproliferative glomerulonephritis (n=14), IgA nephropathy (n=4), post-infective glomerulonephritis (n=4), hypertensive nephropathy (n=1), diabetic nephropathy (n=2), rapidly progressive glomerulonephritis (n=3), lupus nephritis (n=3)). These results indicate the absolute specificity and sensitivity (100%) of C4d antibody in diagnosis of MN regardless of the etiology. However, despite an absolute sensitivity, PLA2r failed to differentiate primary from secondary MN due to extremely low specificity (2.5%).
Conclusion: Confirmation of membranous nephropathy could be done by C4d in each case, without false results, either positive or negative. However, differentiation of primary from secondary MN is not reliable using the proposed PLA2r method, thus seeking a better biomarker is warranted.

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OFP-17-002
Morphology of childhood and adult-onset lupus nephritis
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Background & objectives: Systemic lupus erythematosus (SLE) could affect the integrity and function of many organs, including the kidneys. Although the frequency of SLE is less common in children than in adults, affected children develop lupus nephritis (LN) significantly more often.
Methods: In order to analyse relevant clinical (gender, frequency of LN as the first manifestation of SLE, proteinuria and serum creatinine values) and pathohistological parameters (LN classes, activity and chronicity index), this study included 217 biopsy samples of kidney tissue. Patients were divided into two groups: patients under (n=35) and over (n=183) 18 years.
Results: Among investigated clinical data, serum creatinine values were significantly lower in the paediatric population (71.6±16.4 μmol/l) than in adults (115.5±64 μmol/l), p<0.001. Parameters which define disease activity index were similar in both groups with exception of interstitial infiltration that was significantly higher in the adult group, p=0,003. Chronicity index (p=0,002) as well as the tubulointerstitial parameters that determine it (tubular atrophy (p<0,001) and interstitial fibrosis (p=0,011)) were also higher in adults. Blood vessel involvement was frequently detected in adult biopsies (p<0,001).
Conclusion: Serum creatinine values are significantly higher in the adult population of LN. Pathohistological findings indicate that glomerular LN lesions do not differ significantly in regard to activity and chronicity index in paediatric and adult populations, but degrees of tubulointerstitial lesions, either active or chronic, are significantly higher in adult-onset LN.

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OFP-17-003
NanoString transcriptome analysis with the B-HOT panel for clinical diagnostics on for-cause kidney transplant biopsies
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Background & objectives: Transcriptome analysis could help in diagnosing rejection and is an Additional Diagnostic Parameter for AMR. NanoString is a novel and promising technique. We evaluated the commercially available Banff-Human Organ Transplant Panel (B-HOT panel) using NanoString on for-cause kidney transplant biopsies.
Methods: Transcriptome analysis using the B-HOT panel (770 transcripts) of NanoString was performed on 96 formalin-fixed paraffin-embedded for-cause kidney transplant biopsies retrieved from the archives of the Erasmus MC Rotterdam and the University Hospital of Cologne. Three groups were compared: antibody-mediated rejection (AMR, n=32), T cell-mediated rejections (TCMR, n=32), and non-rejection (controls, n=32). Data was analysed using the nSolver analysing software.
Results: 22 mRNA transcripts (CXCL1, FCGR3A, GNLY, ROBO4, CCL3, CXCL10, TNF, CD74, PLAT, ICAM2, PSMB10, LST1, CRIP2, EMP3, CX3CR1, HSPA12B, SH2D1B, LHX6, CD160, S1PR5, TBX21, TRDC) were found to be differentially regulated (upregulated) between AMR and controls after false discovery rate (FDR) corrections. Eight (PSMB10, CX3CR1, TNF, CXCL11, GNLY, CCL3, CD160, CXCL10) of these 22 transcripts were also found to be upregulated in TCMR vs controls. No transcript was found to be differentially regulated between AMR and TCMR after FDR correction. Notably, even promising transcripts (TNFSF8, C9, TOX2, CD70) showed overlap in expression between AMR and TCMR.
Conclusion: The B-HOT panel can help to distinguish kidney transplant biopsies with rejection from biopsies without evidence of rejection. Caution should be taken regarding the clinical value of this platform regarding the more challenging and clinically important distinction between diagnosis of AMR (most cases of which show an additional component of Borderline or TCMR) and pure TCMR or Borderline. The B-HOT panel could help us identify the most promising transcripts for this differential diagnosis on larger cohorts.

OFP-17-004
An audit of Electron Microscopic (EM) evaluation of native renal biopsies
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Background & objectives: Aim: To carry out a retrospective survey of native renal biopsies to determine the percentage of cases in which a) EM evaluation was necessary to make the correct diagnosis; and b) EM evaluation provided clinically relevant additional information.
Methods: Methods: We retrospectively reviewed 100 consecutive native renal biopsies. We excluded cases in which no sample was available for EM or the EM sample was inadequate. We classified the EM as necessary for diagnosis; adding information to diagnosis; and not necessary/not adding information.
Results: In 81 cases, the main diagnosis was glomerular; tubulointerstitial in 10; and in 9 it was mixed. In 20% of cases, correct diagnosis and classification would not have been possible without EM evaluation. 19/20 were glomerular diseases, and 1/20 was a tubulointerstitial disease. In an additional 44% cases, EM evaluation provided clinically relevant information. Amongst cases where the main diagnosis was glomerular, EM was necessary in 23% cases and helpful in other 47% and where it was tubulointerstitial EM was necessary in 10% and added information in 30%. The most common situations where EM was neither necessary

nor helpful were ANCA- or anti-GBM- glomerulonephritis (n=5/5) and IgA nephropathies (n=14/23)
Conclusion: EM is reported as essential for diagnosis in around 20% of biopsies, and to add value in about 50%, although recent data is not available. Our Trust carries out EM evaluation on all native renal biopsies, giving us the impetus to audit the contribution of EM in native renal biopsy reporting. Our audit confirms the accuracy of published figures for when EM is necessary or useful and supports continued practice of taking a sample for EM in all native biopsies.

OFP-17-005
Heterozygous COL4A3 and COL4A4 patients with classic Alport syndrome morphology – unexpected genetic testing results after kidney biopsy
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Background & objectives: Heterozygous Alport spectrum patients with COL4A3 or COL4A4 mutations usually present as thin glomerular basement membrane nephropathy on kidney biopsy. Here we present cases of heterozygous patients with COL4A3 or COL4A4 mutations with classic Alport syndrome morphology.
Methods: Fifteen patients, six males and nine females (age 2-47 years) with pathohistological diagnosis of Alport syndrome (AS) were tested by NGS sequencing (Illumina MiSeq platform) for COL4A3, COL4A4 and COL4A5 mutations as a part of Croatian Science Foundation project "Genotype-Phenotype correlation in Alport's syndrome and Thin Glomerular Basement Membrane Nephropathy".
Results: At the time of kidney biopsy all patients presented with haematuria and 8 of them with proteinuria. Only one patient had severe decline in eGFR while all other patients had normal eGFR. There were 12 different mutations present (7 in COL4A3 and 5 in COL4A4), 6 of them being novel, previously undescribed. In light microscopy 3 patients showed focal segmental glomerulosclerosis. In three patients there were interstitial foamy cells and only the oldest patient had significant interstitial scaring (50%). All patients had classic Alport syndrome morphology on electron microscopy. Immunohistochemical staining for COL4A3 and COL4A5 was performed in four patients and showed normal distribution.
Conclusion: Diagnostic process of Alport spectrum disorders can be challenging. Phenotype variability is very often among patients. Although kidney biopsy gives insight in to the degree of kidney parenchyma damage genetic testing is necessary for complete diagnosis and patient workup.

Funding: Croatian Science Foundation, project Genotype-Phenotype Correlation in Alport's Syndrome and Thin Glomerular Basement Membrane Nephropathy (IP-2014-09-2151)

OFP-17-006
Automated renal structure recognition: Multi-class segmentation of differently stained kidney tissues using convolutional neuronal networks (CNNs)
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Background & objectives: Pathological diagnostics in kidneys are still based on semi-quantitative eye-balling methods. In former studies, we showed predictive value of precise immune cell quantification in allografts using digital semi-automated techniques. We now aim to achieve fully automated segmentation workflow with CNNs.
Methods: Standard routine stains (immuno/histochemistry, immunofluorecence) were digitized (20x) with Metafer, a commercial scanning/imaging platform. Diagnostically relevant anatomical compartments (cortex, medulla, glomeruli, tubuli (proximal/distal/collecting duct), glomerular/peritubular capillaries, nuclei) were manually annotated to generate data sets on human renal biopsies and nephrectomies. Data were used to train multi-class semantic segmentation CNNs with broad data augmentation to achieve a robustness against staining variances.
Results: On Jones-HE stains, a cortex-medulla-extrarenal CNN reveals pixel based hit rates above 98%, detection of glomeruli show a hit rate above 98%, a multi-class CNN for tubules, tubular membranes and peritubular capillaries results in a hit rate close to 93% and pixelwise nuclear-based cell detection shows hit rates above 98%. Identification of cell location in interstitium, tubuli, glomeruli, peritubular and glomerular capillaries reached very high hit rates: Glomerular endothelial cells actually result in 83% true positives, 13% false negatives and 4 % false positives. Ongoing work also includes detection of arteries and development of classifiers for atrophic tubuli and immune-cell typing within respective structures.
Conclusion: Structure segmentation based on CNNs can complement and specify classical nephropathological diagnostics, especially for spatial risk marker evaluation in early transplant biopsies.

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OFP-17-007
Determination of antibodies that can be used in the differentiation of primary and secondary membranous nephropathy and investigation of the relationship of these antibodies with secondary causes
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Background & objectives: Membranous nephropathy (MN) is the most common primary glomerular disease in adults that causes nephrotic syndrome. We aim to evaluate Phospholipase-A2 receptor (PLA2R), Thrombospondin type-1 domain-containing 7A (THSD7A), and Neural epidermal growth factor-like 1 protein (NELL1) in MN patients.
Methods: 122 cases of MN and 21 cases of Class V Lupus nephritis diagnosed at Mersin University Medical Faculty Medical Pathology Department between 2008 and 2020 are included in this study. Immunohistochemical staining for PLA2R, THSD7A, and NELL1 was performed on the tissue sections obtained from paraffin-embedded blocks of renal biopsy materials.
Results: Percentage of cases positive for PLA2R, THSD7A, and NELL1 were found to be 64.9%, 6.7%, and 6.5% respectively. NELL1 positivity was associated with female gender and Diabetes Mellitus. THSD7A positivity was associated with the absence of hypertension clinically and; intraluminal/mesangial polymorphonuclear lymphocytes, interstitial inflammation, evidence of tubular damage, tubulitis, and calcifications histologically. It was also associated with fibrinogen positivity in an immunofluorescence study. PLA2R positivity was associated with lower serum IgA antibody levels.
Conclusion: The traditional classification of membranous nephropathy does not take associated antigen types and their unique clinical, histopathological and immunological profiles into account. Associated antigens of membranous nephropathy patients can be determined in most of the membranous nephropathy patients and therefore should be the basis of histopathological evaluation and clinical management.

OFP-17-010
A decentralised kidney transplant biopsy classifier incorporating different molecular platforms

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Background & objectives: An optimal decentralized molecular kidney transplant biopsy classifier allows the input of different gene expression assays. We developed a classifier using the Banff-Human Organ Transplant (B-HOT) gene panel extracted from a historical Molecular Microscope® Diagnostic system (MMDx) microarray data set.
Methods: Gene expression data (GEO: GSE98320) from 1208 kidney transplant biopsies was used to develop a classifier with genes that matched those from the B-HOT panel. Tree-based models, random forest and XGBoost, were trained to predict kidney transplant biopsy Banff categories, including non-rejection, antibody-mediated rejection (ABMR), T cell–mediated rejection (TCMR), and mixed rejection (ABMR+TCMR). Performance was evaluated using nested cross-validation.
Results: A multilabel random forest model trained on B-HOT panel genes achieved a mean accuracy of 76.2%. However, both classifiers could not predict ABMR+TCMR Banff category. Accuracy was improved to 77.1% using only the MMDx genes included in the B-HOT panel. Classification of rejection versus non-rejection and rejection subtypes separately vastly improved overall performance for both random forest and XGBoost. The best performance was achieved by XGBoost using the B-HOT panel and synthetic minority oversampling for ABMR+TCMR samples, with an accuracy of 93.6% for non-rejection and 95% for rejection subtypes. Balanced accuracies of prediction were 95.9% and 90.8% for ABMR and TCMR, respectively.
Conclusion: A kidney transplant biopsy classifier using molecular data of a historical data set obtained for the MMDx was developed using only the genes included in the B-HOT panel. While comparison of performance should be treated with caution due to differences in validation sets, the performance of this classifier was higher compared to MMDx. This work is one step closer to the development of a decentralized kidney transplant biopsy classifier that is effective on data derived from different gene expression platforms.

OFP-17-011

Kidney biopsy findings in SARS-Cov2 infected patients: a single center case series of post/co-Covid glomerulopathies & kidney injury

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Background & objectives: Covid19 is a multisystem disease, which may also present with acute tubular injury. Besides, glomerular pathologies associated with Covid-19 can be seen as a "second-hit" phenomenon. Herein, we present 8 post/co-covid cases with glomerular, tubular and vascular injury.
Methods: H&E, JMS, PAS, PAMS, MTC and immunofluorescent slides (IgG, IgA, IgM, C3, C4, C1q, Kappa and Lambda) of 8 cases with kidney dysfunction after or during Covid19 proven by PCR positivity were re-evaluated. Then, clinical findings (such as proof of covid19 pneumonia via thorax CT, interval between beginning of Covid19 symptoms and kidney dysfunction etc) were correlated with histopathological findings.
Results: The mean age of our cases were 64,1 yrs (27-90), and included 4 female and 4 male. Two patients (61 and 71) died while hospitalized in intensive care unit. Six cases had covid19 pneumonia, almost all cases had elevated serum creatinine levels, while some showed proteinuria. Two cases were post-transplant while others were native biopsies. Kidney biopsy findings demonstrated 3 main groups: 1) Post-covid glomerulopathies with immune complexes: Anti-GBM disease (1 case), IgA nephropathy (2 cases), Post-infectious glomerulonephritis (1 case), IgG-kappa and C3-associated glomerulonephritis (1 case). 2)Post-covid kidney findings without immune complexes: ANCA-associated pauci-immune crescentic necrotizing glomerulonephritis (1 case), Acute tubular injury (1 case) 3) Co-covid intimal endarteritis (1 case).
Conclusion: Even though, acute tubular injury is the most common histopathological finding in kidney involvement of covid19, viral induced glomerulopathies must be kept in mind in SARS-Cov2 infection. Especially in post-covid period, glomerulopathies associated with Covid-19 can be seen as a "second-hit" phenomenon. Indirect damage seems to have a role in endothelial injury via coagulation mechanisms, and immune system-inflammation pathways (including complement). Much more remains to be learned to elucidate the exact mechanisms causing acute kidney injury in patients with COVID-19.

OFP-18 | Neuropathology

OFP-18-001

No brachyury expression in atypical teratoid/rhabdoid tumour

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Background & objectives: Atypical teratoid/rhabdoid tumour (AT/RT) shares some morphological, immunohistochemical, and molecular features with poorly differentiated chordoma (PDC). Here, we investigate the expression of brachyury, which is known as a sensitive and specific marker for notochordal differentiation, in AT/RT.
Methods: Forty-four tumour samples from 40 patients, diagnosed as AT/RT between 2001-2020 were included in 3-mm tissue microarrays. Immunohistochemical stainings for INI1 and two different clones of brachyury (Abcam-ab209665 and Santa Cruz-A4) were performed. Nuclear staining is counted as positive for both stains.
Results: Twenty-three patients were male and 17 were female. Patients were aged 0 to 15 years (mean:2,85 years and median:1 year). Twenty-seven of 44 tumour samples were located supratentorial; 15 were infratentorial and 2 were spinal. Three cases (7,5%) were found to retain INI1 expression. Two cases (4,5%), located at dorsal sellar region and clivus, were found to be positive with brachyury, one of which demonstrated diffuse and strong positivity, while the other showed focal (30%) expression. These 2 cases were reclassified as PDC. Two different clones of brachyury demonstrated similar results for all cases.
Conclusion: AT/RT's one of the most challenging differential is PDC, a recent entity characterized by sheets of epithelioid/rhabdoid cells with accompanying inflammation, INI1 loss and brachyury positivity, when located particularly in the infratentorial and spinal region. Brachyury is a reliable marker in differentiating AT/RT from PDC, knowing that none of the unquestionable supratentorial AT/RTs in our series showed brachyury expression.

OFP-18-002

Elesclomol-induced increase of mitochondrial reactive oxygen species impairs glioblastoma stem-like cell survival and tumour growth

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Background & objectives: It has been widely demonstrated glioblastoma stem-like cells (GSCs), a subpopulation of tumour cells endowed with stem-like propertiesis responsible for tumour maintenance, progression and contribute to GBM-associated neovascularization processes, through different mechanisms including the trans-differentiation into GSC-derived endothelial cells (GdECs).

Methods: In order to identify druggable cancer-related pathways in GBM, we assessed the effect of a selection of 349 compounds on both GSCs and GdECs. As a result of this screening, we selected elesclomol (STA-4783) as the most effective agent in inducing cell death on both GSC and GdEC lines tested.
Results: Elesclomol has been already described to be a potent oxidative stress inducer. In depth investigation of the molecular mechanisms underlying GSC and GdEC response to elesclomol, confirmed that this compound induces a strong increase in mitochondrial reactive oxygen species (ROS) in both GSCs and GdECs ultimately leading to a non-apoptotic copper-dependent cell death. Finally, we used our experimental model of mouse brain xenografts to test the combination of elesclomol and temozolomide (TMZ) and confirmed their efficacy in vivo.
Conclusion: In conclusion we think that our results support further evaluation of therapeutics targeting oxidative stress such as elesclomol with the aim of satisfying the high unmet medical need in the management of GBM.

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OFP-18-003
Adult diffuse gliomas in the era of morphomolecular diagnosis – lessons from a 2-year experience in a Portuguese reference centre
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Background & objectives: IDH1/2-mutations are frequent in adult diffuse gliomas (ADG), particularly in younger patients (≤55yo). Both IDH-mutation-status and 1p/19q-codeletion-status are strong prognostic/therapeutic stratifiers. We aimed to evaluate: a)prevalence of IDH-mutations across all age groups of ADG; b)morphophenotypic correlations with IDH-mutation-status and 1p/19q-codeletion-status.
Methods: All consecutive cases of ADG with concurrent molecular testing for IDH-mutation/ 1p/19p-codeletion diagnosed between March 2019 and February 2021 were reviewed and morphologically classified: a)pure astrocytic (PA); b)oligoastrocytic/ambiguous (OA); c)oligodendroglioma-like (ODG). An immunohistochemical (IHQ) panel was applied to all cases: IDH1-R132H (iIDH), ATRX and p53. IDH1/2 molecular testing was performed by PCR-based sequencing. 1p/19q-codeletion was evaluated by FISH.
Results: A total of 153 cases were reviewed: 34 were IDH-mutated (n=16 PA, n=3 OA, n=15 ODG), 27 in younger adults (prevalence=43.6%), 7 in older adults (prevalence=7.7%, the oldest with 72yo) (n=1-PA non-1p/19q-codeleted/n=6 OA/ODG-1p/19q-codeleted); 31 (91.2%) IDH-mutations corresponded to IDH-R132H form, 3 to the IDH-R132S mutation variant. iIDH-positivity was 100% specific and 100% sensitive for IDH1-R132H mutation. The patterns iIDH-negative/ATRX-negative (n=6) and OA/ODG-morphology/ATRX-positive/p53-negative (n=15) were 100% sensitive to detect potential IDH mutations, iIDH-negative/ATRX-negative pattern with overall specificity=50% and specificity=100% in non-midline ADG. OA/ODG-morphology-ATRX-positive/p53-negative pattern had sensitivity=100% and specificity=93.3% in predicting 1p/19q-codeletion. PA, ATRX-negativity and p53-positivity were mutually exclusive with 1p/19q-codeletion. PA morphology-iIDH-negative/ATRX-positive (n=117) and OA-iIDH-negative/ATRX-positive/p53-positive (n=2) were IDH-wildtype lacking 1p/19q-codeletion.
Conclusion: Prevalence of IDH-mutations in ADG with astrocytic morphophenotypes (PA, iIDH-negative/ATRX-negative, OA-iIDH-negative/ATRX-positive/p53-positive) was lower than expected for younger adults, rare in older adults as expected. Prevalence of R132H mutation was similar to the literature.
IDH-mutation-status is reliably predicted/identified combining morphology and immunophenotype, regardless of age.
1p/19q-codeletion is reliably predicted/excluded by specific morphophenotypes.
The majority of ADG (89,5%) don´t need molecular testing for IDH-mutations/ 1p/19q-codeletion, an important rationale to preserve tissue in the foreseeable era of deeper molecular testing for targeted therapy.

OFP-18-004
Prognostic factors of the rare papillary tumour of the pineal region: a systematic review and analysis
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Background & objectives: Tumours of pineal region are rare, representing less than 1% of all intracranial tumours in adults. Here, we aimed to compile current knowledge on the Papillary Tumour of the Pineal Region (PTPR) to identify factors that influence death and recurrence.
Methods: A search was performed in the databases PubMed, Scopus, Web of Science and Google Scholar using the keywords "papillary pineal tumour" and "papillary tumour of the pineal region". 169 potentially relevant articles were identified. The most relevant inclusion criteria were the presence of histopathological and immunohistochemistry characterization and information on tumour size. Exclusion criteria comprised systematic reviews and Radiology-oriented articles.
Results: Twenty articles were included in the final analysis. A database was created containing information on patient characterization, treatment, follow-up, histopathological and immunohistochemistry data. Thirty patients were included, between 1 and 70 years, 14 of which were females and 16 males. The descriptive and analytical statistics performed showed that the presence of areas of necrosis, the expression of cytokeratins, higher proliferative index and mitotic activity are associated with recurrence.
Conclusion: In patients with TPRP, the presence of necrosis seems to be the factor that most influences the recurrence of the neoplasia, an aspect that should be considered in the decision to start more aggressive therapies earlier. This study has limitations conditioned by the reduced number of cases published in the medical literature, so more comprehensive studies will be needed to confirm these findings.

OFP-18-005
Prognostic significance of the sarcomatous component in gliosarcomas: clinicopathological and prognostic analysis of 25 cases
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Background & objectives: Gliosarcoma is a rare central nervous system neoplasm with biphasic glial and mesenchymal components.It is accepted as a variant of glioblastoma multiforme(GBM) in the World Health Organization 2016 classification. We aimed to evaluate the clinicopathological and prognostic features of gliosarcomas.
Methods: All patients operated by our neurosurgery clinic between January 2007 and January 2021 were retrospectively analysed. The demographic, clinical, radiological, histopathological, immunohistochemical and molecular data of 25 patients diagnosed with gliosarcoma were retrospectively analysed and statistically evaluated. The sarcomatous component was grouped depending on the histopathological appereance and prognostic studies were performed regarding these groups.
Results: There were 986 central nervous system tumours operated in our hospital within 14 years. GBMs(n=232) constituted 23.5% wheras gliosarcomas were 10.7% of GBMs (n=25,mean age 57,3,M/F:17/8). The most common localization was the temporal region. The mean tumour diameter was 5,7(2-9)cm. The primary tumour was gliosarcoma in 12 patients,and it developed secondary to GBM in 13 patients. The sarcomatous component was grouped as conventional spindle cell sarcoma(n=13),pleomorphic sarcoma containing pleomorphic cells(n=6) and high-grade sarcoma with heterologous differentiation(n=6).

Recurrence was seen after an average of 3,6(±3,1)months. The mean survival time was 4,8 months,those with a previous diagnosis of GBM had shorter survival(p=0.028)and those with heterologous components in sarcoma had longer survival. The shortest survival was in sarcoma containing pleomorphic cells(p=0.024).
Conclusion: Gliosarcomas are extremely rare tumours which are only available as case reports in the literature. Our study contributes to the literature in terms of incidence and histopathological differentiation data. Gliosarcomas should be diagnosed with a careful histopathological examination and differentiated from entities such as epithelioid sarcoma and carcinoma. When mesenchymal differentiation is seen,the entire tissue should be examined and the glial component should be searched, and molecular studies such as IDH,as well as PTEN, TP53, TERT mutations and CDKN2A deletion should be performed.

OFP-18-006

The immunohistochemical expression of Serin and Arginine-Rich Splicing Factor 1 (SRSF1) is helpful in distinguishing diffuse astrocytomas and oligodendrogliomas from other gliomas

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Background & objectives: The aim of this study was to investigate the immunoexpression of SRSF1 in a series of 102 cases of diffuse and circumscribed adult gliomas, emphasizing the potential diagnostic role of this protein in the differential diagnosis of brain tumours.
Methods: 42 IDH-wild type glioblastomas (GBMs), 21 IDH-mutant and 1p/19q codeleted oligodendrogliomas, 15 ependymomas, 15 pilocytic astrocytomas (PAs), 5 sub-ependymal giant cell astrocytomas (SEGAs) and 4 pleomorphic xanthoastrocytomas (PXAs) were retrospectively retrieved from the neuropathological archive of our Institution and stained with anti-SRSF1 immunohistochemically antibody. The presence of brown chromogen within the cell nuclei was interpreted as positive SRSF1 staining.
Results: Most GBMs (34/42; 81%), oligodendrogliomas (15/21; 71%), SEGAs (4/5; 80%) and PXAs (3/4; 75%) showed strong SRSF1 immunoexpression, while no detectable staining was found in the majority of ependymomas (13/15; 87%) and PAs (10/15; 67%); the remaining ependymoma and PA cases exhibited weak and focal SRSF1 immunoexpression in 2/15 (13%) and 5/15 (33%) cases, respectively. Interestingly, no high SRSF1 immunohistochemical expression was found in any case of PA or ependymoma. Based on our findings, SRSF1 was a reliable immunomarker, both in confirming the diagnosis of diffuse astrocytoma and oligodendroglioma and in excluding other neuropathological entities, such as ependymomas and PAs.
Conclusion: Apart from the morphological and molecular features of gliomas, there are currently no specific immunohistochemical markers for this heterogeneous group of tumours: thus, there is the need to identify more specific and useful immunomarkers to distinguish each histological subtype from the others. The present study strongly emphasizes the role of SRSF1 as a new and promising immunomarker of diffuse gliomas and suggests that SRSF1 can be exploitable as a diagnostic adjunct to conventional markers in neuropathological daily practice.

OFP-18-007

Histone 3 thrimetilated in lysin 27 (H3K27me3) immunostaining is a diagnostic and prognostic marker in diffuse gliomas with mixed or oligodendroglial morphology

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Background & objectives: Surrogate immunohistochemical markers for 1p/19q codeletion could simplify the differential diagnosis between astrocytoma and oligodendroglioma. H3K27me3immunohistochemical loss has been associated with 1p/19qcodeletion.
We analysed the diagnostic and prognostic value of H3K27me3 immunostaining in gliomas with oligodendroglial or mixed morphology.
Methods: H3K27me3 immunoexpression was analysed in 69 diffuse gliomas with oligodendroglial or mixed morphology. All cases were immunostained for IDH1 R132H, ATRX and P53.
IDH1 R132H-negative cases underwent IDH1/2 gene sequencing. The presence of 1p/19q codeletion was investigated with FISH or PCR-based assays.
Statistical analyses were performed to assess the correlation between H3K27me3 staining and clinical-pathologic data.
Results: H3K27me3 was lost in 58/60 oligodendroglial tumours with retained (n=47) or non-conclusive (n=11) ATRX staining, 3/6 astrocytic IDH-mutant with ATRX loss and 3/3 IDH-wt tumours. H3K27me3 was retained in 2/60 oligodendroglial tumours, that also retained ATRX, and in 3/6 astrocytic IDH-mutant tumours, two of which had lost and one retained ATRX.
H3K27me3 retention was associated with a significantly shorter recurrence-free survival (P< 0.0001), independently from IDH mutational status, histological grade or 1p/19q codeletion.
Conclusion: A diagnostic workflow including H3K27me3 immunostaining, after the assessment of IDH1/2 mutational status and ATRX staining, is useful to reduce the number of diffuse gliomas that necessitate 1p/19q codeletion testing.
According to this algorithm, gliomas IDH-wt and IDH-mutant with ATRX loss are classified astrocytic; gliomas IDH-mutant with ATRX retention and H3K27me3 loss are classified oligodendroglial; only gliomas IDH-mutant with retained or non-conclusive ATRX and retained H3K27me3 necessitate 1p/19q codeletion testing. H3K27me3 loss is associated with longer recurrence-free survival.

OFP-18-008

Prognosis of patients with IDH-wildtype and IDH-mutant diffuse gliomas: data from the King Hussein Cancer Center (2014–2019)

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Background & objectives: Mutations in isocitrate dehydrogenase (IDH) signal a better prognosis in diffuse astrocytic and oligodendroglial tumours. Our aim was to study the prognosis of patients with IDH-wildtype and IDH-mutant diffuse gliomas at the King Hussein Cancer Center.
Methods: We performed a retrospective chart review of all Jordanian patients with diffuse gliomas who were managed at our center (2014–2019) and underwent IDH1 (R132H) immunostaining. We included the following entities: diffuse astrocytoma, anaplastic astrocytoma, glioblastoma, oligodendroglioma, and anaplastic oligodendroglioma. We used the Kaplan–Meier method to estimate the overall survival rates and the log-rank test to perform pairwise comparisons.
Results: We included 181 patients. Glioblastoma was the most common entity (n = 104), followed by anaplastic astrocytoma (n = 29), diffuse astrocytoma (n = 24), oligodendroglioma (n = 15), and anaplastic oligodendroglioma (n = 9). IDH-wildtype tumours outnumbered IDH-mutant tumours 112 (61.9%) to 69 (38.1%). IDH mutation was most common in oligodendroglioma (93.3%), followed by anaplastic oligodendroglioma (77.8%), diffuse astrocytoma (62.5%), anaplastic astrocytoma (51.7%), and glioblastoma (17.3%). IDH status statistically significantly stratified the overall survival of the full cohort ($p < 0.001$), patients with any astrocytic tumour ($p < 0.001$), patients with a grade II or III astrocytic tumour ($p = 0.035$), and patients with glioblastoma ($p = 0.049$).
Conclusion: IDH mutation signals a better prognosis in patients with a diffuse glioma. This finding is concordant with the published international literature.

OFP-19 | Ophthalmic Pathology

OFP-19-001
Lacrimal gland pleomorphic adenoma: factors leading to recurrence and malignant potential

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Background & objectives: Lacrimal gland pleomorphic adenomas (LGPA) can undergo malignant transformation, most often in recurrent cases. Complete excision is thus the recommended definitive diagnostic/therapeutic approach when clinically/radiologically suspected.
This paper will investigate the potential factors associated with LGPA recurrence and malignant transformation.
Methods: A retrospective review of histologically confirmed LGPA cases occurring between September 1975 and January 2021 (46 years) in a national tertiary referral centre for ophthalmic pathology was undertaken. Where residual/recurrent LGPA or malignant transformation was identified, patient records were accessed and further information including; socio-demographics, presenting symptoms, diagnostic procedures, radiology and clinical course was analysed.
Results: A total of 13 cases of LGPA were identified. Recurrent LGPA occurred in 3 patients, no cases of malignant transformation were reported. The recurrence time for LGPA ranged from 6 months to 15 years post initial diagnosis. Recurrence occurred in 2 males and 1 female, all were Irish Caucasians with ages ranging from 13 to 72 at the time of first biopsy. The initial diagnostic procedure in all recurrences was incisional biopsy. The reasons for incisional biopsy versus the recommended primary en bloc resection included clinical uncertainty and broad radiologic differential. No recurrences were identified in LGPA cases which had undergone outright complete excision.
Conclusion: LGPA should be considered as a potential diagnosis in lacrimal lesions at all ages. In cases of clinical or radiological ambiguity, second opinion from a specialist centre should be sought. Where necessary, fine needle aspiration cytology is preferable to incisional biopsy due to the associated potential for tumour displacement and subsequent increased risk of recurrence. In situations where incisional biopsy is undertaken, the suture track should be marked to facilitate identification and removal of the entire track during subsequent resection.

OFP-20 | Other Topics

OFP-20-001
Quick sectioning-free H&E imaging of bulk tissue using multiphoton microscopy

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Background & objectives: Labour and time-intensive paraffin sectioning is the foundation of today's routine pathology workflow. To accelerate this process, we create H&E images from bulk fresh or formalin-fixed tissue without sectioning using a home-built multiphoton microscope based on fibre laser technology.
Methods: To evaluate whether our multiphoton microscopy technique can provide a fast alternative to paraffine or frozen sectioning, we compare images of our system using H&E-stained formalin-fixed tissue as well as acridine orange and sulforhodamine 101-stained fresh tissue to classical formalin-fixed paraffin embedded sections.
Results: Our multiphoton microscope can acquire images of bulk acridine orange and sulforhodamine 101 stained skin and kidney samples within less than 1 hour. We gross the tissue block and stain it for 10 min without any further processing. Afterwards the tissue is scanned by the microscope and converted into a digital H&E image. The digital image can now directly be analysed by a pathologist. Additionally, we compared multiphoton microscope images of formalin-fixed H&E-stained tissue to paraffin-embedded sections of the same block to assess the quality of our technique.
Conclusion: We create H&E-like images without sectioning the tissue using a home-built multiphoton microscope. Two different staining mechanisms have been tested to acquire high quality images. In the future, we want to further improve our measurement speed and start a clinical study on basal-cell carcinoma. The potential combination with other imaging modalities such as fluorescent lifetime imaging and the application of AI algorithms on the digital data might allow us to increase the diagnostic accuracy of our method.

OFP-20-002
Taking undergraduate pathology research education to the Cloud

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Background & objectives: COVID-19 pandemic has created the largest disruption in education in human history. Quick and efficient modifications to teaching and assessment were devised to maintain biomedical education continuity. We created a virtual pathology research project for undergraduate (UG) biomedical sciences students.
Methods: The bespoke research project was based on fixed field images from 20 digitised human nonalcoholic fatty liver disease (NAFLD) biopsies (n=40, training set and n=60, test set). Students were trained using a web-based teleconference platform in four group sessions, followed by one-to-one meetings, and self-studied using the free LITMUS NAFLD Histopathology Atlas at the European Society of Pathology website (https://tinyurl.com/LITMUS-Histology).
Results: Inter-observer variability between 3 stage 3 UG students and three pathologists on semi-quantitative histological scoring of steatosis, lobular inflammation (LI), hepatocyte ballooning (HB) and fibrosis was assessed. The NASH CRN histological scoring system and Fleiss's and Cohen's kappa statistics were applied. Results were discussed during online adjudication meetings and multiple annotations were used on the images in difficult cases. Following training, steatosis was the feature with highest agreement (k=0.63) in the whole group, while moderate agreement was achieved for LI (k=0.52), fibrosis (k=0.57) and HB (k=0.46). All students efficiently prepared on time a 5,000-word dissertation, organized as an original research publication, and a power-point presentation required for project assessment.
Conclusion: Novel educational initiatives have been employed to sustain UG student theoretical and practical learning during Covid19 pandemic. We have successfully modified a "wet" UG pathology research project into a virtual "dry" project applying Cloud-based digital pathology imaging and providing online pathology training and feedback sessions using web-conference tools. Our methodology offers a digital alternative to laboratory-based research teaching in pathology and may be further improved for application in larger student groups.

OFP-21 | Paediatric and Perinatal Pathology

OFP-21-001
Placental and placental bed pathology caused by SARS-CoV-2

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Background & objectives: The impact of coronavirus infection SARS-CoV-2 on pregnancy and perinatal outcomes is particular interest for obstetricians, paediatricians and other scientists. The aim of study was to reveal changes in the placenta and placental bed of women with confirmed SARS-CoV-2 infection.
Methods: The main group included 34 women (SARS-CoV-2 confirmed by real-time PCR), a comparison group included 15 healthy women. Histopathological examination of placenta and placental bed was carried out. Staining method was performed on serial sections of paraffin blocks with H&E. Immunohistochemistry with CD8 and CD3 was performed, as well as real-time PCR. Statistical processing by Fisher's test
Results: In the main group an increase of complications (anaemia (48%) and isthmic-cervical insufficiency (11.8%), preeclampsia (2.9%) and threatening premature birth (11.9%)) was found. Microscopic examination showed an increase in the incidence of maternal malperfusion (central infarctions ($p = 0.00032$), agglutination of villi ($p = 0.00043$), decidual arteriopathy ($p = 0.00069$), intervillous thrombi ($p = 0.00005$)) and foetal stromal-vascular lesions (obliterative angiopathy ($p = 0.00033$), chronic willitis ($p = 0.00002$), chronic chorioamnionitis ($p = 0.00001$), massive fibrinoid deposits in the uteroplacental region ($p = 0.00001$)). Biopsys of the placental bed showed foci of lymphohistiocytic infiltration and focal hemorrhages in the perivascular areas. Decidual arteriopathy was detected in 18 cases.
Conclusion: Changes in the placenta in women with confirmed SARS-CoV-2 infection in the third trimester of pregnancy are characterized by the development of maternal vascular malperfusion, chronic inflammation in the form of focal villitis and interillusitis, obliterative angiopathy and lesions of the decidual spiral arteries. These changes reflect an increased risk for transplacental transmission of the virus and can lead to long-term negative consequences for the foetus.

OFP-21-002
Impact of SARS-COV-2 on foetus and placenta of pregnant women affected by COVID-19. Study of 177 cases received during the pandemic
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Background & objectives: Placental pathology and vertical transmission in pregnant women infected by SARS-CoV2 has generated many reports with nonspecific or contradictory results. The objective is to identify histological and molecular findings of infected placentas and its impact on the course of pregnancy.
Methods: Placentas from 177 women infected with SARS-COV-2 were reviewed, 66 of them with active infection within 10 days prior to delivery and 111 with past infection beyond this period. Two foetal autopsies were submitted for pathological study. Placental infection was investigated by immunohistochemistry (IHC) in all cases, RT-PCR in 27 cases, and in situ hybridization (ISH) in 5 cases.
Results: Five placentas showed trophoblast necrosis with villous stroma preserved, collapse of the intervillous space, intervillous fibrinoid deposition and variable polymorphous inflammatory infiltrates. These 5 placentas were the only ones with SARS-CoV-2 infection identified by IHC and ISH (granular cytoplasmic villous trophoblast staining) and RT-PCR. These 5 cases with placental infection belonged to the group of pregnant women with active infection within 10 days prior to delivery. Two had focal lesions (<20%) and the other three, which resulted in stillbirth, showed diffuse lesions (> 80%). In two of the three deaths, an autopsy was performed and infection of the foetal tissues was not demonstrated by IHC.
Conclusion: Placental SARS-CoV-2 infection has a characteristic histological pattern with villous trophoblast necrosis, intervillous space collapse, and variable degrees of mixed inflammation and intervillous fibrinoid deposition. Placental infection can be confirmed by trophoblast cytoplasmic positivity with IHC and/or ISH for SARS-CoV-2. We propose the term "Diffuse Trophoblastic Damage" for extensive lesions, which can be the cause of foetal death due to placental insufficiency. In this study we have not been able to confirm the possible vertical transmission of the virus.

OFP-21-003
Diffuse trophoblast damage is the hallmark of SARS-CoV-2-associated foetal demise
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Background & objectives: Placenta pathology in SARS-CoV-2 infected pregnancies seems rather unspecific. However, the identification of the placental lesions due to SARS-CoV-2 infection would be a significant advance in the management of these pregnancies and the identification of the mechanisms in vertical transmission.
Methods: The pathological findings in placentas delivered from 198 SARS-CoV-2 positive pregnant women were investigated for the presence of lesions associated with placenta SARS-CoV-2 infection. SARS-CoV-2 infection was investigated in placental tissues through immunohistochemistry and positive cases were further confirmed by in situ hybridization. SARS-CoV-2 infection was also investigated by RT-PCR in 33 cases, including all the immunohistochemically positive cases.
Results: Nine cases were SARS-CoV-2 positive by immunohistochemistry, in situ hybridization, and RT-PCR. These placentas showed lesions characterized by villous trophoblast necrosis with intervillous space collapse and variable amounts of mixed intervillous inflammatory infiltrate and perivillous fibrinoid deposition. Such lesions ranged from focal to massively extended in five cases, resulting in intrauterine foetal death. Two of the stillborn foetuses showed some evidence of SARS-CoV-2 positivity. The remaining 189 placentas did not show similar lesions.
Conclusion: The strong association between trophoblastic damage and placenta SARS-CoV-2 infection suggests that this lesion is a specific marker of SARS-CoV-2 infection in placenta. Diffuse trophoblastic damage, massively affecting chorionic tissue, can result in foetal death associated with COVID-19 disease.

OFP-21-004
Paediatric Hodgkin Lymphomas: a 10-year retrospective study from Coimbra
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Background & objectives: Hodgkin lymphomas are common lymphoid neoplasms in children and adolescents worldwide. Two major types are recognized: classic Hodgkin lymphoma and nodular lymphocyte predominant Hodgkin lymphoma. The improved therapeutic approach, according to the correct diagnosis has led to a better prognosis.
Methods: From 2010 to 2020, there were 50 patients in total with histopathological diagnosis of Hodgkin lymphoma. The neoplasm had a clearly predilection for females, representing 62% of this retrospective study. The youngest case was diagnosed in a 3 year-old child and the oldest one in a 17 year-old adolescent.
Results: Classic Hodgkin lymphoma (CHL) represented 86% of cases while nodular lymphocyte predominant Hodgkin lymphoma accounted (NLPHL) for 10%. As for CHL, the vast majority were nodular sclerosis subtype, representing almost 96% of the total cases, with mediastinal involvement in almost all patients. There was also one case of mixed cellularity subtype and another of lymphocyte-rich CHL.
Two patients had recurrent disease, one died without response to bone marrow transplant and the other is currently being managed. Other two cases had its diagnosis reviewed and modified to B-cell lymphoma

unclassifiable, one patient died due to progression of the disease and the other had an effective response to treatment.
Conclusion: Hodgkin lymphoma remains a neoplasia with great overall survival mainly at paediatric age. In our series, we conclude that it is necessary to review some cases when treatment is not effective because it might be present overlapping morphological and immunophenotype features that represent exceedingly difficult cases, resulting as B-cell lymphoma unclassifiable.
Recurrent disease and immunosuppression related to treatment also represented defiant cases in our study, however, the majority of patients remain relapse free after treatment, as expected.

OFP-21-005
Hepatoblastoma: a clinicopathological review of 17 cases from a single centre
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Background & objectives: Hepatoblastoma, the most common primary malignant liver tumour in children, occurs mainly in the first three years of life, being associated with good survival rates. Since some subsets are not responsive to therapy, understanding predictors of tumour behaviour is mandatory.
Methods: Clinicopathologic features of 17 patients diagnosed with hepatoblastoma at Portuguese Oncology Institute of Porto (1999-2021) were reviewed. Material was composed of liver biopsies (n=14), and resection specimens (n=15) of primary tumour, as well as recurrence/metastatic resection specimens (n=10). Besides the descriptive results stated below, we further aim to correlate detailed histological findings with tumour behaviour and clinical outcome.
Results: Mean age at presentation was 2.78 years (range:0.35-8.1) and male:female ratio of 1.43:1. Most patients presented with abdominal mass, fever and/or abdominal pain. AFP was increased in the majority of cases. One with normal AFP was diagnosed with SCUD subtype. AFP decreased in all patients after treatment. Two carried APC gene mutations.
Hepatoblastomas were classified as epithelial (47%) or mixed epithelial and mesenchymal (53%). Most common patterns were foetal (29,4%) and mixed foetal and embryonal(37%); one SCUD and one macrotrabecular case were identified. 23.5% had extramedullary hematopoiesis. Heterologous elements present in 53%.
Metastasis occured in 23,5%; persistence in 5,8%. Survival rates were 92% at 5-years and 77% at 10-years follow-up.
Conclusion: Our data is in accordance with the literature, mostly demonstrating good survival rates, primarily due to therapeutical improvement. However, prognostic factors are still limited and mainly dependent on clinical and imagiology factors, with limited pathology input. Due to the rarity of disease, large multicentric collaborative studies are essential to identify potential molecular markers and pathological features that could predict tumour behaviour and improve even further therapy success or develop targeted therapy strategies.

OFP-21-006
Small-for-gestational age placentas – a clinical-pathological correlation
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Background & objectives: Small-for-gestational age placentas comprises placentas whose weight is below 10th percentile and they are correlated with various risk factors, most of them of maternal cause. Our work attempt to characterize the maternal clinical conditions and correlate with macroscopic/microscopic findings.
Methods: We retrospectively reviewed 418 singleton placentas from the last year, excluding those which weight was above 10th percentile or below 20+6 week gestational (WG) age. In those cases, we reviewed maternal history, macroscopic and histologic report and if there was an associated foetal autopsy.
Results: We obtained 137 small placentas (33%), with mean of 35WG age; eighteen with autopsies (11 stillbirths; 7 medical termination of pregnancy). Only 19 cases were concomitant with foetal weight <10thpercentile. Median maternal age was 32 years old (range 16-45 years old), most of them were healthy (52cases - 38%). The large number of cases were placentas with weight below 3rd percentile (102cases - 75%), the majority were healthy mothers followed by the group with multiple pathologies. The most frequent histologic features in the first group was maternal malperfusion (38%). Ten cases had no prior maternal history and no pathological findings; one was from an autopsy due to genetic alterations.
Conclusion: There are several well-known risk factors associated with small-for-gestational age placentas, the majority associated with maternal malperfusion; and our results are concordant. In 7.29% of the cases there were no clear reasons for placenta's low weight, not even maternal history, which suggests other factors may play a role. Despite some risk factors can be manageable, cases still exist with increased risk of foetal morbidity and foetal mortality.

OFP-21-007
Skin lesions in children: evaluation of clinicopathological findings
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Background & objectives: Paediatric skin diseases may show various manifestations, occasionally affecting the patients' quality of life. Histopathological examination may be required for the diagnosis. The aim of this study was to evaluate the spectrum of clinicopathological features in paediatric skin lesions.
Methods: A total of 180 biopsies of 171 consecutive patients were included. The clinicopathological findings were retrospectively evaluated and retrieved from clinical and pathological data. Neoplastic/proliferative lesions (NPLs) (n=97) were grouped per their origin while non-neoplastic (inflammatory) lesions (ILs) (n=83) were grouped based on their pattern. The clinical and histopathological characteristics were statistically analysed.
Results: 53% were male and median age was 10±4.9 y.o. (range 0-17). ILs mainly involved the head and neck while NPLs were predominantly located in lower extremity (p=0.001). The most common NPLs were benign nevus (23%, n=22) and pilomatrixoma (15%, n=15). The most frequent IL was spongiotic/psoriasiform dermatitis (45%). The mean diameter of NPLs was 2.3 cm, connective tissue/skin appendage tumours being the largest (p=0.02). Melanocytic lesions and cutaneous cysts were significantly more common in children >12 y.o. ($p<0.05$). Juvenile xanthogranuloma occurred only in children <6 y.o. Only one patient had histopathological findings suspicious for mycosis fungoides. The discordance rate between clinical and histopathological diagnoses was higher for ILs (32% vs.21%).
Conclusion: Although the spectrum of skin lesions is very broad in paediatric patients, most are benign in nature. The higher frequency of melanocytic and/or cystic lesions among children >12 years old may be attributed to increased self-care during puberty. Neoplastic/proliferative lesions seem to be more easily and accurately recognized by clinicians. However, multidisciplinary approach remains to be the optimal method in diagnosis of skin lesions among children, considering the relatively high rate of discordance between the clinical and histopathological diagnoses.

OFP-23 | Pulmonary Pathology

OFP-23-001

A multi-modality approach for biopsy-based diagnostic and prognostic prediction in early-stage lung adenocarcinomas

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Background & objectives: Lung adenocarcinomas are variable in morphology and genetics. In resected tumours, these parameters correlate with prognosis and development of metastases. Deriving as much information from a biopsy as possible could facilitate an early stratification of patients for therapy and follow-up.
Methods: 200 patients with stage I and II adenocarcinomas were retrospectively included. Specimens (biopsies n=200; paired resections n=125) were evaluated for growth pattern, nuclear grade, fibrosis, inflammation and genomic alterations. Findings were compared using non-parametric testing for categorical variables. Model performance was assessed using the area under the curve for biopsies and resection specimens and overall and progression free survival calculated.
Results: The overall growth pattern concordance between biopsies and resections was 69.6%. Nuclear grade and degree of fibrosis correlated with different types of growth pattern and had higher scores in paired resections. EGFR mutations and MET exon 14 skipping mutations were mainly found in lepidic predominant tumours. The dominant growth pattern correlated with overall and progression free survival in resected adenocarcinomas but not in biopsies. We further demonstrated similar findings for nuclear grade and amount of fibrosis. Model performance for the prediction of overall and progression free survival using all available information from biopsy specimens only was poor and resulted in an average AUC of 0.58 and 0.57 respectively.
Conclusion: Our data confirm the prognostic relevance of growth pattern and nuclear grade in resected adenocarcinomas. We further demonstrated that the amount of fibrosis may predict overall and progression free survival. Contrary to our hypothesis, we could not confirm these findings for biopsy specimens. Combining all biopsy specimen information did not improve prediction of overall and progression free survival. For daily practice, more robust (bio)markers are needed in biopsies to predict prognosis and stratify patients for therapy and follow-up.

OFP-23-002

Different types of immune system regulations in severe Coronavirus disease 2019

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Background & objectives: Coronavirus disease 2019 (Covid-19) is a severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2). While most patients exhibit mild or moderate symptoms, approximately 10-20 % progress to severe disease and 0.5-1 % of infected die.
Methods: To gain insight into the immune mechanisms underlying Covid-19 related lung damage a systematic, pathological and whole transcriptome analysis of autopsy materials was done collected from lung samples of 20 individuals, who died from Covid-19. These were compared to 13 patients from a different hospital, and reports on patients from South America for differences in the type of immune reaction.
Results: Distinct pathological and molecular signatures were observed, characterized by different stages of diffuse alveolar damage and disseminated intravascular coagulation with hyperinflammation, enabling stratification of the deceased individuals. CD4+ lymphocytes predominated during the early inflammation stages, in part expressing a memory signature. Natural killer cells (NK) and B lymphocytes were absent. Upregulation of the JAK3-STAT1-cGas-Sting-IL6 pathway was identified. This pathway upregulates class one interferons, and prolongs inflammation, and can activate coagulation by platelets. Genes involved in enhanced production of cGAS and stability of cGAS and STING were upregulated in Covid-19 cases. Downregulation of cytokines regulated by vitamin D (VitD) was also found, pointing to a potential role for VitD deficiency.
Conclusion: This integrated, multi-tiered analysis of autopsy materials provides insight into the lethal manifestation of Covid-19. It allowed to separate patients prone to disseminated intravascular coagulation from those with a classical respiratory viral pneumonia such as SARS-Cov1.

OFP-23-003

EGFR-mutated non-small-cell lung cancer transformation into small-cell lung cancer after tyrosine kinase inhibitors: let us think about liquid biopsy!

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Background & objectives: Tirosine kinase inhibitors (TKI) are employed extensively in mutant non-small cell lung cancer (NSCLC), showing an indisputable benefit on tumour response. However, disease progression always occurs after approximately 9–12 months of treatment due to different mechanisms of resistance.
Methods: Herein, we describe two cases diagnosed as lung adenocarcinoma harbouring epidermal growth factor receptor (EGFR) mutations and treated by TKI with clinical benefit for a short time. In each case, liquid biopsy and subsequent transbronchial biopsy performed at the time of disease progression were processed by molecular analysis.
Results: CASE 1: A 39-year-old male nonsmoker with lung adenocarcinoma, harbouring an EGFR exon 19-deletion mutation was treated with Erlotinib. At recurrence after two years, a liquid biopsy detected the T790M mutation, switching the treatment to Osimertinib. After two months of unresponsiveness to Osimertinib, a re-biopsy was carried out. CASE 2: A 63-year-old female nonsmoker with lung adenocarcinoma, harbouring an EGFR exon 19-deletion mutation, was treated with Osimertinib. After a short period of clinical benefit, the patient underwent liquid biopsy and an EGFR wild type was found without any resistant mutant form. The mass was then re-biopsied. In both cases, the re-biopsy showed a switch to small cell lung carcinoma (SCLC).
Conclusion: Several mechanisms of resistance can affect TKI treatment, most commonly the acquisition of new mutations that overcome and/or bypass the inhibition of the specific molecular pathway and/or the histological transformation into more aggressive forms (e.g. SCLC). At the present time, "tissue is the solution": histological analysis should be considered the first choice, whenever possible. Currently, liquid biopsy is indeed unable to detect any histotype switch thus delaying alternative treatments.

OFP-23-004

Oncogene driver testing in surgically early/locally advanced non-small-cell lung cancer: a single centre experience

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Background & objectives: Oncogene driver screening in advanced non-small-cell lung cancer (NSCLC) is a standard in practice in molecular pathology. Herein, we describe our experience of biomarker screening in surgically resected early/locally advanced NSCLC, whose molecular status is presently largely unknown.

Methods: The study included naïve surgically resected NSCLC cases consecutively recruited at the University Hospital of Padova (from 2017 to 2018; adenocarcinoma, stage I-IIIA). Must oncogene drivers, EGFR gene alterations, ALK/ROS1 translocations, and PDL-1 tissue expression were analysed in all cases. After surgery patients were treated with adjuvant radiotherapy and/or chemotherapy as opportune. Data on follow-up and treatments were collected.
Results: Ninety-five cases (55 males, 40 females, median age: 70 years) were studied. Four cases were ALK translocated (4%). Eighteen cases (19%) showed EGFR gene alterations in exons 18 (1 case), 19 (9 cases), 21 (6 cases), and in both 18 and 20 (2 cases). In 6 of them (30%) PD-L1 was positive (tumour proportion score >1%). At the average follow-up (45 months), 31 patients (33%) showed an adverse event: death in 16 (17%) cases and disease recurrence in 15 (16%) cases, also in stage I (13 out of 31, 42%). Four of them (13%) had an oncogene driver alteration.
Conclusion: Molecular analysis of oncogene drivers in surgically resected NSCLCs, whose incidence is similar to that of advanced stages, will be an additional important task for pathologists. This is reinforced by successful data obtained from the recent trial that demonstrated a benefit of adjuvant target therapy in completely resected EGFR mutation-positive NSCLCs (Wu et al, NEJM, 2020). Oncogene driver alterations and PDL-1 analysis in resected NSCLC may allow a better prognostic stratification, ensuring the administration of the most effective targeted treatments.

OFP-23-005
Lower gene expression of angiotension-converting enzyme 2 receptor in lung tissues of smokers with COVID-19 pneumonia
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Background & objectives: Angiotensin-converting enzyme 2 (ACE-2) is the main cell entry receptor for SARS-CoV-2 and plays a critical role in causing COVID-19. The role of smoking is controversial, thus we correlated lung ACE-2 expression with several data to explore susceptibility to infection.
Methods: This is a retrospective observational study on 29 consecutive COVID-19 laboratory-confirmed autopsies performed at the University Hospital of Padova from March to October 2020. SARS-CoV-2 genome and ACE-2 mRNA expression were evaluated by Real-Time polymerase chain reaction in lung tissue samples obtained from all patients and correlated with several clinical/pathological data with main focus on smoking habit.
Results: Smoking habit was shown to be less frequent in high than low ACE-2 expressors (14% vs 67%, p=0.014). Bayesian logistic regression including smoking, age, gender, hypertension, and virus quantity confirmed that smoking was the most probable risk factor associated with low ACE-2 expression. A direct linear relation was found between viral quantity and ACE-2 expression (p=0.028). No other significant differences were found when ACE-2 expression was correlated with remaining clinical data. Finally, considering morphological features, high ACE-2 expressors showed more frequently a prevalent pattern of vascular injury than low expressors (56% vs 31%, p=0.049).
Conclusion: In conclusion, ACE-2 levels were decreased in the lung tissue of smokers with severe COVID-19 pneumonia. These results point out complex biological interactions between SARS-CoV-2 and ACE-2 particularly concerning the aspect of smoking habit and need larger prospective case series and translational studies.

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OFP-23-006
Forms and stages of progression of pulmonary pathology in novel SARS-COV-2 coronavirus infection
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Background & objectives: Lungs are the main portal of entry for COVID-19.
Methods: Study was performed on lung tissue from 232 autopsy patients with COVID-19 confirmed by PCR during life and/or by examining paraffin blocks of lung tissue. Conducted macro-, microscopic and immunohistochemical (IHC) analysis (CD3, CD20, TLR4, TLR9, ki67, p63, OCT4, ALDH1) revealed the particularities of pathological changes in the lungs.
Results: Morphological examination revealed diffuse alveolar damage (DAD) (in 86% of cases); disseminated coagulopathy in all cases with thrombosis or thromboembolism of the pulmonary artery and haemorrhagic infarcts and haemorrhages; lymphocytic alveolitis with concomitant vasculitis of medium- and small-calibre pulmonary arterial branches in 92 %, viral-bacterial pneumonia (20%), interstitial fibrosis (10%), and disregeneration changes of the lung epithelium. IHC showed high expression of CD3, CD20, TLR4, TLR9 in inflammatory infiltrate in all cases; low or negative expression of ki67, p63, OCT4, ALDH1 in foci of disregeneration.
Conclusion: Discussed pathological processes in lung tissue may be considered as stages of COVID-19 progression. The process in the lungs can develop along three morphogenetic pathways, starting with the development of DAD or lymphocytic alveolitis, or coagulopathy. The latter variant of the onset of infection is most likely associated with intestinal portal of entry. Wherein lung damage is secondary, and develops after viremia, disseminated intravascular coagulation and cytokine storm.

OFP-23-007
Transthoracic fine needle aspiration and clot core biopsies of pulmonary spindle and mesenchymal lesions: a Pandora's box
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Background & objectives: Pulmonary spindle cell and mesenchymal lesions represent a significant group of heterogeneous neoplasms with differentials ranging from benign to malignant lesions. This study highlights the role of FNAC and clot core biopsy in diagnosis of spindle-cell lesions in lung.
Methods: Present study is a retrospective study in which lung FNA with spindle and mesenchymal cells from 2015-2020 were retrieved from cytopathology archives and reviewed. Granulomatous lesions, FNA from mediastinum and chest wall were excluded. In our institute, fine-needle aspiration (FNA) cytology was the first material available while final diagnosis was rendered on clot core and IHC.
Results: 60 cases of FNA lung having spindle and mesenchymal cells as key morphological feature were identified. Six (10.0%) benign and fifty-four cases (90%) malignancies including 23 primary and 31 metastasis on clot core and IHC. FNA was paucicellular in 12 cases, reported as benign in 8 cases and malignant in 52 cases. One case of pulmonary blastoma was reported as inflammatory pseudotumour on cytology, other case of chondrosarcoma was reported as chondroid tumour. Most common primary malignancies sarcomatoid carcinoma and most common metastasis was malignant peripheral nerve sheath tumour. A single case of alveolar soft part sarcoma, epitheloid sarcoma and neuroblastoma arising in a teratoma were also identified.
Conclusion: FNA along with clot core plays a pivotal role in the subsequent pathway taken for diagnostic or therapeutic management of these patients.

OFP-23-008
Interobserver concordance of PD-L1 clones SP263 and E1L3N in non-small cell lung carcinoma (NSCLC): two centre study
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Background & objectives: The use of PD-L1 immune-checkpoint inhibitors in NSCLC has marked an era. Testing for PD-L1 expression of NSCLC is widely used, there may be inconsistencies between different immunohistochemical assays, moreover, between different observers. In this study, we aimed to measure inter-pathologist variability.
Methods: Pathological specimens that were diagnosed with NSCLC between 2017-2021 and had enough tumour tissue to stain with two clones were included to study. According to the percentage of positive tumour cells detected in each PD-L1 clone , semi-quantitative scoring was performed by two pathologists individually and blindly. Cohen's kappa analysis was performed to measure consistency between two pathologists, EB and SB.
Results: There were 19 female and 83 male patients, with an average age of 63.25 years. Of the 102 cases 47(46%) were small biopsy, 37(36,2%) as resection and 7(6,8%) as cytology. The distributions of SP263 and E1L3N scoring of EB and SB were as the following (respectively): for 1% cut-off negative n=15/18 and n=20/34 and positive n=87/84 and n=82/68, for 50% cut-off negative n=15/18 and n=44/62 and positive n=87/84 and n=58/40. Interobserver agreement for the two clones, at 1% cut-off, agreement was 82,4%,for E1L3N and 93% for SP263, respectively (Cohen κ:0,55 and 0,76, respectively); at 50% cut-off, agreement was 91.2%and 86,3% for E1L3N and SP263, respectively (Cohen κ:0,81 and 0,72, respectively).
Conclusion: The highest interobserver variability was observed for the ≥1% cut-off for positivity in assessment of NSCLC tissues stained by E1L3N clone. We have shown a substantial to almost perfect interobserver agreement in evaluating PD-L1 using SP263 for any cut-off value, and a substantial agreement in evaluating PD-L1 using E1L3N clones when we used ≥50% cut-off for positivity.

OFP-23-009
MUC4 and GATA3 immunohistochemical staining in the diagnosis of sarcomatoid mesotheliomas: Case series of 5 patients with clinical and pathologic correlation, and literature review
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Background & objectives: Diagnosing mesotheliomas is challenging, especially sarcomatoid subtype, which poses a differential morphological diagnosis with sarcomatoid carcinomas (SC) and sarcomas, and usually lacks positive effusions. GATA3 and MUC4 expression has been described as useful in the diagnosis of sarcomatoid mesothelioma (SM).
Methods: We studied 5 cases, previously diagnosed as SM based on clinical and pathological criteria, between 2014 and 2020. Confirmation was made with, at least two mesothelial markers (calretinin, WT1 or D2-40) and two epithelial markers (BerEP4 and MOC31) in addition to, GATA3 (clone L50-823), BAP1 (clone C-4), MUC4 (clone SP241, with external control), EMA, Desmin and CKAE1-AE3 on complete sections.
Results: All cases were male, with ages ranging between 56-84 years at diagnosis. Different presentation forms were seen: pleural masses (3), pleuro-pulmonary nodule (1) or pleural nodule (1) with combined hemothorax (1) or pleural effusion (4). None had positive pleural effusions. Diagnosis was made by transthoracic core needle biopsy (2) or videothoracoscopic biopsy (3).
Three showed focal positive immunostaining for epithelial markers (EMA or CKAE1-AE3) and two showed focal positivity or complete loss for mesothelial markers (calretinin, WT1, D2-40).
GATA3 expression was found in all cases (5/5). No obvious immunostaining for MUC4 could be demonstrated (0/5), while up to 40% of sarcomatoid carcinomas are described as MUC4 positive.
Conclusion: Several risk factors were identified, such as smoking history (4/5), prolonged asbestos occupational exposure (1/5) and working in construction (2/5). All SM (100%) expressed GATA3 staining (only focal and weakly in two of them), what suggests that GATA3 is a very sensitive immunohistochemical marker, for the integrated clinical-radiological diagnosis of these neoplasms. Negativity for MUC4 does not exclude sarcomatoid carcinoma, requiring additional techniques (BAP1, homozygous deletion of P16 / CDKN2A, GATA3) to confirm/rule out MS.

OFP-23-010
The bronchoalveolar lavage in COVID-19 acute respiratory failure: the role of pathologist
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Background & objectives: The occurrence of respiratory superinfections represents an additional risk factor for fatal outcome in COVID-19 patients. In this study we evaluate the role of the cytological examination of the bronchoalveolar lavage (BAL) in a cohort of patients with severe COVID-19.
Methods: BAL from 10 mechanically ventilated patients were collected following one of these criteria: radiology discordant from typical COVID-19 pneumonia; immunosuppression; no improvement after 10 days of ventilation; microbiological tests suspected for superinfection. For each case the following parameters were evaluated: adequacy; quantification of the inflammatory cells and lipid-laden macrophages index (LLMI); presence of microorganisms, hyperplastic pneumocytes, erythrocytes, necrotic material, fibrin.
Results: Ten millilitres of liquid were used to prepare cytological smears and cytoblock. Nine out the ten samples were adequate (upper airway contaminants <7%). Fungal hyphae (two morphologically compatible with Candida spp and one with Aspergillus spp) were detected in three cases through the special stains (i.e. PAS, Grocott). The LLMI was high (300) in a patient in whom a lung aspiration was subsequently confirmed. The remaining cases showed variable increases in neutrophilic granulocytes, hyperplastic pneumocytes, fibrin or necrotic material. These latter features are compatible with diffuse alveolar damage, due to SARS-CoV-2 infection.
Conclusion: The COVID-19 pandemic still represents a worldwide sanitary challenge, particularly regarding the severe forms characterized by acute respiratory distress syndrome. The occurrence of respiratory superinfections represents an additional risk factor for fatal outcome. The cytological evaluation of the BAL could represent an important surrogate of biopsy to investigate pathological lesions of the deep lung compartment in these severely compromised patients.

OFP-23-011
PD-L1 expression in squamous cell lung carcinoma in small biopsy specimens
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Background & objectives: Programmed death ligand-1 (PD-L1) is a predictive marker for immunotherapy of non-small cell lung cancer, including squamous cell carcinoma (SqCC). The aim of this study is determining immunohistochemical PD-L1 expression in patients with SqCC in small biopsy specimens.
Methods: There were 50 patients in this retrospective study. All the patients were diagnosed SqCC on small biopsy specimens sampled during bronchoscopy and confirmed on histologic material after surgical resection. Small biopsy samples were stained immunohistochemically with PD-L1 clone 28-8 antibody. Membranous PD-L1 expression on tumour cells was evaluated and positivity was considered when expression was in more than 1% cells.
Results: Among patients 86% were male and 14% female. 52% were smokers, 30% were former and 18% were non-smokers. Small-biopsy samples of 26% patients were PD-L1 positive and 12% had histological type in surgical specimen with- and 14% without keratinization. Most of

patients with PD-L1 positivity ,76.92% were male and 23.08% were female. The majority of patients were former smokers (53.85%), following smokers (30.77%) and non-smokers (15.38%). There was no statistically significant difference neither between gender (p=0.522) nor different histological types of SqCC (p=0.624) between patients with PD-L1 positive and negative specimens. There was statistically significant difference between smoking habits of patients with PD-L1 positive and negative specimens (p=0.042).
Conclusion: PD-L1 expression was positive in about one quarter of patients with squamous cell lung carcinoma. PD-L1 expression in squamous cell lung carcinoma is linked to smoking habits and has no connection neither with histological type in surgical specimens of tumour nor with gender.

OFP-23-012
Evaluation of STING immunohistochemistry as a potential biomarker to predict immunotherapy efficiency in lung non small cell carcinoma
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Background & objectives: STING (STimulating INterferon Gene) plays a key role in anti-tumoral immune response. PD-L1 is an imperfect biomarker for immunotherapies. Our objective was to evaluate STING immunohistochemical expression in non small cell lung carcinoma as a biomarker to predict pembrolizumab efficacy.
Methods: We performed a retrospective study on 56 patients treated in our institution by pembrolizumab as first line monotherapy. These patients had a locally advanced or metastatic NSCLC with TPS PD-L1 > 50%. STING immunhistochemistry was evaluated on tumoral cells and on tumour infiltrating lymphocytes (TIL). Pembrolizumab efficiency was assessed using the CT scan for patient follow-up.
Results: STING expression by the tumoral cell was heterogenous: 21 samples dysplayed no STING expression, 3 dysplayed strong expression 32 weak to moderate. In most cases TIL dysplayed weak to moderate STING expression. We did not observe any statistically significant correlation between tumoral STING expression and clinical response to pembrolizumab. There was no correlation between TIL STING expression and clinical response. Importantly, according to current recommandations, all patients treated by pembrolizumab as first line monotherapy dysplayed high PD-L1 expression. This PD-L1 high immuno-expression in our patients could induce a bias explaining our results.
Conclusion: Although pre-clinical studies tend to show a correlation between STING expression by tumoral cells and clinical efficiency of immune check point inhibitors (ICI), we found no correlation between STING immunohistochemical expression and response to pembrolizumab. Considering, the small number of patients studied, enlarging this study to patient with other ICI treatment protocols could be interesting.

OFP-24 | Soft Tissue and Bone Pathology

OFP-24-001
Detection of MDM2 gene amplification on tissue microarray-based fluorescence in-situ hybridization (FISH) in well-differentiated and dedifferentiated liposarcomas, displaying a wide morphological spectrum: a validation study
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Background & objectives: Liposarcomas, including atypical lipomatous tumour(ALT)/well-differentiated liposarcomas(WDLPS) and dedifferentiated liposarcoma(DDLPS) display a histomorphological spectrum with their several diagnostic mimics. MDM2 gene amplification characterizes ALT/WDLPS and as well as DDLPS. This study was conducted to validate MDM2 gene testing in these tumours.
Methods: Twenty-eight cases, diagnosed as ALT/WDLPS(n=5) and DDLPS(n=23), along with 10 other tumours were tested for MDM2 gene amplification, using fluorescence in-situ hybridization FISH) on tissue microarrays (TMAs). Fourteen cases, diagnosed as ALT/WDLPS and DDLPS, along with 49 other tumours were tested for MDM2 (IF2 clone) immunostaining. Twenty tumours were tested for p16INK4a immunostaining.
Results: FISH was interpretable in 25(89.2%) cases. Among 20 cases diagnosed as DDLPSs, 19 displayed MDM2 gene amplification. Among 5 cases diagnosed as ALT/WDLPS, four showed MDM2 gene amplification. Finally, 19 cases were confirmed as DDLPS and 4 as ALT/WDLPS. Furthermore, 7/19 cases, confirmed as DDLPS and all 4 cases as ALT/WDLPS, tested for MDM2 immunostaining, displayed its diffuse immunoexpression, while a DDLPS showed its focal immunostaining. None of the 49 controls displayed diffuse MDM2 immunoexpression. ALL 16 DDLPSs and 4 ALTs/WDLPSs displayed p16INK4a immunostaining. Sensitivity for diffuse MDM2 immunostaining was 87.5% and specificity was 100%. The sensitivity for MDM2 gene amplification was 94.7%. Sensitivity for p16INK4a was 100%.
Conclusion: This constitutes the first sizable study on MDM2 testing in ALT/WDLPS and DDLPS from our subcontinent, using TMAs. MDM2 gene amplification testing is the diagnostic gold standard for ALTs/WDLPSs and DDLPSs, particularly during diagnostic dilemmas. Diffuse MDM2 and p16INK4a immunostaining, together seem useful for triaging cases for FISH.

OFP-24-002
Dermatofibrosarcoma protuberans: ten years' experience of a Portuguese tertiary institution
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Background & objectives: Dermatofibrosarcoma protuberans (DFSP) is a mesenchymal neoplasm, characterised by locally aggressive growth, frequent recurrences, and extremely rare metastases. We aimed to assess the clinicopathologic features of all DFSPs diagnosed at our hospital in the last 10 years.
Methods: A retrospective search of our database yielded a total of 68 DFSPs, diagnosed at our institution from 2011 to 2020. All cases were reviewed clinicopathologically (including age, size and site of tumour, morphology, surgical margins status, number of local recurrences and distant metastases) and submitted to FISH analysis.
Results: Median age was 43.5 years (range 1-77) and male-to-female ratio was 1.48:1. There was marked predilection for the trunk (62.7%), with the remainder cases affecting limbs (23.9%) and head and neck (13.4%). Median tumour size was 2.35cm (range 0,7-24). The cohort included cases with classic morphology (54.4%), fibrosarcomatous transformation (29.4%), melanin pigmentation (7.4%), myxoid change (3.0%) and/or myoid nodules (3.0%). Hybrid morphology (DFSP with areas of giant cell fibroblastoma) represented 8.8% of cases. Surgical margins were positive in 40.3%. Local recurrence was seen in 53.0%, with multiple relapses in 13,2%. Distant metastasis occurred in one case of fibrosarcomatous DFSP (1.48%). COL1A1 gene rearrangements were identified in 95.5%.
Conclusion: Being aware of the wide morphological spectrum of DFSP is necessary for a correct diagnosis. In harmony with literature, and probably due to the difficulty of achieving negative margins, recurrence rates were remarkably high in our cohort, while distant metastases were exceptional. COL1A1 gene rearrangements were present in the vast majority of

cases. FISH analysis provided valuable information for the diagnosis in challenging cases.

OFP-24-003

Clinicopathological features of dermatofibrossarcoma protuberans treated with Imatinib

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Background & objectives: Dermatofibrosarcoma protuberans (DFSP) is a fibroblastic neoplasm carrying a COL1A1-PDGFB fusion and often presenting with multiple recurrences. Although surgery remains the standard treatment, the recent introduction of Imatinib as a treatment option has shown significant activity against locally advanced DFSP.
Methods: We retrospectively assessed five cases of DFSP diagnosed and treated with Imatinib in our institution from 2010 to 2020. We reviewed the medical records regarding demographics, clinical and radiologic features of the tumour, treatment course and clinical response. Histological findings from pre and post-Imatinib treatment surgical and biopsy specimens were reviewed and morphological treatment response was recorded.
Results: All patients were male. Median age was 50 years (range 27-53). All underwent treatment with Imatinib 400mg. Clinical reduction in tumour size was seen in all cases. Fibrossarcomatous DFSP was diagnosed in 3 patients, with COL1A1-PDGFB fusion detected in 2. One of these cases showed significant response with hipocellularity, hyalinization, fibrosis, necrosis, chronic inflammation and hemosiderin deposition. Two fibrossarcomatous cases had poor responses. The two remaining cases of conventional DFSP showed partial response with areas of hypocellularity, hyalinization and fibrosis, with focal residual tumour. Four patients are alive and disease-free after a median of 46.4-months follow-up and one patient died with metastatic disease
Conclusion: DFSP often presents with unresectable tumours. Some cases benefit from adjuvant treatment with Imatinib, showing clinical responses and allowing surgical resection with wider margins. Scarce data is available regarding histological features of treated DFSP. Most cases show areas of hypocellularity, myxoid stroma, fibrosis, hyalinization and necrosis, with variable foci of viable tumour. Larger series of treated DFSP are needed in order to validate an adequate and standardized evaluation system of histological treatment response.

OFP-24-004

Angiosarcoma of the breast: a single institution experience

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Background & objectives: Breast angiosarcoma is a rare tumour. It may occur de novo, as a complication of prior radiotherapy for breast cancer or in association with chronic lymphedema (Stewart-Treves syndrome). Herein we describe a single institution experience over the past 20 years.
Methods: Retrospective analysis of all cases diagnosed at Portuguese Oncology Institute of Porto between 2000-2020. Evaluation of clinicopathologic features, including age at diagnosis of breast cancer and angiosarcoma, interval between radiotherapy and diagnosis of angiosarcoma, treatment rendered for each neoplasm and time from diagnosis of angiosarcoma to death. Tumour size and grade, number of local recurrences and metastasis were also assessed.
Results: Twenty cases were identified: 4 primary angiosarcoma (PAS) and 16 secondary angiosarcoma (SAS), 2 associated with Stewart-Treves syndrome. Median age (41 years vs 70 years) was lower in PAS and median tumour size (5.85cm vs 4.3cm) was higher. The vast majority of tumours (n= 17) were high grade. Median time from radiation to SAS diagnosis was 6.3 years. Total mastectomy was the main surgical treatment. Follow-up (median, 18.5 months) revealed that 4 patients (3 SAS) recurred locally, 6 patients (4 SAS) had distant metastasis, and 11 patients (9 SAS) died of disease, on average, 20 months after diagnosis. Median overall survival: 29 months for PAS and 18 months for SAS.
Conclusion: Breast angiosarcoma is an aggressive tumour with poor long-term prognosis. Primary tumours occur in younger patients. Secondary tumours are more frequent and the incidence of radiation-associated angiosarcomas seems to be increasing. The results of our series are similar to those described in the literature.

OFP-25 | Uropathology

OFP-25-001

An international validation study of automated cancer detection in prostate biopsies

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Background & objectives: Digital pathology provides an opportunity for computational analysis of histological slides and the standardized automation of some pathological tasks. In this retrospective study, we validate a deep learning-based tool for prostate cancer detection from patient biopsy samples.
Methods: A prostate cancer detection tool was developed and implemented in HALO AI® and HALO AP® software (Indica Labs, Albuquerque, US). Two external validation cohorts of patients with multifocal prostate biopsy were analysed: Cohort 1/Dataset 1 (n full cases = 65) digitized by Hamamatsu S360, Cohort 2 (n = 57) digitized by Hamamatsu S360 (Dataset 2) and Leica GT450 (Dataset 3).
Results: Similar high accuracy metrics were received for all three datasets implying good generalization among cases from different institutes and digitized by different scanner systems. For Dataset 1, Dataset 2, and Dataset 3, respectively: the negative predictive value was 0.99, 0.98, and 0.97; sensitivity was 0.97, 0.94, and 0.91; specificity was 0.93, 0.94, and 0.96; overall accuracy was 0.941, 0.942, and 0.946. Domain adaptation strategies for institution and scanner system improve the final accuracies. Several cores were detected where tumour was missed by pathologists (Cohort 1: n=7, Cohort 2: n=5). The average analysis time was 1 minute / core in Cohort 1, and 2 minutes / core for Cohort 2.
Conclusion: The prostate cancer detection tool reported high accuracy for prostate cancer detection in biopsy cases during external validation; independent of the institute or scanner used. It is fully integrated into Indica Labs' digital pathology platform and can assist pathologists in the form of pre-screening or quality control during analysis of prostate biopsy cases.

OFP-25-002

Large cribriform growth pattern does not have additional prognostic value above small cribriform architecture on prostate cancer biopsies

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Background & objectives: Invasive cribriform and intraductal carcinoma (IDC) are associated with adverse features in prostate cancer patients, with large cribriform fields having the worst outcome in prostatectomies. Our objective was to determine the impact of large cribriform pattern in prostate cancer biopsies.
Methods: A prostate biopsy cohort (n=1887) with long-term clinical follow-up was reviewed for Grade Group according to the 2014 ISUP guidelines. Presence of small and large cribriform pattern were monitored, with large cribriform pattern having at least twice the size of adjacent benign glands.

Hazard ratios (HR) for metastasis-free survival and prostate cancer-specific mortality were calculated using Cox proportional hazards regression.
Results: Cribriform growth was found in 280/1887 men: 1.1% in Grade Group 1, 18.2% in Grade Group 2, 57.1% in Grade Group 3, 55.4% in Grade Group 4 and 59.3% in Grade Group 5. Large cribriform growth was found in 47/1887 men: 0.5% in Grade Group 2, 9.8% in Grade Group 3, 18.1% in Grade Group 4 and 17.3% in Grade Group 5. Presence of cribriform growth showed significantly worse metastasis-free survival (small cribriform/IDC: HR 3.04; large cribriform: HR 3.17) and prostate cancer-specific mortality (small cribriform/IDC: HR 4.07; large cribriform: HR 4.13). Large cribriform fields did not have additional adverse prognostic value for metastasis-free survival (P=0.77) or prostate cancer-specific mortality (P=0.96).
Conclusion: We demonstrate that both invasive cribriform and intraductal carcinoma are associated with worse metastasis-free and disease specific-free survival in a large prostate biopsy cohort. In contrast to radical prostatectomies, the presence of large cribriform fields does not have additional adverse prognostic value in prostate biopsies. This discordance could be explained by cribriform pattern sampling artifacts and limitations of size estimation on biopsies. Any cribriform growth pattern should therefore be reported in prostate cancer biopsies without size limitations.

OFP-25-003

Epigenetics in renal cell tumours – expression patterns of histone H2AX

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Background & objectives: Epigenetic effects have been widely recognized in Renal Cell Tumours (RCT), thus we investigated the expression of H2AX histone in RCT and its correlation with demographic, clinical and pathohistological characteristics regarding immunohistochemical positivity.
Methods: The analysis included a total of 168 RCT (102 clear cell Renal Cell Carcinomas (RCC), 7 papillary type I RCC, 15 papillary type II RCC, 23 chromophobe RCC, 5 multilocular-cistic RCC, 6 collecting duct carcinoma, 10 oncocytomas) and was performed on tissue microarray slides using H2AX (1:1000, clon ab11175, Abcam) histone.
Results: Expression of H2AX in RCT was variable: in some tumours it was not detected, while other tumours expressed it in diffuse or focal patterns. Diffuse patterns were observed among patients with significantly lower mean age (48.1 ± 25.2 years) compared to those with focal (58.6 ± 16.2 years) and absent (59.7 ± 14.5 years) patterns, p=0.003. Moreover, diffuse H2AX expression pattern was frequently associated with high immunostaining intensity, while focal form mostly exhibited low H2AX intensity level, p<0.001.
Conclusion: H2AX is decreased with aging, suggesting an involvement of the current epigenetic mechanism in RCT development without specific influence on tumour morphology and biological behaviour.

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OFP-25-004

Novel double staining (OCT4/CD34) for the detection of lymphovascular invasion in OCT4(+) Germ Cell Tumours: technical aspects, results and future prospective

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Background & objectives: Lymphovascular invasion (LVI) is prognostically relevant in germ cell tumours (GCT) but studies showed discrepant results and low agreement with H&E. We tested double staining (DS) for OCT4/CD34 in GCT, providing the methodological aspects, the results and its potential implications.
Methods: We retrospectively analysed 25 GCT [15 OCT4(+) and 10 OCT4(-)] diagnosed between January 2019-February 2021 at our Institution. DS was performed on FFPE, 3-μm-thick sections (BenchMark ULTRA), with OCT4 stain visualized with DAB and CD34 one with FastRed. The slides (H&E and DS) were assessed by two uropathologists (M.F., C.R.) to assess the LVI with the two different techniques.
Results: Of the 15 OCT4(+) GCT tested, 15 (100%) stained with OCT4 at DS. Conversely, 0/10 (100%) of the OCT4(-) GCT showed any nuclear stain at DS. The normal parenchyma [OCT4(-)] and GCNIS [OCT4(+)] served as internal controls. According to its nature of "pan-lymphovascular" marker, C34 stained both lymphatic and vascular structures. In all cases, DS showed results superimposable to the single ones (OCT4 and CD34), with no discrepancies of nuclear and cytoplasmatic stains. In the groups of OCT4(+) GCT, LVI was detected in 5/15 (33.3%) and 7/15 (46.7%) cases with H&E and DS, respectively; as results, one of the latter two changed its pT stage (1b to 2).
Conclusion: In conclusion, DS for OCT4/CD34 showed to be technically reliable and potentially suitable for the evaluation of LVI in a significant subgroup of GCT. Future studies on larger case series and with long-term follow-up are needed to validate its prognostic implications (increase in the number of cases positive for LVI and so pT2 at TNM staging, with crucial therapeutic implications) and its effects on inter- and intra-observer agreement in the LVI assessment of GCT.

OFP-25-005

Vessels encapsulating tumour clusters (VETC) in renal cell carcinoma (RCC). prognostic role and predictive value to tyrosine kinase inhibitors (TKI) therapy. A Bayesian retrospective clinico-pathological study

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Background & objectives: VETC is a new metastatic mechanism in HCC where it is prognostic and predictive of sorafenib response. VETC is also present in RCC. We aim to investigate its prognostic and to model its predictive to TKI response in RCC.
Methods: To evaluate the overall survival (OS) effect, we included 92 primary RCC from 2005 to 2007 (Surgical-Series) and all RCC patients treated with first line TKIs at our center (TKI-series; Sunitinib, n=39; Pazopanib n=17), and recorded the progression free survival (PFS). VETC was assessed with CD34 immunohistochemistry and defined as a continuous endothelial lining around tumour clusters.
Results: VETC+ cases had a worse prognosis in the Surgical-Series, with a posterior probability density (PPD) of median OS of 88 months (mo) (standard deviation, SD:16mo) for VETC+ Vs 136mo (SD:26mo) for VETC-; the expected loss of median OS was 48mo (SD:31mo) for VETC+RCC. Conversely in the TKI-Series, VETC+ showed longer PFS: Sunitinib had a PPD of median PFS of 35mo (SD:11mo) for VETC+ Vs 19mo (SD:5mo) for VETC-. Under Pazopanib a PPD of median PFS of 20mo (SD:8mo) for VETC+ Vs 11mo (SD:7mo) for VETC-. The expected gain of median PFS for of VETC+RCC, was 17mo and 9mo (SD: 12mo and 9mo), respectively for Sunitinib and Pazopanib.
Conclusion: Our results confirmed the general adverse prognostic role of VETC in RCC, however this phenotype gave a substantial PFS gain for patients treated with TKI, similarly to what have been observed in HCC. VETC could be a new predictive bio-marker that allows the delivery of a personalized treatment: patients affected by RCC might directly benefit from a better selection of already approved drugs.

OFP-25-006

PD-L1 expression and tumour-infiltrating lymphocytes: combined use as urothelial carcinoma biomarkers

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Background & objectives: Programmed death ligand-1 (PD-L1) has been associated with an increased survival rate and can be evaluated by immunohistochemistry (IHC). The main goal is to correlate the expression of PD-L1 with tumour Infiltrating Lymphocytes (TILs) (CD8 expression) in urothelial carcinoma (UC).
Methods: Forty-three samples of high grade UC diagnosed in 2019 and 2020 were selected from archive of the Pathological Anatomy Service (SAP) of Centro Hospitalar Universitário de Coimbra(CHUC) and tissue microarray (TMA) were constructed. PD-L1 immunostaining was performed with different clones (SP142, SP263 and 22C3). The information collected were organized in a database and subjected to statistical analysis using the SPSS.
Results: TILs are greater in female patients, when using 20 lymphocytes / High Power Field (HPF) cutoff (median expression). TILs positive cases are lower in basal IHC subtype carcinomas ($p=0.045$, $p<0.05$) when considering the cutoff of 50 lymphocytes / HPF and have a tendency to be higher in histologic grade 2 tumours ($p=0.0814$). Positive correlations between PD-L1 22C3 with CD8 expression (cutoff 50) ($p=0.024$, $p<0.05$) and PD-L1 SP263 with CD8 (cutoff 50) ($p=0.002$, $p<0.05$) were found.
Conclusion: Higher TILs (CD8 expression) levels are correlated with higher PD-L1 expression, highlighting their use as biomarkers.

OFP-25-007

Digital pathology reporting of TRUS biopsies of prostate

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Background & objectives: Digital pathology is an integrated component of primary reporting in Clinipath Pathology, Malaysia for the past two years. Due to the Covid 19 pandemic outbreak in 2020, most of the TRUS biopsies were reported digitally, away from the office.
Methods: An advanced Aperio AT2 slide scanner (Leica), which has been approved by FDA , is in usage for digital pathology reporting in Clinipath. A total number of 119 TRUS biopsy cases, many of which had a minimum of 12 cores and also targeted biopsies with MRI mapping for precision and accuracy were reported, individually, as per latest International guidelines.
Results: Digital pathology reporting of TRUS biopsies is as accurate as conventional microscope reporting, and in many instances, more advantageous. With an integrated Dragon Speech software, all cases were reported with ease, without resorting to the conventional microscope for a review. The response and acceptance from the urologists have been over whelming.
Measurements of percentage of small malignant foci, and interpretation of Gleason pattern, coupled with digital photography has made the system more rewarding. Constant and perpetual practice has made the digital reporting 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 OF TRUS biopsies of prostate is simple, dependable, accurate and should be incorporated as a regular primary reporting procedure, where digital pathology is available. The accuracy and effectiveness are very advantageous for the current demand of uropathology in many laboratories. This will become the norm of future diagnostic digital pathology and artificial intelligence(AI).

OFP-25-008

Incidental prostatic adenocarcinoma in cystoprostatectomy specimens for bladder cancer: a 21-year institutional case review

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Background & objectives: Radical cystoprostatectomy is recommended as a treatment modality in high-risk non-invasive bladder cancer and in muscle-invasive bladder cancer. Herein, we aimed to review all cystoprostatectomy specimens received by our institution in a 21-year period (2000-2020) for incidental prostatic neoplasia.
Methods: We reviewed the reports of 232 cystoprostatectomy specimens for urothelial cancer and evaluated the prostate for the following parameters: presence of prostatic adenocarcinoma, Gleason score, prostatic intraepithelial neoplasia (PIN), prostate volume and percentage occupied by tumour, number of tumour foci, laterality, invasion of extra-prostatic tissues or seminal vesicles, positive surgical margins, staging, PSA levels before surgery, relapse and metastases.
Results: In total, there were 67 patients (28.9%) with incidental prostatic acinar adenocarcinoma, with a mean age of 70 years and an average total PSA level of 2.2 ng/ml. There were 50 cases (74.6%) graded Gleason 6 and 17 cases (25.4%) graded Gleason 7. Prostatic intraepithelial neoplasia (PIN) was highly associated with prostatic adenocarcinoma (85.7%) while being present in only a minority of specimens without it (21.6%). The tumours occupied, on average, 12.6% of the prostatic volume, were mostly multifocal (53.7%), bilateral (59.7%) and stage pT2 (94.0%), with only 4 cases (6.0%) being pT3. Only one patient showed biochemical relapse (PSA: 146 ng/ml) and cervical bone metastases.
Conclusion: In our series, the incidental prostatic carcinomas were all acinar adenocarcinomas, mostly small, bilateral, Gleason 6 and stage pT2. These results are similar to the findings reported for radical cystoprostatectomy specimens and autopsy series. The detection of these tumours on cystoprostatectomy specimens is not an uncommon finding and is to be expected in older patients. Although follow-up is warranted, the concomitant urothelial carcinoma and its complications remain the major risk factors to the patients' overall survival.

OFP-25-009

ACO2 expression as a common characteristic of primary and metastatic renal cell carcinoma

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Background & objectives: Renal cell carcinoma (RCC) continues to pose a great challenge due to our limited understanding of its underlying pathophysiology. We explored relationships between ACO2 protein expression and the clinical courses of RCC using the tissue microarray (TMA).
Methods: The TMA contained 94 cores of primary tumour, matched metastases and matched adjacent tissues derived from 31 RCC patients. The mean follow-up was 84.1 months. Tumour samples were evaluated for ACO2 expression using the H-score, and its correlations with clinicopathological data and survival data were analysed.
Results: All of the tissue samples showed ACO2 cytoplasmic expression, with the median value of 139.7, 130.3 and 166.7 in primary tumour, metastatic tissue and control group, respectively. Normal adjacent tissues were characterized by significantly higher ACO2 expression comparing to primary or metastatic RCC ($p<0.05$). The analysis demonstrated a significant positive correlation between ACO2 expressions in primary tumour and its metastases ($p<0.05$). The correlation between two variables was strong ($r = 0.7301$). The expression of ACO2 did not

significantly correlate with overall survival, tumour size or incidence of capsular or vain invasion (p>0.05).
Conclusion: Significant alterations in ACO2 expression presumably occur in the early stages of RCC carcinogenesis. Taking into account the physiological role of ACO2, its downregulation may constitute an adaptive trait of RCC to escape the equilibrium phase of immunoediting.

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OFP-25-010
PTEN loss And PD-L1 expression among morphology patterns of Gleason grade 4 prostate cancer
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Background & objectives: The Gleason grading system is clearly accepted for the evaluation of prostate cancer architectural patterns. We aimed to find out whether PTEN immunohistochemical loss of expression and PD-L1 expression is associated with specific histological patterns.
Methods: The current study included consecutive 98 radical prostatectomy specimens between 2011 and 2017. We selected 151 foci with different patterns from 98 radical prostatectomies. PTEN and PD-L1 immunohistochemistry were assessed on the different architectural patterns.
Results: There were foci with grade 3 pattern in 18 slides, foci with fused gland pattern in 39 slides, foci with cribriform pattern in 28 slides, foci with irregular gland pattern in 47 slides, foci with glomeruloid pattern in 4 slides, and foci with grade 5 pattern in 15 slides. Fifty foci (%33.3) exhibited PTEN loss. PTEN loss was substantially associated with cribriform pattern (<0.001). Combined PDL-1 score was positive in 13% of patients (1 foci with grade 3 pattern, 3 foci with fused gland pattern, 1 foci with cribriform pattern, 7 foci with irregular gland pattern, 1 foci with glomeruloid pattern, and 3 foci with grade 5 pattern).
Conclusion: Between the five different grades, Gleason grade 4 is certainly a heterogeneous group, containing different architectural patterns. Lately, the cribriform pattern has attracted more attention as an independent negative risk factor. The results of our study showed that PTEN loss was significantly associated with cribriform patterns. We observed that PD-L1 was most commonly seen in foci with irregular gland pattern(44%) There was no statistically significant difference between six histological patterns regarding PD-L1 positivity.

OFP-25-011
Should we report the distance to the anterior margin for PSA recurrence prediction?
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Background & objectives: Since anterior aspect of prostate tissue is irregular, measuring distance to anterior margin is controversial. Our aim is to investigate the relation between PSA recurrence and distance to the anterior margin in anterior dominant Grade Group 1(GG1) prostate cancers.
Methods: A number of 20 GG1 radical prostatectomy specimens (RPs) with anterior dominant tumour were included in this study from 836 RPs from 2010 to 2016. PSA recurrence was defined as PSA level of greater than or equal to 0.2 ng/mL. Slides were re-viewed in order to select the closest margin. Scanned slides were marked by pathologists to acquire digital measurements.
Results: Tumours of 9/20 cases were closer than 1 mm to the margin. Among these 9 cases 3(33.3%) of them had PSA recurrence. The distance from tumour to margin was greater than 1 mm in 11 cases. Out of these 11 cases one (9.09%) had PSA recurrence. The mean and median follow-up for PSA recurrences of the cases was 6.8 and 6.5 years (range, 5-11 years). The PSA recurrence was found in 4(20%) cases. And 3 out for 4 had margin closer than 1 mm. The mean distance of recurrent 4 cases was 1.15 mm (median 0.7;range, 0.26-2.93) compared to 1.64 mm (median 1.085; range, 0.05-4.29) for cases without PSA recurrence.
Conclusion: Although there are few numbers of anterior-dominant tumour cases, the surgical margin distance at the anterior aspect of prostate may have an impact on prognosis of such cases. The long-term follow-up of the patients with GG1 P-Ca may reveal that the tumour distance to the anterior margin can be an important prognostic feature, which should take place in the radical prostatectomy reports in the future.

OFP-25-012
Solitary fibrous tumour (SFT) of kidney and renal hilus: 15 cases with special emphasis onSTAT6 and PAX8 expression
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Background & objectives: SFT is a fibroblastic tumour characterized by a haphazard proliferation of spindled to oval cells, staghorn hemangiopericytoma (HPC)-like vasculature and STAT6 expression. Although already published in case reports or small series, a comprehensive series of primary renal SFT is lacking.
Methods: Fifteen primary kidney SFTs were reviewed for clinical, morphological, and immunohistochemical features. STAT6 (BioSB, EP325, 1/250 and Santa Cruz, D-1, 1:800), CD34 (Leica, QBEND-10, 1/100) , BCL-2 (Invitrogen, BCL-2-100, 1/600) and PAX8 (CellMarque, MRQ-50, 1/150 and Proteintech, 10336-1-AP, 1:800) immunostainings were performed.
Results: Mean age was 50,3(17-83) with equal sex distribution. Mean size was 9,3(2,5-23) cm. Tumours were mainly well-demarcated and located at the hilus. Morphologically, they were grouped as 1) SFT-like (5 cases) characterized by hypocellularity and abundant collagen; 2) HPC-like(6 cases) showing hypercellular proliferation of small-ovoid cells lacking collagen; 3) mixed SFT/HPC(4 cases). 40% had myxoid degeneration and/or accompanying lymphocytes. All cases were positive for CD34, BCL-2, and STAT6(focal, 27%). PAX8 was positive in 27%. According to Demicco-grading, 12 cases(80%) were low-risk (all cases of groups 1-2), while 2(13%) and 1(7%) were intermediate- and high-risk, respectively. One high-risk patient died while 7 were alive for an average follow-up period of 57 months.
Conclusion: Renal SFTs can exhibit SFT-like, HPC-like or mixed morphology. Most cases (especially SFT-like and mixed HPC/SFT) are benign but occasional malignant examples occur and it seems that current SFT classification schemes effectively predict such behaviour in this anatomical location as well. PAX8 positivity and only focal STAT6 expression in a subset of cases is an important diagnostic pitfall.

OFP-25-013
Significant inter- and intra-laboratory variation in Gleason grading of prostate cancer: a nationwide study of 35,258 patients in The Netherlands
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Background & objectives: Gleason grading (GG) of prostate cancer (PCa) is essential for patient treatment and prognosis. Studies showed inter-observer variation in GG. As GG variation between pathology laboratories has not been investigated, we analysed inter- and intra-laboratory grading variation using nationwide data.
Methods: Needle biopsy reports (n=42,774) and corresponding prostate specific antigen (PSA)-values were retrieved for January 2017–

December 2019 from the Dutch Pathology registry and The Netherlands Cancer Registration.
We determined laboratory-specific proportions per histologic grade and unadjusted odds ratios (OR) for International Society of Urological Pathologists (ISUP) Grades 1 versus 2-5. Logistic regression was performed to correct for case-mix variables.
Results: 38,321 Reports of 35,258 patients were included, of which 25,367 were narrative reports and 12,954 standardized, synoptic reports. Laboratories assigned ISUP Grade 1 to 34.1% of patients on average, ranging from 19.7-44.3%. Laboratory-specific ORs were significantly deviated for 22/40 laboratories, ranging from 0.48 (95% confidence interval (CI) 0.39-0.59) to 1.54 (CI 1.22-1.93). Case-mix correction was performed for 10,294 synoptic reports of 21 laboratories for variables PSA, age, diagnosis year, number of biopsies and positive cores. Case-mix correction altered the status of three laboratories. The range of adjusted laboratory-specific proportions increased compared to unadjusted proportions (20.8% vs. 17.7%). Within 15/21 (71.4%) laboratories that consented to intra-laboratory analysis, significant inter-pathologist variation existed.
Conclusion: Substantial variation in PCa grading was observed between and within Dutch pathology laboratories. Case-mix correction changed the status of individual laboratories but did not change the magnitude of the observed variation. Grade is an essential for treatment strategy and patient prognosis. The observed variation suggests that patients might receive different grading and subsequently different treatment depending on laboratory and pathologist. Better standardization of PCa grading is warranted to optimize and harmonize treatment.

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OFP-25-014

Unexpected low metastatic potential to lymph-nodes of isolated tumour cell and cluster-cord in ISUP 5 prostate adenocarcinoma (PC): morphological analysis of a mono-institutional cohort of radical prostatectomy (RP) with lymph-node metastasis (LNM)

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Background & objectives: Gleason pattern 5 (GP5) includes distinct morphologies, namely undifferentiated solid pattern (US), cribriform with necrosis (CN), cluster and cord (CC), and isolated single tumour cells (ISTC). We histologically characterized these different subtypes in LNM comparing them with the primary tumour.
Methods: ISUP 5 were collected from a mono-institutional cohort of 2784 pts between 2014 and 2020, from which 79 PC with LNM cases were identified. The different subtypes of GP, tumour volume, topographical distribution, intraductal component, pT, margin status, and vascular invasion were determined both in LNM and primary tumour.
Results: In LNM, GP5 was documented in 22/79 cases, either alone or in combination with other patterns. US, CN, ISTC and CC were documented in 13 (16.4%), 8 (10%), 5 (6.3%), and 4 (5%) cases, respectively. Primary PC harboured ISTC in 35/79 cases, but the same pattern was rare in the associated LNM (3/35), only as minor component (alone in one case, with CC in one, with US in one). ISTC did not show differences in lymph-node topographical distribution (parenchymal, capsular, extracapsular) compared with other patterns. Overall, 53/79 (67%) LNM were dominated by GP4, mostly represented by cribriform pattern. The presence of ISTC/CC did not correlate with pathological parameters analysed.
Conclusion: Our results showed that ISTC and CC patterns, although not uncommon in the primary tumour, are unfrequently observed in the loco-regional lymph-nodes. Although in limited cases, these preliminary data could suggest that ISTC and CC use a different spreading way to disseminate when compared with cribriform pattern. This low intrinsic capability to spread into loco-regional lymph nodes could be modulated on a genomic level, and further studies are ongoing to better understand the biology of these subtypes of GP5.

OFP-25-015

The switching phenotype and intratumor plasticity in urothelial bladder carcinoma (UC): a mono-institutional analysis of 211 muscle-invasive tumours with considerations for therapy

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Background & objectives: UC classification into Basal and Luminal categories has shown variable sensitivity to chemotherapy. We conducted a phenotypical analysis of UC cases from transurethral resection specimens to evaluate the intra-tumour plasticity (switch) between the superficial and deep component of the tumour.
Methods: High grade UC cases were analysed using a simple immunohistochemical score (Piescore) focusing on the expression of CD44, CK5/6, CK20 and pPARg in superficial (pTa/T1) and muscle-invasive (pT2) component of tumour to identify Luminal, Basal, Mixed, Null (Neu-like) categories. To increase the specificity of the analysis, 20 cases were also investigated with RT-PCR.
Results: Two hundred-eleven cases were collected. Superficial component showed Luminal, Basal, Mixed and Neu-like phenotype in 99 (46.1%), 61 (28.9%), 33 (15,6%) and 18 (8.5%) cases, respectively. RT-PCR analysis confirmed immunohistochemical results. From superficial to deep component, a switch of phenotype was observed in 80/211 (38%) cases, from Luminal (42/80, 52.5%) to Neu-like (20), Basal (16), and Mixed phenotype (6); from Mixed (29/80, 36.2%) to Basal (21), Luminal (3), and Neu-like phenotype (5). Among 18 Neu-like, 4 (22.2%) acquired new phenotypes, while only 6/61 Basal tumours switched. Papillary tumours switched more frequently than not-papillary (52/112, 46.4% vs 26/99, 26.3%) (p=0.0385). Phenotypical transition did not correlate to OS and PFS.
Conclusion: Piescore system revealed phenotypic plasticity through the evaluation of a switch between superficial and deep component of the same tumour. The switch is frequent in Luminal but not in Basal tumours. After cystectomy, a protective effect of CD44 expression in OS (p=0.0016) and in PFS (p=0.0042) was observed. This variability could partially explain the sensitivity of a subset of Luminal UC to chemotherapy: good responders could be "non-real" Luminal UCs, which acquire Basal markers such as CD44.

OFP-25-016

Immunohistochemical and molecular comparative characterization of ipsilateral synchronous papillary renal cell neoplasm with reverse polarity and clear cell renal cell carcinoma

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Background & objectives: Ipsilateral synchronous renal clear cell renal cell carcinoma (CCRCC) and papillary renal cell neoplasm with reverse polarity (PRCNRP) is an exceptional finding in renal pathology. PRCNRP, characterized by a hallmark mutation in KRAS, displays unique morphology and immunoprofile.
Methods: We present an extremely rare case of coexisting PRCNRP and CCRCC in the same kidney on a 77-year-old patient with no oncologic medical history. Morphological and immunohistochemical features of both tumours are described. Molecular analysis using an in-house next

generation sequencing (NGS) panel was performed in samples of normal renal parenchyma and both neoplasms.
Results: Histologically, CCRCC showed a classic morphological and cytological features and so did PRCNRP. The latter displayed a pure papillary architecture with hyalinized fibrovascular cores. Papillae were lined by a single layer of non-stratified tumour cells with large, eosinophilic cytoplasm and apically located nuclei. Immunohistochemical studies showed positive staining for MUC1 and GATA3. Negative staining for a-methylacyl-coenzyme A racemase (AMARC) and vimentin was described. NGS results evidenced mutations in CDH19, COL1A1 and EGFR in both tumours and normal kidney. CCRCC also showed a mutation in TAF1 gene. PRCNRP demonstrated the hallmark mutation in KRAS.
Conclusion: To the best of our knowledge, this is the second reported case of collided CCRCC and PRCNRP. Immunohistochemical and molecular studies evidenced not only characteristic features of both tumour but confirmed the diverse oncogenic origin of each entity. PRCNRP has arisen as a new and underdiagnosed entity in renal pathology, with distinctive molecular and pathologic findings. Early follow-up studies have suggested better data in terms of recurrence and metastasis in comparison with other papillary neoplasms.

OFP-25-017
Power to the pathologist - immunofluorescence or chromogenic antibody-guided annotations improved the analytical performance of the algorithm compared to manual annotated whole H&E slide images in prostate cancer core-needle biopsies
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Background & objectives: To better the concordance and objectivity in the evaluation of prostate core-needle biopsies, we developed an AI-based decision-support tool and algorithm to specifically detect and outline neoplastic glandular tissue using an in-house high-resolution staining and annotation method - Master Annotation.
Methods: To reduce the turnaround time and improve the objectivity of our training data, we developed a patented multiplex-staining method to train our algorithms to detect and outline suspicious glandular tissue without basal cells and intraductal cancer.
Pathologists annotated, in high-resolution mode, of H&E whole-slide images, assisted by re-stained and aligned immunofluorescence or consecutive chromogenic IHC whole slide images.
Results: The semantic segmentation algorithm, in INIFY® Prostate (ContextVision, Sweden) was trained within a deep learning framework developed in-house at ContextVision.
The algorithm was evaluated on 58 prostate slides, stained at five different laboratories and scanned on three different WSI-scanners. It achieved a median pixel-level sensitivity and specificity of 98.4% and 97.5%, respectively, on cancer images, and a specificity of 99.0% on benign images, using a tolerance of 3 pixels (or approximately 21 μm).
Conclusion: Master Annotation enabled a micron-level region of interest and an augmented segmentation ground truth for our input-data of the deep learning algorithm.
Using this approach, we have developed INIFY® Prostate, a CE marked AI-based software that a clinical setting, predicts, outlines, and quantifies suspected cancer areas in prostate biopsy H&E stained whole slide images.

Funding: The work was in part funded by Verification for collaboration, Uppsala University and the European Regional Development Fund

OFP-25-018
First results of a retrospective observational performance study of INIFY® prostate screening in the clinical pathology workflow: FIRST-PATH
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Background & objectives: Prostate cancer is the second most frequent cancer for men in Europe but grading suffers from discordance and low objectivity in the histopathologic evaluation.
FIRST PATH study aims to evaluate performance and usability of INIFY-Prostate in the clinical pathology workflow.
Methods: The feasibility phase of the FIRST PATH study included 100 WSI's (59 benign, 41 cancer) from 12 retrospective anonymised cases. Two study pathologists diagnosed all WSI's without INIFY, and then after wash-out-period with the support of INIFY. A panel of 3 senior pathologists did the final consensus diagnosis. All diagnoses in the study were blinded (inter- and intra-pathologists).
Results: The diagnostic accuracy as well as diagnostic concordance of pathologists with INIFY was higher than the corresponding values without INIFY. The two study pathologists judged INIFY's performance as good/acceptable for 12 of 12, and 11 of 12 cases, respectively. In comparison to the reference diagnosis, seven (7) whole slide images (WSIs) that were incorrectly diagnosed without INIFY, but were then correctly diagnosed with INIFY, while only one (1) correct diagnosis without INIFY rendered incorrect with INIFY.
The % tissue area of cancer given by the INIFY algorithm correlated well with the pathologists' estimates of % cancer length within the respective cores (Spearman rank correlation 0.80, $p<0.001$).
Conclusion: Preliminary results indicate that INIFY Prostate Screening performs well and gives good support to pathologists in the clinical workflow. The observed improvements of diagnostic accuracy and concordance between pathologists need to be confirmed in the full FIRST PATH clinical study.

OFP-MD-01 | Molecular Pathology Diagnostics Symposium Orals

OFP-MD-01-001
Detection of on-target ALK inhibitor resistance mutations and treatment options for patients with non-small cell lung cancer
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Background & objectives: Non-small cell lung cancer (NSCLC) patients with Anaplastic Lymphoma Kinase (*ALK*) gene fusions respond well to ALK inhibitors but commonly develop on-target resistance mutations. The objective of this study is to collect clinical evidence for subsequent treatment with ALK inhibitors.
Methods: Local experience with on-target *ALK* resistance mutations and review of the literature identified 387 patients with ALK inhibitor resistance mutations and subsequent treatment results. Clinical benefit of mutation-inhibitor combinations was assessed based on reported response, progression-free survival and duration of treatment. Furthermore, this clinical evidence was compared to previously reported *in vitro* sensitivity of mutations to the inhibitors.
Results: Of the 387 patients included in this analysis, 239 received a different ALK inhibitor after developing on-target resistance to first line ALK inhibitor therapy. Clinical benefit was reported for 177 (68%)

patients but differed for each mutation-inhibitor combination. Agreement between in vitro predicted sensitivity of six published models and observed clinical benefit ranged from 64 to 87%. The observed clinical evidence for highest probability of response in the context of specific on-target ALK inhibitor resistance mutations is presented.
Conclusion: Molecular diagnostics performed on tissue samples that are refractive to ALK inhibitor therapy can reveal new options for targeted therapy. The comprehensive overview of clinical evidence of drug actionability of ALK on-target resistance mechanisms may serve as a practical guide to select the most optimal drug for individual patients.

OFP-MD-01-002
NTRK gene fusions in MLH1 deficient and BRAFV600E wild-type colorectal cancers
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Background & objectives: NTRK fusions are oncogenic drivers and offer targets for cancer therapy. Since they are rare in colorectal cancer (CRC), universal screening for these fusions in CRC seems impractical. Our aim was to investigate NTRK fusions in a subset of CRC.
Methods: Pan-Trk (clone EPR17341, Roche, Ventana) immunohistochemistry (IHC) and MLH1 promotor hypermethylation (MLH1ph) were analysed in 63 CRC cases with deficient MLH1 (dMLH1) and BRAFV600E wild-type (wt) status from CRCs resected at the Helsinki University Hospital in 2018-2020. Pan-Trk immunopositive cases were evaluated by targeted RNA-based NGS (Fusion Plex Comprehensive Thyroid and Lung Kit, ArcherDX Inc.).
Results: Of the 63 dMLH1/BRAFV600Ewt CRCs seven (11.1%) cases were Pan-Trk IHC positive and each of them was confirmed to harbor NTRK1 fusion by NGS. Detected fusions involved LMNA-NTRK1, TPM3-NTRK1 and PLEKHA6-NTRK1 each in two cases and IRF2BP2-NTRK1 in one. MLH1ph status was determined using methylation-specific multiplex ligation-dependent probe amplification (MS-MLPA) with SALSA MS-MLPA Probemix ME011-D1 Mismatch Repair Genes kit (MRC Holland) comprising 44 dMLH1/MLH1ph/BRAFV600Ewt CRCs. All NTRK1 fusions were in the subgroup of MLH1ph (7/44; 15.9%). Pan-Trk immunostaining pattern showed strong or moderate cytoplasmic staining in TPM3-NTRK1 and IRF2BP2-NTRK1 cases, stronger membranous than cytoplasmic staining in PLEKHA6-NTRK1 cases, and the only cases showing perinuclear staining were the fusions for LMNA-NTRK1.
Conclusion: Our study shows that Pan-Trk IHC detects NTRK1 fusions with 100% specificity in CRC. Our results confirm that NTRK1 fusions are frequently detected in dMLH1/BRAFV600Ewt (11%) and especially in dMLH1/MLH1ph/BRAFV600Ewt (16%) CRCs justifying screening for NTRK fusions in these subsets of CRCs. Our findings of NTRK1 fusions with partners LMNA, PLEKHA6 and TPM3 in CRC are consistent with previous studies but noteworthy, we introduce a novel IRF2BP2-NTRK1 fusion in CRC.

OFP-MD-01-003
Nationwide evaluation of mutation-tailored treatment of gastrointestinal stromal tumors in daily clinical practice
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Background & objectives: Molecular analysis of *KIT* and *PDGFRA* is critical for tyrosine kinase inhibitor treatment selection of gastrointestinal stromal tumors (GISTs). We performed a nationwide real-world data study into the application of predictive mutation testing and its impact on treatment decisions.
Methods: Real-world clinical and pathology information was obtained from GIST patients with initial diagnosis in 2017–2018 through database linkage between the Netherlands Cancer Registry and the nationwide Dutch Pathology Registry.
Results: Predictive mutation analysis was performed in 89% of the patients with high risk or metastatic disease. Molecular testing rates were higher for patients treated in expertise centers (96%) compared to non-expertise centers (75%, $P<0.01$). Imatinib therapy was applied in 81% of the patients with high risk or metastatic disease without patient's refusal or adverse characteristics, e.g. comorbidities or resistance mutations. Mutation analysis, that was performed in 97% of these imatinib-treated cases, did not guarantee mutation-tailored treatment: 2% of these patients had the *PDGFRA* p.D842V resistance mutation and 7% initiated imatinib therapy at the normal instead of high dose despite of having a KIT exon 9 mutation.
Conclusion: In conclusion, nationwide real-world data show that over 81% of the eligible high risk or metastatic disease patients with GIST receive targeted therapy, which was tailored to the mutation status as recommended in guidelines in 88% of cases. Therefore, still 27% of these GIST patients misses out on mutation-tailored treatment. The reasons for suboptimal uptake of testing and treatment require further study.

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Computational Pathology Symposium Orals

CP-03 | Computational Pathology Symposium: Evening Session

CP-03-001
Clinical level AI-based solution for primary diagnosis and reporting of prostate biopsies in routine use: a prospective reader study
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Background & objectives: This study aimed to clinically validate the use of an AI-based tool by pathologists for reviewing and reporting prostate core needle biopsies (PCNBs) as compared with Standard of Care review on microscope, also assessing improvements in efficiency and turnaround time.
Methods: A two-arm prospective reader study comparing the performance of pathologists using an AI-based solution workflow compared with the use of standard of care (pathologists using a microscope). Both arms were compared to ground truth (GT) established by consensus of two subspecialist uropathologists. Rates of major discrepancies between each arm and GT, as determined by an adjudicating expert uropathologist, were compared.
Results: Eight pathologists participated in the study and reported on 785 H&E slides from 100 PCNB consecutive cases. Each case was reported twice, once in each study arm. The major discrepancy rates of the microscope and of the AI-based solution arms against GT were 7.15% and 4.84%, respectively. The AI solution demonstrated very high performance on prostate cancer detection with AUC=0.99, sensitivity of 95.5%, and specificity of 96.2%. Other endpoints included sensitivity and specificity of both arms on cancer detection and grading. The study demonstrated that reporting with the AI-based solution leads to >30% efficiency gains and a significant decrease in TAT.

Conclusion: This is the first large-scale study, in which pathologists perform full primary diagnosis with the support of an integrated AI-based solution in a real world-like clinical setting, in a large network of pathology laboratories. Importantly, diagnostic accuracy improvements are observed in addition to significant efficiency gains for the pathologists reviewing and reporting with the integrated AI solution.

CP-03-002

Multiple-instance learning for assessing prognosis of ductal carcinoma in situ

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Background & objectives: We propose a Deep Learning-based pipeline to aid pathologists in the task of distinguishing Ductal Carcinoma in Situ (DCIS) cases with low versus high risk of progression to ipsilateral Invasive Breast Cancer (iIBC), using H&E whole-slide images (WSIs).
Methods: We use a Multiple-Instance Learning-based Deep Learning pipeline to predict 10-year iIBC recurrence of DCIS from H&E stained WSIs. We also explore automatic mammary duct detection as an input selection strategy, and we compare it to standard WSI tiling. The resulting models are trained and evaluated on 414 H&E stained WSIs provided by the Netherlands Cancer Institute.
Results: All classification results are obtained on a validation set which remains untouched until after model training and selection, and which contains good balance between the positive and negative class. When using detected ducts as its input, the proposed pipeline achieves up to 0.71 in area under the Receiver Operating Characteristic curve (precision: 0.68; sensitivity: 0.61; specificity: 0.75). Classification performance increases significantly when we exclude patients treated with adjuvant radiotherapy from both the training and validation sets. In this case the pipeline achieves up to 0.86 in ROC-AUC (precision: 0.89; sensitivity: 0.71; specificity: 0.89).
Conclusion: Our pipeline achieves remarkable classification performance, substantially improving over both human assessment and over the only comparable recent machine learning-based approach. Our results show that a Multiple-Instance Learning pipeline using score average-pooling aggregation is more likely to produce correct classifications for the low-risk group when applying duct detection as an input selection strategy as opposed to dense tiling, showing promise for tackling the problem of over-treatment of DCIS.

Funding: This work was supported by Cancer Research UK and by KWF Kankerbestrijding (ref. C38317/A24043).

CP-03-003

Computer aided assessment of melanocytic lesions by means of a mitosis algorithm

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Background & objectives: An increasing number of pathology laboratories are fully digitised. In this study a mitosis algorithm primarily developed for breast carcinoma is applied to melanocytic lesions. This study aims to study the added value of this algorithm in diagnosing melanocytic lesions.
Methods: A set of 99 digitally scanned melanocytic skin lesions for which a consensus diagnosis was reached was subjected to a mitosis algorithm based on convolutional neural networks. Two academic and six non-academic surgical pathologists specialized in dermatopathology examined the WSI cases, first without and after a washout period of at least 2 months with mitosis annotations based on the algorithm.
Results: The overall concordance of the pathologists with the consensus diagnosis for all cases excluding nevoid melanoma (n=89) appears to be comparable with and without the use of artificial intelligence (AI) (89% vs. 90%). However, the concordance increases by using AI in nevoid melanoma cases (n=10) (75% vs 68%). All but one pathologist reported more dermal mitoses with the mitosis algorithm which on a regular basis were incorrectly attributed to mitoses from mainly leukocytes. In 3 cases the algorithm indicated a correct dermal mitosis in a melanocyte that was not in accordance with the consensus diagnosis.
Conclusion: This study shows that in general cases pathologist perform similarly with the aid of a mitosis algorithm. In nevoid melanoma cases, pathologists perform better with the algorithm. This study shows that pathologists need to be aware of potential pitfalls using CAD, e.g. misinterpreting dermal mitoses in non-melanotic cells.

CP-03-004

Single-cell architecture of the tumour microenvironment predicts response to cancer immunotherapy

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Background & objectives: Immunotherapies can induce long-lasting remissions in advanced-stage cancer patients, but many patients do not benefit. We reasoned that characterizing the tumour microenvironment (TME) architecture at the single-cell level should reveal novel spatial biomarkers of immunotherapy response.
Methods: We performed CODEX highly multiplexed tissue imaging to investigate the TME in cutaneous T cell lymphoma (CTCL) patients treated with pembrolizumab anti-PD-1 immunotherapy. 55 protein markers were visualized simultaneously in a tissue microarray of matched pre- and post-treatment skin biopsies from 7 responders and 7 non-responders. RNA sequencing was performed to extract cell-type specific gene expression profiles by CIBERSORTx analysis.
Results: We identified and characterized 21 spatially resolved tumour and reactive immune cell clusters in the CTCL TME. Advanced computational analysis of tumour architecture revealed cellular neighbourhoods that dynamically changed during pembrolizumab therapy and were correlated with response. Furthermore, a spatial signature of cell-cell distances between tumour cells, regulatory T cells (Tregs) and PD-1+CD4+ effector T cells predicted therapy outcome. After treatment, in pembrolizumab responders PD-1+CD4+ effector T cells up-regulated the cytotoxic molecule granzyme B, whereas in non-responders the frequency of ICOS+ Tregs increased. In addition, CIBERSORTx analysis revealed that tumour cells in responders, but not in non-responders, enhanced the expression of immune-activating genes, particularly the T cell chemoattractant CXCL13.
Conclusion: The pre-existing immune status of the CTCL TME is associated with specific immune cell types, cellular neighbourhoods and architectural features that correlate with pembrolizumab response. Multidimensional analysis of the TME enables discovering spatial predictive biomarkers and generating novel mechanistic hypotheses of immunotherapy response, paving the way for future studies functionally addressing these cell types and their interactions.

CP-03-005

Histocartography: an entity-based workflow for histology image analysis

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Background & objectives: Cancer diagnoses rely on phenotype and topological distribution of histological entities. However, deep learning

techniques for cancer analysis operate at pixel-level which disregards the notion of such entities. We propose Histocartography, a generalized entity-based paradigm to address the aforementioned issue.
Methods: Histocartography begins with tissue pre-processing. Subsequently, we construct entity-graph representation, where nodes and edges depict histological entities and inter-entity interactions in the tissue. The choice of entity type, entity embedding, and topological formulation can be customized using task-specific pathological prior. Afterward, Graph Neural Network (GNN) is employed to map structure-to-function relationship. Finally, post-hoc graph explainability techniques explain the GNN's decision.
Results: We released Histocartography python package, a collection of image-to-graph translation, state-of-the-art GNNs, and graph explainers to facilitate interpretable entity-based analysis. A REST API prototype with user-friendly interface is deployed to seamlessly onboard pathologists. Currently, Histocartography supports entity-graphs using nuclei, tissue regions, or both as entities for arbitrary image dimensions. We included pre-trained GNNs to map breast tumour regions-of-interest onto 7 breast carcinoma subtypes. We include 4 graph explainers to generate post-hoc explanations, and an explainability module to produce pathologist-friendly quantitative measures. Average processing time for a 1K´1K region-of-interest on an NVIDIA P100 GPU is 2s, 0.01s, 0.3s, and 0.2s for cell-graph generation, GNN inference, explanation generation, and quantitative measurements respectively.
Conclusion: Histocartography lays the foundation for a one-stop solution to access graph-based analysis in computation pathology. It enables developers to build customized graph representations and task-specific GNNs. It provides an interpretable input space in terms of relevant histological entities to pathologists which they can relate to and reason with. Finally, the explainability module generates easy-to-understand localized explanations. Currently, the service only includes solutions for breast carcinoma, and we are in process of extending to other organs, disease types, and pathology tasks.

Posters

PS-01 | Autopsy Pathology Posters

PS-01-001
Adrenal gland developmental anomalies – rare necroptic findings
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Background & objectives: Adrenal gland is formed of two embryological-distinct layers: the cortex and medulla. Adrenal gland anomalies are relatively rare and most cases are incidental autopsic findings. We present two cases of developmental anomalies of the adrenal gland diagnosed in our Department.
Methods: Necroptic examination has been associated to collection of tissue specimens for microscopy, followed by routine hematoxylin-eosin staining.
Results: The developmental anomalies of the adrenal gland occurred in two subjects, a 69 and a 76-years old men. The histopathological examination revealed a fusion between renal and adrenal cortex in one case and an area of adrenal tissue which was located under the liver capsule in another case. Considering the adrenal gland embryological development, ectopic adrenal tissues are usually found in the vicinity of the adrenal gland or along the trajectory of embryonic migration, within or near the urogenital tract. However, ectopic adrenal in the liver is also a possibility, although extremely rare, as in a case of our report.
Conclusion: Incidental anomalies of adrenal gland are occasional findings in forensic pathology. Adrenal-renal fusion and ectopic adrenal tissue may be incidentally discovered during the necropsy, the microscopic examination being important in certification of diagnosis. The differentials from benign lesions to malignant and potentially lethal conditions are important in the context of tanatogenesis.

PS-01-002
Incidental haemangiomas in forensic pathology
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Background & objectives: Haemangioma is a common benign vascular tumour derived from blood vessel cells. The objective of our study is to report the particular features of incidental haemangiomas necroptically diagnosed, from our files.
Methods: The autopsic reports of our Department, from the last 5 years, have been reviewed, and 47 cases of haemangiomas have been selected. These cases have been investigated by routine paraffin-embedding, followed by hematoxylin-eosin staining.
Results: The cases were diagnosed in 31 males and 16 females, age ranging between 41 weeks gestational age up to 78 years old. Gross findings were that of small, well delimited red-brown masses, of up to 2 cm diameter. The microscopic examination revealed the proliferation of thin-walled blood vessels, lined by a single layer of flat endothelial cells, without atypia, within the liver tissue, in a subcapsular location, in 84.09% of cases, with characteristic features for cavernous haemangioma in 91.48% of cases and of capillary haemangioma in 8.51%. The other cases revealed three rare locations, as following: left atrium cavernous haemangioma, renal corticomedulllary junction capillary haemangioma, and umbilical cord cavernous haemangioma.
Conclusion: Haemangioma is the most common benign liver tumour, but it may develop in any location. Differentials should include other vascular tumours, such as lymphangioma, benign (infantile) haemangioendothelioma, hemangioblastoma, epithelioid haemangioendothelioma, and angiosarcoma. Haemangiomas may be significant in legal medicine when large, compressing vital organs or when spontaneously or traumatically ruptured, if it prevents the foetal development (e.g. umbilical cord location), or if it determines sudden death (e.g. cardiac location).

PS-01-003
Cerebellum metastasis mimicking the dissemination of a malignant pheochromocytoma
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Background & objectives: Central nervous metastases are relatively frequent in forensics. We present the particular features of a female subject, of 69 years old, which presented multiple tumours, located in adrenal gland, lung, pleura, and cerebellum, associated with lymphadenopathy.
Methods: Necroptic examination has been associated to collection of tissue specimens for microscopy. Routine hematoxylin-eosin staining, along with immunohistochemistry using a panel of markers (Cytokeratin AE1/AE3, CK5, CK7, CK20, p63, TTF-1, Synaptophysin, Chromogranin, Melan A, Calretinin, Inhibin, and S100) have been used in order to discriminate between primaries and secondaries.
Results: The gross findings were that of multiple tumour masses with variable areas of necrosis and adenopathy. The microscopic examination of tumour cells showed variable nuclear atypia, eosinophilic cytoplasm, the differential between a metastatic lung squamous cell carcinoma and a metastatic malignant pheochromocytoma being investigated. The tumour cells expressed diffuse, strong positivity of AE1/AE3 and CK5, focal

Melan A positivity, and also focal adrenal CK7 positivity. Negative stains included CK20, p63, TTF-1, Synaptophysin, Chromogranin, Calretinin, Inhibin, and S100. Accordingly, the diagnosis of poorly differentiated lung squamous cell carcinoma with pleural invasion and lymph nodes, adrenal gland, and cerebellum metastases has been certified.
Conclusion: Central nervous system metastases are mainly located in brain hemispheres and spinal cord but, rarely, they may be located in cerebellum, as seen in this case report. Immunohistochemistry is useful to distinguish primary and metastases in cases with multiple disseminations, including adrenal gland, and AE1/AE3 and CK5 association shows a high specificity in metastatic lung squamous cell carcinomas.

PS-01-004
Location variability of incidental hydatid cysts
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Background & objectives: Hydatid cysts are incidental findings in forensics, involving liver and rarely lung, abdomen cavity, spleen, ovaries, uterus, cervix, fallopian tubes, and broad ligaments. The aim of our study is to report the features of incidental hydatid cysts from our files.
Methods: The reports from autopsies performed in the last 5 years in our Department, have been reviewed, selecting 19 cases of hydatid cysts, with cases age distribution between 37 to 89 years old, 4 females and 15 males. The cases have been investigated by routine paraffin-embedding sections, followed by hematoxylin-eosin and trichrome staining.
Results: The gross findings showed single cysts with maximum diameter of 80mm, low consistency, with subcapsular liver location in 17 cases (89.47%), while another case showed a subcapsular splenic location. In one case, multiple cystic structures, of up to 30mm diameter, with partially calcified wall, forming a tumour-like mass have been detected within the anterior right ribs 1-3. The microscopic exam revealed laminated membrane, inflammatory infiltrate rich in lymphocytes and eosinophils, pericystic fibrosis, necrosis, and dystrophic calcifications. The endocyst with the inner germinal layer and partially lithic scolices have been detected in 63.15% of cases. Differential diagnoses included inflammatory cysts, neoplastic diseases, and trauma-related lesions.
Conclusion: Incidental hydatid cysts or echinococcosis are relatively rare in forensic pathology, usually being located in liver. These appear as single or multiple cysts, associated with variable inflammation, fibrosis, and calcification. However asymptomatic echinococcosis progression may result in unexpected findings and locations and, as a consequence, this diagnosis should be considered in endemic areas. The differentials, from benign lesions to malignant and potentially lethal conditions, are important in the context of causes of death.

PS-01-005
COVID-19 and autopsy, a case series
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Background & objectives: The novel coronavirus has caused million of deaths since the start of the global pandemic. In this situation, the pathological examination is more important than ever to understand the pathophysiology of this new disease.
Methods: 31 autopsies of patients who died with COVID-19 infection were performed between May 2020 and February 2021. There were performed 27 thoracic and 4 thoracoabdominal autopsies. All of them were carried out in BSL-3 rooms. Patients had an age range between 44 and 89 years old, 28 of them were male and 3 were female.
Results: Lungs had a congestive appearance and were heavy. Microscopically the most consistent finding in all cases was the presence of diffuse alveolar damage. It was seen in an exudative phase with the presence of hyaline membranes, in a proliferative phase with reactive type II pneumocytes and even in a fibrotic phase. Eight patients showed acute organizing and fibrinous pneumonia and sixteen patients showed thrombotic phenomena. Microbiological cultures were performed and 28 patients had viral, bacterial and fungal superinfections what lead to pneumonia and lung abscesses. The lung parenchyma also showed the presence of multinucleated giant cells in ten cases. Emphysema, squamous metaplasia and lambertosis were seen in 16 patients.
Conclusion: This study reveals the importance of the autospy in understanding the changes produced in the body by the SARS-CoV-2. The lungs were the most affected organ with the presence of acute and chronic processes. Also, as mentioned, many patients showed thrombotic phenomena with lung thromboembolism. These findings are consisten with the fact that the new coronavirus affects the vasculature exerting a prothrombotic effect. All in all, further investigation are necessary in order to shed light on this pandemic.

PS-01-006
Histopathological clues in a case of ethylene glycol ingestion
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Background & objectives: Ingested ethylene glycol(EG) is metabolised into four organic acids: glycolaldehyde, glycolic acid, glyoxylic acid and oxalic acid(OA), causing severe acidosis, central nervous system depression, cardiopulmonary and renal failure. OA precipitates as calcium oxalate monohydrate(COM) in the kidneys and other tissues.
Methods: We present a case of fatal EG poisoning of a 44-year-old male found dead in his home. An autopsy was performed and samples of brain, lung, heart, liver, spleen, stomach, kidney and adrenal were taken. The organs were fixed in formalin, processed, embedded in paraffin and examined on H&E. Blood, urine and gastric content samples were sent for toxicological examination.
Results: Microscopic examination revealed that the kidneys were the most affected showing moderate chronic pyelonephritis, nephroangiosclerosis, areas of acute tubular necrosis with extensive intratubular deposition of translucent, colourless, refractile crystals of COM, with multi-coloured birefringence under the polarized light.
Other findings were: cerebral cortex stasis, perineuronal and perivascular oedema; meninges with arachnoid fibrosis, meningothelial hyperplasia and psammoma bodies; atherosclerosis of the coronary artery branches, hypoxic changes in cardiomyocytes, with moderate perivascular and interstitial fibrosis and lipodystrophy; massive stasis and alveolar oedema in the lungs with few vascular fibrin thrombi; a small cavernous hepatic haemangioma and an adrenal cortical adenoma of 2 cm diameter.
Toxicological tests revealed lethal levels of EG.
Conclusion: EG can be found in many agents, such as antifreeze. Ingestion of EG, accidental or in suicide attempts, causes poisoning which can be fatal. COM accumulates in the kidney by attachment of crystals to tubular cell membranes, followed by endocytosis, resulting in structural damage of cell membranes, production of free radicals and lipid peroxidation, malfunction in the mitochondria of proximal tubule cells and consequently, renal tubular necrosis. Microscopic findings together with the toxicologic report are diagnostic for EG poisoning.

PS-01-007
Determination of survival time following isolated head trauma by histopathological method
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Background & objectives: The objectives of this study were determine the demographic characteristics of patients who died from isolated head injuries having no surgery and to determine their survival time based on histopathological changes in the injury hematoma and brain.
Methods: Between 2018 and 2019 the Department of Forensic Medicine of the National Institute Forensic Science recorded 3895 deaths of which 810 cases had head trauma. A subset of 398 of these patients with isolated head trauma were analysed. The tissues from 50 of these patients underwent histopathological analysis to determine the time from injury to death.
Results: Out of 398 cases studied, 326 (82%) were male, 72 (18%), were female (male to female ratio 4.5:1) and most (n=119, 30%) were within 40-49 years of age (mean age 42±13.2). Trauma to the anterior head was the most common location of injury (259, 65%). We identified 50 cases to estimate time from injury to death by histological examination using Martius Scarlet Blue stain. Among these cases 15 died between 0-6 hours after head trauma, 3 died between 6-12 hours, 22 cases died between 12-18 hours, 3 cases died between 18-24 hours, 2 case died 24-48 hours, and 5 cases died 48 hours after head injury.
Conclusion: Males who suffered death from traumatic head injuries from blunt objects were most frequently identified in our research. Brain oedema, subarachnoid haemorrhage, frontal skull fracture and brain contusion were most common. The interval of time from the head trauma to death was determined by the age of the fibrin using histochemistry stain.

PS-01-008
Haematolymphoid malignancies in clinical autopsy - our institution experience
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Background & objectives: In the past decades, autopsy rates have declined for a multitude of reasons. Despite technological diagnostic advances, the number of malignancies missed during clinical evaluation has not declined. Hereby, we focused on haematolymphoid malignancies (HLM) due the challenges they present.
Methods: The present study was an observational record-based study, with consult of autopsy reports and patient's medical files. We evaluated all the autopsies performed at our institution over the last 12 years (2009-2020), with the purpose of characterizing HLM in autopsy context. All the data was analysed as frequency and proportion.
Results: During this research, we found that, since 2009, 366 autopsies were performed at our institution. Of those, 98 were associated with neoplasms: 80 epithelial malignancies and 18 HLM. Regarding HLM, 6 were female and 12 were male with a mean age of 69 years old. 2 had been previously diagnosed [Non-Hodgkin Lymphoma (NHL) and Plasma cell neoplasms (PCN)], 5 were under study for occult malignancy [(4 NHL and 1 Myeloproliferative/myelodysplastic neoplasm/syndrome (MM/NS)] and the remaining 11 were not diagnosed/suspected clinically (8 NHL, 2 PCN and 1 MM/NS).
Conclusion: HLM usually course with nonspecific clinical manifestations being most of the time diagnostically challenging. Generally, they have a poor clinical outcome and prompt treatment may be lifesaving. With the present study we try to emphasize the persisting relevance of the traditional postmortem examination, by shedding some light not only in current pathology practice but also by contributing to the improvement of the diagnostic approach in HLM.

PS-01-009
The analysis of mortality among patients with SARS-CoV-2 infection in concomitance with malignant neoplasms
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Background & objectives: The aim of study was to determine the mortality structure in the autopsy cases of concomitant SARS-CoV-2 infection and malignant neoplasms.
Methods: We assessed 4695 autopsies. In all cases there was post-mortem histological examination and the data of reverse transcriptase-polymerase chain reaction (RT-PCR). The SARS-CoV-2 was determined by RT-PCR in 95% of cases. In 5% of cases there was just typical for COVID-19 clinical and morphological findings without RT-PCR determination.
Results: The overall number of autopsies with SARS-CoV-2 infection and malignant neoplasms was 94/4695 (2%). The median age was 66 years (LQ-58,25; HQ-77,5). The coexisting SARS-CoV-2 infection and hemoblastosis was observed in 46% cases (ICD-10 C91 – 18%; C92-93 – 12%; C90 – 9%; C81-85 – 7%), colorectal cancer in 12% cases (C18-C20), lung cancer in 10% (C34), CNS malignancy in 5% cases (C70-72). The others malignancies were observed in less than 5% of cases.
Pneumonia (31% cases), pulmonary embolism (25% cases), cancer metastasis (13% cases) and shock (13% cases) occurred as a complication.
Conclusion: The most common concomitance of SARS-CoV-2 infection and hemoblastosis was revealed among all types of malignancies. It may be connected with the immune dysfunction associated with hemoblastosis.

PS-01-012
The importance of death verification services in Ceara, a state in the Northeast of Brazil
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Background & objectives: Death verification services (DVS) supply important epidemiological data to improve the healthcare system. In Ceará, it has an important role in decreasing the index for death by ill-defined causes. This study aims to understand the importance of this institution's implementation.
Methods: The present study consists of a literature review. The articles studied were retrieved from the Scielo database. The descriptors Death, Verification, Services and Importance were applied, utilizing the boolean operator and. Government databases like DATASUS, official government websites and literary works on the subject were also considered. The period from 1996 to 2020 was the search limit.
Results: The DVS in Ceará was created in 2005. It works by identifying the natural causes of death, providing data to the health system and improving its coverage area throughout the state in 2014 with the Mobile Death Verification Service. According to the government's mortality information system, in the nine years prior to the service's implementation, the rate of ill-defined causes of death was 10% above the national target. After the institution's first year of operation, the index dropped to 6.2%. During the dengue outbreaks between 2011 and 2012, 214 post-mortem examinations were performed of which 121 were confirmed as dengue and 42.05% of those had no clinical suspicion.
Conclusion: The death verification service of Ceara has played a fundamental role in collecting data on the diverse types of natural deaths, helping to trace an epidemiological profile that contributes to the improvement of public healthcare in the state.

PS-01-013
Primary amoebic meningoencephalitis (PAM) in North-eastern Brazil: an autopsy report
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Background & objectives: We report autopsy findings of primary amoebic meningoencephalitis (PAM), caused by Naegleria fowleri, a rare reported disease in Brazil with high mortality, associated with bathing on still hot water.
Methods: Clinical, imaging, and autopsy recordings were reviewed. The patient was a 19-year-old, male college student, immunocompetent, who presented with progressive headache for three days, evolving with aphasia and motor deficit, after bathing on a lagoon during an expedition to the state of Piauí, Brazil. MRI showed multifocal lesions with T2 hyperintensity, intralesional haemorrhage, and heterogeneous pattern of enhancement.
Results: The patient was transferred to the ICU after presenting progressive clinical worsening with intracranial hypertension. After three days, brain biopsy was performed showing necrotizing encephalitis without any identified microorganism. Despite corticosteroid, antifungal and antibiotic therapy, the patient rapidly progressed to death. Autopsy gross findings were: purulent leptomeningeal exudate with haemorrhage along the cerebral hemispheres, brain stem, cerebellum and upper spinal cord, congestion of meningeal vessels, brain oedema with herniation of the uncus and cerebellum. Cerebral hemispheres and cerebellum exhibited multiple necrotic and lytic lesions. A diagnosis of primary amoebic meningoencephalitis caused by Naegleria fowleri was based on epidemiological and histopathological findings of multiple amoeba trophozoites without cystic forms.
Conclusion: Primary amoebic meningoencephalitis is associated with swimming in warm and fresh water where the free-living and thermophilic amoeba Naegleria fowleri may enter the central nervous system through the olfactory nerve epithelium. This is a rare case reported in Brazil that shows the importance of considering PAM in the differential diagnosis of necrotizing lesions of the central nervous system.

PS-01-014
Gastrointestinal tract damage in fatal cases of COVID-19
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Background & objectives: The COVID-19 infection now is spreading globally, threatening public health worldwide. Patients with COVID-19 experience acute respiratory syndrome accompanied by several extrapulmonary symptoms. The aim of present study was to reveal digestive system pathology in fatal cases of the COVID-19.
Methods: A full pathological post-mortem examinations were performed in 47 fatal cases of the COVID-19. Medical records and clinical data were studied. Gross pathology of the lungs, digestive system, other internal organs and brain were examined. Tissue samples were taken for histological study. Microscopy of H&E stained slides performed at x10, x20, x40. Gastrointestinal tract pathology features were recorded and analysed.
Results: Our study has shown the features of pulmonary pathology in majority of cases, including interstitial pneumonia, diffuse alveolar damage and hyaline membranes formation. Gastrointestinal tract pathology was found in 21% of cases (nine men and one woman). Foci of dystrophy and necrosis, covered with fibrin films with an admixture of neutrophils and mononuclear cell revealed in stomach and intestines. The glands of the stomach were overflowing with mucous secretion, mucostasis was noticeable in the goblet cells. In addition, lymphocytes, monocytes, leukocytes infiltrations were common findings in oesophageal mucosa, stomach, intestines lamina propria. These changes were accompanied with interstitial oedema, acute plethora of blood vessels, stasis of erythrocytes.
Conclusion: COVID-19 infection responsible for the significant growth of patient's morbidity and mortality worldwide. Post-mortem examination is an essential tool in understanding pathogenesis and pathomorphology of severe acute respiratory syndrome coronavirus 2. Although the infection primarily affects the respiratory system, it is also a multi-organ pathology, including gastrointestinal pathology. The virus associated cells and tissue injuries along with presence of hemodynamic disturbances, inflammatory reactions significantly contributed to death. Further studies of the relationship between gastrointestinal tract disorders and COVID-19 are considered necessary.

PS-01-015
Disseminated trichinosis - case report of an uncommon parasitosis
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Background & objectives: Trichinosis is an often unrecognized parasitosis and public health hazard, transmitted by ingestion of the nematode Trichinella. Although it is uncommon in well-developed countries, it is still present in Europe in the XXIst century.
Methods: A 56-year-old Nepalese man presented to the emergency department with a 1-month history of generalized myalgia, fatigue and diarrhoea: his last visit to Nepal occurred 7 months prior to the onset of symptoms. He presented with fever and a rash in his left thigh, and laboratory studies showed a white-cell count of 17,000/μL with 10.1% eosinophils.
Results: The patient was admitted to the Intensive Care Unit with severe sepsis and submitted to lower extremity fasciotomy - after 7 days of treatment with antibiotics and supportive therapy, to which he did not respond favourably, muscle biopsies were performed (left quadriceps femoris): histopathological analysis showed muscle tissue with countless encapsulated cysts of Trichinella species.
15 days after presentation the patient died and an autopsy was performed: samples of various skeletal muscles were obtained, which showed muscle tissue with encapsulated cysts of Trichinella species on the left quadriceps, pectoral muscles, intercostal muscles, diaphragm and temporal muscles. A diagnosis of disseminated trichinosis was made.
Conclusion: Trichinosis is a parasitic disease transmitted by ingestion of viable Trichinella larvae in undercooked meat, with pork and wild boar meat being the primary sources of infection worldwide. Symptoms are nonspecific, which hinders the diagnosis, and severity depends on the amount of larvae consumed and conditions of the host. Histopathological analysis of skeletal muscle samples may, along with serologic testing, confirm the diagnosis.

PS-01-016
The importance of specialist autopsy service in identification of cause of failure and adjustment of structure of novel mechanical assist device
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Background & objectives: After years spent on development of an optimised mechanical assist device, few fatal outcomes associated with malfunctioning of this novel device were reported. The aetiology of the device malfunction remained unidentified at the early stage of the product launch.
Methods: After product launch of Heartmate 3, end-stage left ventricular heart failure of an elderly patient was initially successfully treated with mechanical unloading of the left ventricle by this novel device. But soon after surgical implantation, the clinical condition of the patient deteriorated, with a fatal outcome. With consent of the patients' relatives an autopsy was performed by a cardiovascular pathologist.
Results: A to date of necropsy not photodocumented twisting of the inner membrane of the pumps' outflow graft was detected, which likely would have remained undetected by trainee pathologists. The finding was met with scepticism by cardiologists and surgeons, as well as by industry, and was suggested to represent an autopsy artefact.
Conclusion: This case highlights the importance of specialist autopsy service, proper (photo-)documentation and open interdisciplinary communication in a highly specialised university hospital setting, together with the importance to keep updated on novel clinical developments, in

order to diagnose and communicate postmortem findings confidently, even if they appear alogical or unlikely, and proves the role of pathology in preventing further fatal outcomes caused by design flaws of novel devices in the follow-up phase of the product launch.

PS-02 | Breast Pathology Posters

PS-02-001

Immunohistochemical expression of vascular endothelial growth factor (VEGF-A) in triple negative breast carcinoma and its correlation with clinical and pathological factors

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Background & objectives: Triple-negative breast carcinoma (TNBC) is a BC subtype with no "tailored" therapy. Our objective is to evaluate immunohistochemical expression of VEGF-A and to correlate it with other prognostic factors, in order to establish its potential role as a predictive/prognostic biomarker.
Methods: The present study is a retrospective research encompassing 35 cases of TNBC selected from our hospital, during 1995-2020. Clinical and morpho-pathological data were extracted from electronic records. All cases were retrospectively reviewed and selected samples were submitted for immunohistochemical analysis using VEGF-A; P53; Ki67 biomarkers. The SPPS23.0 software for Windows was used to run the statistical analysis
Results: The mean age of cases included in our research was 64 years-old and the overexpression of VEGF-A was noticed in 65.7% of cases. The most important clinic-morphological features which have been correlated with this pattern of expression were lymph node status, angiolymphatic invasion and TNM stage ($p < 0.001$). The vast majority of TNBC had a high proliferation rate (82.85%) and it was established a perfect association with overexpression of VEGF-A ($p<0.001$). Immunohistochemical evaluation of p53 mutational status revealed that 37.14% presented a mutated immunostaining pattern, most of them with "over-expression" p53 type (69.23%). The mutational pattern of p53 was also correlated with overexpression of VEGF-A ($p=0.010$).
Conclusion: The need to discover new therapeutic targets for TNBC is imperative because chemotherapy alone is not sufficient to significantly improve the survival of these patients. An additional therapy based on VEGF inhibitors may have an important clinical response, improving the quality of life for these patients. VEGF-A biomarker can be used as a prognostic and predictive biomarker, but further studies and clinical trials are required.

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PS-02-002

Mammary tuberculosis masquerading as a primary breast tumour

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Background & objectives: Although over one billion people suffer from tuberculosis worldwide, mammary tuberculosis is an uncommon disease even in countries where the incidence of pulmonary and extrapulmonary tuberculosis is high, accounting for less than 1% of breast conditions.
Methods: We report the case of a 49-year-old female patient presenting with a solitary, palpable, ill-defined, firm lump situated in the central quadrant of the right breast and measuring approximately 2 cm. Imaging examination reported a BI-RADS 4c lesion and the patient was referred to the surgery department where she underwent right breast lumpectomy.
Results: Histopathological examination revealed multiple epithelioid cell granulomas composed of Langhans cells, caseous necrosis and lymphocytes, scattered throughout fibroadipose tissue. There was no evidence of microcalcifications, epithelial hyperplasia or malignancy. The pattern of distribution, presence of necrosis and lack of suppurative inflammation excluded a granulomatous lobular mastitis. Immunohistochemical stains confirmed the presence of epithelioid cells (CD68 positive) accompanied by a polyclonal lymphocyte population (CD3 and CD20 positive). Since anti-MPT64 was not available, Ziehl-Neelsen stain was performed, which revealed several acid-fast bacilli. Based on our findings, the patient underwent subsequent CT scans, which revealed patchy pulmonary consolidation as well as poorly defined linear and nodular opacities, consistent with a post-primary pulmonary tuberculosis.
Conclusion: Extrapulmonary tuberculosis occurring in the breast is very rare and it is an uncommon disease even in countries where the incidence of pulmonary and extrapulmonary tuberculosis is high. The first case of breast tuberculosis was reported in 1829 by Sir Astley Cooper. The disease occurs far more frequently in women, especially in their reproductive period. Clinical and imaging data may mimic a malignant neoplasm, but primary breast tuberculosis should be taken into consideration in patients from endemic areas.

PS-02-003

Neuroendocrine neoplasms of the breast: study of 12 cases

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Background & objectives: Neuroendocrine neoplasms are a rare subtype of breast cancers. It includes all tumours with predominant neuroendocrine differentiation. These neoplasms are classified into neuroendocrine tumour and neuroendocrine carcinoma. The aim of our study is to discuss the clinico-pathological characteristics.
Methods: This is a retrospective study of 12 cases. Data was collected from files of pathology Department of Farhat Hached University Hospital over a period of 2001 and 2020.
Results: The mean age was 66.47 years with extremities ranged between 43 and 89 years. The mean size was 3.76 cm (1- 8.4 cm). Nodule was the most common symptom. Tumours were bifocal in 4 cases. 2 cases had mucinous differentiation and 10 cases were pure neuroendocrine carcinomas. 8 cases were neuroendocrine tumours and 4 cases were neuroendocrine carcinoma. All tumours were positives for synaptophysin and chromogranin A. 6 tumours were classified as stage I, 4 were stage II, one was stage III and one was stage IV. There were 7 cases of luminal A type, 4 cases of luminal B type and 1 case of basal type.
Conclusion: Neuroendocrine neoplasms of the breast affect postmenopausal women in the sixth to seventh decade of life. Clinical presentation is similar to NOS. The diagnosis of neuroendocrine differentiation requires expression of the neuroendocrine markers synaptophysin or chromograninA. The main differential diagnosis is a metastatic neuroendocrine tumour from a non-mammary site. Neuroendocrine tumours are low grade tumours with an outcome similar to NOS. Neuroendocrine carcinomas are high grade tumours. Its morphology and prognostic is similar to small cell carcinoma of the lung.

PS-02-004

Desmoid-type fibromatosis of the breast: A report of 7 cases

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Background & objectives: Mammary fibromatosisis a rare and locally aggressive benign tumour; it originates from fibroblasts / myofibroblasts within the breast parenchyma and does not metastasize.
Through this study we tried to improve and add to the knowledge of this disease.
Methods: This study included 7 women with desmoid-type fibromatosis of the breast collected over a period of 5 years (2016- 2020) in the department of pathology of the university hospital of Monastir.
Results: Patient's ages ranged from 26 to 46 years. Breast imaging examinations suggested an invasive breast tumour, likely carcinoma, infiltrating the muscles of the chest wall. An ultrasound-guided core needle biopsy revealed a low-grade myofibroblastic proliferation consistent with breast fibromatosis in two cases. Other patients did not have needle biopsies and underwent surgery. They underwent tumourectomies, with a partial resection of the underlying musculature. Macroscopically, tumours were firm and white measuring between 2 and 9 cm. A definitive diagnosis of breast fibromatosis was established from serial paraffin sectioning and immunohistochemistry using β-catenin. In three cases surgical margins were positive and one among these cases showed a relapse after 12 months.
Conclusion: Desmoid-like fibromatosis is a rare breast neoplasm. Despite its classification as an intermediate soft-tissue tumour, breast fibromatosis does possess the potential for aggressive local behaviour. Breast imaging examinations are not specific for fibromatosis and often imitate breast cancer. Surgery remains a valid option, however, preservation of function and quality of life are essential. The role of adjuvant therapy is also not entirely clear, and the optimal regimes, doses and durations of systemic treatment of the disease require elucidation.

PS-02-005
Male breast carcinomas – a 20-year long series in a tertiary Portuguese hospital
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Background & objectives: Male Breast Carcinomas (MBC) account for <1% of all cancers in men, largely characterized based on data from female counterparts. This study aims to review several cases of MBC from 2000-2020 registered in our department and contribute to their portrayal.
Methods: Through the National Oncologic Registry, we compiled every case of MBC registered in our hospital between 2000 and 2020, and 45 out of 87 cases were selected to our study; only cases with a pathology report from our department were chosen. Both biopsies and surgical specimens were considered and all available clinicopathological features were summarized and analysed, accordingly.
Results: Median age of diagnosis was 66,1 years (range 36-86 years), occurring equally on both sides, mainly in the subareolar region (n=30). 32 cases were diagnosed with invasive breast carcinoma of no special type, 3 were invasive special types (2 mucinous and 1 micropapillary), 3 were invasive encapsulated papillary carcinomas and 7 were in situ lesions. Pertaining to invasive carcinomas, 33 were Luminal A, 4 were Luminal B and 1 was triple-negative; 15 had lymph node metastasis (sentinel/axillary nodes) and 4 had distant metastasis reported. To date, 17 patients passed away but it was not possible to evaluate overall survival since most cases did not have information regarding cause of death.
Conclusion: Our study provided data consistent with current knowledge of MBC, with the majority of cases being invasive breast carcinomas of no special type, with a higher frequency of Luminal A molecular subtype; we additionally concluded that most cases were classified as stage I. Noticeably, this cements our understanding of these neoplasms and while female breast carcinomas remain the main source of evidence for treatment algorithms, further research is needed on the optimization of management and therapeutic decision-making in men.

PS-02-006
One-step-nucleic-acid amplification (OSNA) for intraoperative evaluation of sentinel lymph node in breast cancer patients treated with neoadjuvant therapy
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Background & objectives: The evaluation of sentinel node (SN) in breast cancer (BC) by one-step-acid-nucleic-amplification (OSNA) after neoadjuvant treatment (NAT) is controversial. We evaluate the results obtained from the incorporation of OSNA for the study of GC in BC patients treated with NAT
Methods: Since June 2018, a total of 163 BC patients have undergone surgery after NAT. In 42 of them, GC study was performed intraoperatively using the OSNA method. Data on the primary tumour, its phenotype, response grade, GC involvement, axillary involvement in positive cases and post-neoadjuvant cytokeratin 19 are studied.
Results: OSNA was feasible in all the 42 patients, displaying grade 1, 2 and 3 in 1, 20 and 21 cases, respectively. One case was luminal A, 6 luminal B phenotype, 16 luminal B-HER2, 8 pure HER2 and 11 triple negative. They showed a Miller-Payne grade 5,4,3 and 1 in 25, 4, 12 and 1, respectively. All the cases with residual tumour were Cytokeratin 19 positive.
Nodes studied by OSNA were negative in 34 patients. Isolated cell group, micrometastases and macrometastases were detected in 1, 5, and 2 cases, respectively. Lymph nodes at subsequent lymphadenectomy were negative in 7 cases and micrometastasis was observed in one case.
Conclusion: it is necessary to detect small metastases after NAT to be treated with lymphadenectomy. We consider that OSNA has all the characteristics that have led to its implementation in non-NAT:
-It is carried out intraoperatively and allows the study of the whole lymph node, avoiding surgery.
-It allows the detection of small metastases associated with false-negative cases.
-The only disadvantage we observe is the impossibility of obtaining the residual cancer burden (RCB) in positive patients, although we can determine the RCB-Class.

PS-02-007
Low grade adenosquamous carcinoma: prevalence in our centre and literature review
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Background & objectives: Metaplastic breast carcinoma corresponds to 0.2-1% of all infiltrating breast carcinomas. We review metaplastic carcinomas diagnosed in our centre the last 7 years, low-grade adenosquamous carcinoma (LGASC) among them, to see their prevalence and clinical or immunohistochemical differences.
Methods: A retrospective study has been carried out of all the breast tumours in our centre diagnosed between 2014 and 2021 and the age at diagnosis was collected as well as the immunohistochemical study of biomarkers (hormone receptors, HER2), P53 and Ki67.
Results: 29 metaplastic carcinomas were identified, 2 cases (6.9%) corresponded to LGASC, 10 (34.5%) to sarcomatoid carcinomas, 9 (31%) to squamous carcinomas, 7 (24.1%) to spindle cell carcinomas, 8%) and 1 (3.4%) to fibromatosis-like carcinoma. The hormone receptors were negative in 89.7% of the cases (100% in the case of LGASC) and P53 showed an altered pattern in 37.9% (50% in LGASC). The average Ki67 was 53.3% [5-95], being 6.5% in the LGASC.
Conclusion: LGASC is a rare tumour within metaplastic breast carcinoma, with 2 cases identified in the last 7 years in our centre. Their age of onset was higher than the average for metaplastic carcinomas and,

although they showed a triple negative immunohistochemical profile, their low proliferative index (6.5%) stood out.

PS-02-008

Circulating soluble HLA-G is increased in HER2+ breast cancer patients: a meta-analysis

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Background & objectives: Soluble plasmatic molecule HLA-G(sHLA-G) is often associated with aggressive cancer types. We aimed to understand the real implication of sHLA-G in aggressive breast cancer (BC), and to resolve the limitation of insufficient statistical power and reduced sample size in individual studies.
Methods: A comprehensive systematic literature search in Pubmed, Medline, Cochrane, Embase, and Web of Science databases was performed to look up for relevant studies. We identified 5 studies with a total of 401 BC patients and 298 healthy controls. The study of sHLA-G levels association to HER2 status is determined by calculating standardized mean differences (SMD) and the corresponding 95% confidence interval(CI).
Results: In overall population, sHLA-G is statistically increased in HER- BC patients as well as in HER+ BC patients compared to healthy controls (Respectively: SMD=1.964; %95CI= 0.368-3.560, P=0.016 and SMD=1.459; %95CI=0.058-2.860, P=0.041). In overall population, the sHLA-G is slightly higher in patients with HER+ vs. HER- without significance (P=0.411). Interestingly, Asians demonstrated significant increase of sHLA-G in HER+ patients compared to HER- patients (SMD=0.477; %95CI=0.104-0.849, P=0.012). This increase may explain the aggressiveness and the rapid progression of HER2+ BC compared to HER2- BC. However, this result should be taken with cautious because of reduced meta-analysed studies.
Conclusion: Our meta-analysis revealed an increased sHLA-G levels in patients expressing HER2 compared to patients HER2- and healthy controls. Our findings suggested the complementary targeted therapy against HER2 and HLA-G in BC expressing HER2 and high sHLA-G levels. Further larger studies and well-designed studies still needed to clearly establish our findings.

PS-02-009

A study on tumour-infiltrating lymphocytes, PD-L1 and BRCA1 immunohistochemical expression in basal-like subtype of breast cancer

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Background & objectives: The aim of the study was to determine basal-like subtype of breast cancer (BC), its tumour expression of breast cancer 1 (BRCA1) protein, the predominant type of lymphocytes and the expression of programmed death ligand 1 (PD-L1) by immune cells.
Methods: We studied 100 patients with invasive BC, grouped into four surrogate molecular subtypes - Luminal A-like and Luminal B-like, HER2 positive non-luminal and triple negative (TN), determined by immunohistochemical (IHC) method.
IHC was performed to find basal-like subtype of BC, to distinguish PD-L1 and BRCA1 antigens and to detect subtypes lymphocytes, using CD20, CD3, CD4, CD8 and FoxP3 antibodies.
Results: In our cases, the basal-like BC were mainly TN ($p<0.05$), mostly with special histological subtypes ($p=0.036$). Their immune response was represented predominantly by high concentration of intratumoral cytotoxic CD8+ T-lymphocytes ($p<0.05$) and stromal PD-L1 positive immune cells ($p=0.008$). In these tumours, the BRCA1 expression was more often absent in the tumour cells ($p<0.001$).
The basal-like subtype of BC and IHC negative expression of BRCA1 were associated with <5-year survival ($p=0.001$ and $p=0.017$, respectively).
Conclusion: The established dependencies can be incorporated in a prognostic algorithm and predictive morphological screening, allowing better selection of patients with BC for subsequent genetic analysis of BRCA1 gene and for application of appropriate therapy.

PS-02-011

Vacuum assisted breast biopsy: diagnostic and therapeutic

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Background & objectives: Vacuum-assisted breast biopsy (VAB) plays a diagnostic and therapeutic role. This study aims to evaluate the efficacy of this procedure in the management of breast lesions at a single institution.
Methods: We carried out a retrospective study, of 221 VAB (guided by stereotaxis or ultrasound) performed at a single institution over 15 months. We reviewed the imaging characteristics of the lesions, as well as the histological slides from VAB and respective surgical specimen, when available. Post VAB surgery was performed based on the imagiological follow-up.
Results: Imaging characteristics pre-VAB: microcalcifications (56,1%); nodules (33%); architectural distortion (4,5%) and density asymmetries (2,3%).
Diagnosis by VAB: benign (44,8%); uncertain malignant potential/B3 (22,2%) including 23 papillomas (10.4%); ductal carcinoma in situ/DCIS (23,5%); invasive carcinoma not otherwise specified/IC (9,5%).
In 70 cases (31,7%) post-VAB surgery was necessary: 2,8% were benign lesions; 15,7% B3 lesions; 54,3% DCIS; 27,1% IC.
No malignancy was found on the surgical specimens of benign and B3 lesions. Of 19 papillomas, only 1 was incompletely excised with VAB.
In DCIS' surgical specimens, there was no residual lesion in 5,2%; microinvasive carcinoma was found in 10,5% and IC in 10,5%, one of these with a 3 mm axillary metastasis.
Conclusion: The low percentage of cases submitted to surgery post-VAB proves its efficacy in the management of benign and also in B3 lesions, with emphasis in the total excision of papillomas. Of the DCIS cases that went through surgery, we found no residual tumour in 5,2% and malignancy in 21,1%, half of these with microinvasion.

PS-02-012

Denosumab as inmunomodulator in early breast cancer: preliminary results of a randomized window of opportunity clinical trial D-BIOMARK (NCT03691311)

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Background & objectives: RANK pathway inhibition could prevent and/or treat breast carcinoma (BC) and regulate the tumour immune crosstalk in BC. We are running D-BIOMARK, a prospective, randomized pre-operative study evaluating denosumab (anti-RANKL) and its biological effects in early-stage BC.
Methods: Early-stage HER2-negative-BC, candidates to tumour excision as first therapeutic approach were included. Patients were randomized into two groups: 2:1 to denosumab: control (no treatment). Experimental arm received 2 doses of subcutaneous denosumab 2-4weeks before surgery. Clinicopathological parameters were recorded. Ki67, cleaved caspase-3 and stromal tumour infiltrating lymphocytes (TILs) were assessed in biopsy and surgical resection specimen (pre- and post-denosumab).
Results: We present results from the first 36 patients enrolled out of 60. Clinical and tumour characteristics were well balanced between the

groups. No clinically relevant differences in Ki67 or cleaved caspase-3 were observed after denosumab treatment. Interestingly, an increase of TILs was observed in the denosumab treated group (p=0.03, Paired t test), but not in the control group (p=0.80). A 33% of patients treated denosumab showed a ≥10% increase in TILs vs 0% in the control group (p =0.05).
Conclusion: Short term neoadjuvant denosumab increases TILs in early BC.

PS-02-013
Insulinoma-associated protein 1 (INSM1) expression in breast carcinomas with neuroendocrine morphologies: application and future prospective
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Background & objectives: INSM1 was recently demonstrated to be a better diagnostic and prognostic indicator for small cell pulmonary carcinoma than the traditional 'gold-standard' neuroendocrine (NE) markers, i.e. chromogranin A and synaptophysin.
Methods: Herein, for the first time, we present three cases with NE phenotype mammary neoplasms in which the NE nature of the tumours was confirmed solely by INSM1. This is also the first analysis to use INSM1, a promising antibody with high sensitivity and specificity, in the field of breast oncology.
Results: Three patients were, respectively, 42-, 58- and 64-year-old Japanese women with breast tumours showing characteristic NE morphologies: 1) Neuroendocrine tumour, grade 2, 2) Cellular mucinous carcinoma, and 3) Neuroendocrine ductal carcinoma in situ. On immunohistochemical examinations, these malignancies showed diffuse nuclear expressions of INSM1, whereas chromogranin A and synaptophysin staining did not correspond to distinct NE features in the neoplastic cytoplasm, despite appropriate positive and negative controls having been provided for these NE stained sections. In addition, we could not detect INSM1-reactive cells in breast parenchyma surrounding the tumours.
Neuroendocrine neoplasms (NENs) could be regarded as a rare, distinctive type of aggressive mammary carcinoma.
Conclusion: Intriguingly, in the lung oncology field, it was very recently reported that outcomes were significantly poorer in NEN patients with high-INSM1 than those with low-INSM1 reactivity.
Based on the establishment of INSM1 accompanied by our current immunohistochemical results, the frequency of detecting NE differentiation in systemic neoplasms, including breast NENs, is anticipated to increase. Our observations might ultimately contribute to the development of novel treatments including molecular-targeted therapies for these invasive tumour entities.

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PS-02-014
Expression of prolactin receptors does not affect the development of benign breast pathology
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Background & objectives: Recently, attention has been given to the study of prolactin receptors (PRL-R) on the development of benign breast tumours (BBT). The aim: to investigate the relationship between PRL-R expression and the development of BBT.
Methods: 16 samples of BBT and 16 samples of intact tissue were taken for the study. We considered serum PRL levels, according to which patients were divided into two groups: group I - with normal serum prolactin (8 women) and group II - with elevated serum prolactin (8 women). BBT tissue was examined using histological, immunohistochemical methods and Western blotting.
Results: The middle age of the women in the BBT study was 27.9 ± 1.55 years, ranging from 19 to 39 years. Expression rates of PRL-R in BBT tissue (39.97 ± 2.1) and intact MG tissue (35.56 ± 3.6) did not differ significantly (p> 0.05). In women of group I, a strong positive association was found between PRL-R expression in BBT tissue and serum prolactin levels (p <0.05; p = 0.8). Comparison of middle PRL-R expression values in benign tumour tissues and intact MG tissues of patients with elevated PRL levels did not show a significant difference between these indicators (p> 0.05).
Conclusion: Therefore, the level of PRL-R expression does not affect benign pathology of the breast.

PS-02-015
NDRG1 and lymph nodes status in breast cancer
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Background & objectives: N-myc downstream-regulated gene1(NDRG1) is widely described as a distant metastasis suppressor in breast cancer(BC). However, the related mechanism has not been fully discovered yet. In our study, we purposed to investigate the relationship between NDRG1 and lymph node BC metastasis.
Methods: NDRG1 levels in tissue microarrays from 358 BC patients were evaluated by immunohistochemical staining with NDRG1 (EP200, Abcam, USA). NDRG1 staining was predominantly cytoplasmic/membranous. NDRG1-scoring was done according to the German semi-quantitative scoring system (intensity and percentage of stained tumour cells). Tumours with score 1–4 were considered as negative (NDRG1-low), whereas tumours with score 5–12 were considered as positive (NDRG1-high).
Results: NDRG1-high BC tumours were significantly more often detected (136 cases, 60.2%) in the patients group without lymph nodes metastases(group 1) than in those with metastases(group 2)(62 cases, 47%)(p=0.015). The absence of NDRG1 expression was observed with the same frequency in the two compared groups(18.1%). The intensity of NDRG1 expression was higher in the group 1(25.7%) compared to the group 2(21.2%). No significant difference was obtained(p = 0.576). The significant difference was found in the two compared groups for moderate and weak NDRG1 expression. In the group 2 weak intensity expression of the marker was more often observed (34.8%), while in the group 1 moderate NDRG1 expression was more common (34.5%).
Conclusion: NDRG1 was a significant independent prognostic factor of lymph nodes metastases in BC. The intensity of the marker expression was statistically significant (p=0.015). In samples with NDRG1- moderate expression the risk of lymph node metastasis was lower than when the staining of tumour cells was weak (p=0.045). NDRG1-low expression has a reverse correlation with breast cancer metastasis and progression, and may serve as a predictive biomarker of lymph node involvement.

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PS-02-016
MMP-2 expression in breast cancer and its association with molecular subtypes and clinicopathological features
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Background & objectives: Matrix metalloproteinase-2(MMP-2) is gelatinase that plays a role in invasion and metastasis of cancer through

the destruction of basal membrane and extracellular matrix. The study is aimed to investigate MMP-2 expression levels in breast cancer(BC) and their relationship with molecular subtypes.
Methods: MMP-2 expression levels were studied in 358 tissue microarrays of BC specimens and their association with 5 molecular subtypes was evaluated by immunohistochemical cytoplasmic staining with MMP-2 (EPR1184, Abcam, USA). MMP2-scoring was done according to intensity of stained tumour cells. The staining scores for MMP-2 were negative in 96 cases(26.8%), mild in 184 cases(51.4%), and strong in 78 cases(21.8%).
Results: MMP-2 expression was increased in BC with HER2/neu overexpression, regardless of hormon receptor status. Strong MMP-2 expression was detected in 66.7% of luminal B HER2-positive subtype BCs and in 53.3% of non-luminal HER2-positive BC subtype. Only 1 case of BC with HER2/neu overexpression was MMP2-negative ($p<0.001$). There were only 10 (6.2%) cases with strong MMP2-expression and 76 (79.2%) MMP2-negative cases in luminal-A subtype BC. Regarding luminal-A subtype, MMP-2-negative and mild expression was observed in 45.8% and 93.8% cases respectively in comparison to luminal-B Her2-negative BC subtype (6.7% and 73.3%) ($p<0.001$). The number of MMP2-negative cases was lower than in TNBC (6.7% and 30.6% respectively), but without statistical significance($p=0.158$).
Conclusion: MMP2-expression is associated with molecular BC subtypes ($p<0.001$). MMP2-negative BC positively correlates with luminal-A subtype. MMP-2 expression is increased in TNBC and in cases with HER2 over-expression ($p<0.001$). Furthermore, strong MMP-2 expression correlates with larger tumour size ($p<0.001$), high-grade ($p<0.001$) and tumours with lymph nodes metastases ($p<0.001$). No correlation was found between MMP-2 expression and patient's age($p=0.061$), tumour localization($p=0,113$), number of tumour nodes($p=0.619$), hystologic BC type ($p=0.417$). These results suggest that MMP-2 plays a role in the biology of BC.

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PS-02-017
Heterogeneity of Ki67 expression in local metastases of breast cancer depends on the surrogate subtype of the primary tumour
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Background & objectives: Ki67 is an important prognostic and predictive marker for breast cancer. Its heterogeneity could affect the treatment results. Objective of the study: to discover Ki67 level stability in local metastasis of Luminal A-like and Luminal B-like breast cancer primary tumour.
Methods: 66 patients having breast cancer with local metastases and Luminal A or Luminal B surrogate subtype of primary tumour were included in the study. Antibodies to ER (1D5), PR (PgR636), Ki67 (MIB-1) and Her2/neu (4B5) were used. Changes of Ki67 expression (threshold – 30%) in primary and metastatic tumours were counted and compared in groups with different primary tumour subtypes.
Results: In the group with Luminal A subtype of primary tumour Ki67-status of primary tumour and metastases was discordant in 8 of 50 cases (16,0%, 95% CI 7,6-29,7%), while in group with Luminal B subtype – in 11 of 16 cases (68,7%, 95% CI 41,5-87,9%). The difference of discovered frequencies is statistically significant (Fisher exact probability test) ($p<0,01$).
Conclusion: Proliferation status of breast cancer is discordant in primary and metastatic tumour depending on the surrogate subtype of the primary tumour. In cases with Luminal B subtype Ki67 status of the metastasis changes more frequently than in cases with Luminal A subtype of the primary tumour.

PS-02-019
Study on the heterogeneity of expression of PD-L1 (Ventana SP142) in breast cancer in space and time
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Background & objectives: Tumour has a certain degree of heterogeneity, which brings a challenge for clinicians to choose PD-L1 detection time for breast cancer patients. Therefore, the heterogeneous expression of Ventana PD-L1 (SP142) in breast cancer needs to be studied in depth.
Methods: 124 surgical specimens, 5 tissues were penetrated in each case. 298 cases of primary breast cancer and its matched metastases were stained with PD-L1 to explore the differences in expression. 71 cases of PD-L1 positive invasive breast cancer specimens were included at different temperatures and different time nodes. Compare the expression of PD-L1 with the corresponding fresh slices.
Results: When the number of punctured tissues increased from 1 to 5, the κ value of PD-L1 expression and PD-L1 expression in surgical specimens gradually increased from 0.165 to 0.615, and κ was 0.499 for 3, reaching a moderate consistency. The positive rate of PD-L1 in different metastatic organs is different. With the extension of the storage time of paraffin sections, the PD-L1 antigen is gradually lost, and the positive rate gradually decreases. The expression of PD-L1 in slices stored at room temperature for 1 and 2 weeks is more consistent than that of fresh slices ($ICC \geq 0.9$).
Conclusion: The expression of PD-L1 in primary breast cancer and paired metastatic breast cancer is different, and the expression of PD-L1 in metastases needs to be reassessed. Long-term storage of paraffin sections will cause the expression level of PD-L1 to decrease and refrigerated storage at 4°C or -20°C is recommended, and the storage time should not exceed one month.

PS-02-020
Changes in the positive rate of HER2 expression may indicate the progression of early breast cancer
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Background & objectives: To explore the relationship between the expression of HER2 and clinicopathological characteristics in patients with microinvasive breast cancer and T1a breast cancer. To analyse the consistency of HER2 expression in carcinoma in situ and invasion foci.
Methods: 217 cases of breast microinvasive carcinoma and T1a patients admitted to the hospital from January 2015 to June 2020 in the Fourth Hospital of Hebei Medical University were collected. Interpret the HER2 expression status of the carcinoma in situ and the infiltrated area respectively. Combining pathological features and morphological features to construct a nomogram to predict the HER2 expression status.
Results: High nuclear grade, comedy type necrosis, high TILs infiltration and high proliferation index are more likely to have HER2 positive expression. There was no significant difference in the expression of HER2 in microinvasive breast carcinoma and T1a in carcinoma in situ and invasive area. The overall agreement rate of HER2 expression of carcinoma in situ and invasive area was 97.7%.The feature with the strongest correlation with the HER2 positive rate is the diameter of the invasion foci. When the diameter of the invasion foci>2mm, the positive rate of HER2 decreases significantly (52.6%-16.1%, $p<0.001$). The molecular type has changed ($c2=9.725$, $p=0.045$), and the lymph node metastasis rate is increased (2.6%-8.9%, $p=0.426$).
Conclusion: The HER2 expression in the carcinoma in situ area can be referred to. Compared with T1a stage breast cancer with an invasion foci of 1-2 mm in diameter, breast cancer patients with an invasion foci of 2-5 mm in diameter are more malignant, and HER2 targeted therapy is recommended for HER2-positive breast cancer patients with an invasion foci of 2 to 5 mm in diameter.

PS-02-021

Establishment and verification of a prognostic prediction model for non-pCR patients after neoadjuvant treatment of breast cancer

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Background & objectives: The purpose is to establishment and verification of a prognostic prediction model for non-pCR patients after neoadjuvant treatment of breast cancer.
Methods: Patients who were diagnosed with invasive breast cancer from 2009 to 2017 and were surgically removed after neoadjuvant therapy. All pathological results included histological grade, Tils, ER, PR, HER2 and Ki67. R language is used to calculate the calibration degree and ROC curve of the prediction model in the training set and the verification set.
Results: In the training set, the prediction model's 3-year and 5-year survival rate AUC values were 0.93 and 0.80, and the RCB classification 3-year and 5-year survival rate AUC values were 0.69 and 0.65. Relative to the RCB classification, the prediction model can more accurately predict the OS of non-pCR patients after neoadjuvant treatment. The same results are also shown in the classification of HR, HER2+ and TN. The RCB classification predicts HR 3-year and 5-year survival rates AUC values of 0.77 and 0.72; predicted HER2+ 3-year and 5-year survival rates AUC values of 0.79 and 0.62; predicted 3-year and 5-year survival rates of TN group AUC value of 0.83, 0.69.
Conclusion: We have combined a variety of prognostic factors related to breast cancer through R software and developed a more accurate prediction model than RCB classification to evaluate the prognosis of non-pCR patients after neoadjuvant treatment of breast cancer and provide further clinical treatment Provide a basis for decision-making.

PS-02-022

Immunohistochemistry for NDRG1 and its phosphorylated form and its relationship with triple negative breast cancer biological features and behaviour

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Background & objectives: Triple Negative Breast Cancer (TNBC) is the most aggressive molecular type of breast cancer. Herein we assess the prognostic role of NDRG1 (a gene of the TGF-beta pathway) and its phosphorylated form (pNDRG1) in a series of TNBC.
Methods: Eighty-three cases of TNBC (All female, age: 23-86 years, follow up: 66-264 months) were included in this study.
Immunohistochemistry for NDRG1 and pNDRG1 was performed, scoring intensity and extension of the staining on digital images obtained with a 3DHISTECH preparation scanner.
Statistical analysis assessed the association of the degree of staining with survival, development of recurrence, metastases, and histological parameters.
Results: Seventy-three cases were infiltrating ductal carcinoma (85.9%), frequently in stages pT1 (31, 36.5%) and pT2 (36, 42.4%) and there were lymph node metastases in 23 cases (28%) and distant metastases in 1 case (1.2%). 34 (40%). patients died from disease (DFD) during follow-up.
NDGR1 and pNDRG1 was detected in 67.5% and 67.5%, respectively mainly at cytoplasmic level, with a lesser nuclear staining.
Nuclear NDRG1 expression is higher in DFD (11.92 vs 2.99%, $p = 0.03$) and cytoplasmic in recurrences (35.82 vs 19.99%, $p = 0.04$). On the contrary, pNDGR1 is higher in survivors without disease (30%) compared to active disease (3.88%) or DFD (18.05%), although without statistical significance.
Conclusion: NDGR1 expression in TNBC seems to be associated with parameters of tumour aggressiveness, in contrast to the expression of its phosphorylated form, which shows a trend to be expressed in cases with better biological behaviour. Further studies on larger series are needed to clarify its prognostic role in this area.

PS-02-024

Digital image analysis is a robust method for evaluation of tumour-associated macrophages in breast cancer

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Background & objectives: Tumour-associated macrophages (TAMs) may be of prognostic value in breast cancer. The objective was to investigate agreement between 1) estimation of CD68+ TAMs by "eyeballing" and digital-image-analysis (DIA) and 2) assessment of TAMs on tissue-micro-arrays (TMAs) and whole-slide-sections (WS).
Methods: Tumour-containing tissue blocks and TMAs (1 core/patient) were available from 1167 BC patients. Immunohistochemistry for CD68 were performed on TMAs (991 pts.) and on corresponding WS from 234 patients. Fraction of CD68+ TAMs was estimated semi quantitatively by 2 observers (KH, TT) using light microscopy ("eyeballing") and quantitatively by DIA on scanned slides as a continuous area-fraction.
Results: Evaluation of CD68 was successful in 991/1167 TMA cores and 223/234 WS. Interobserver agreement for "eyeballing" on WS was moderate with an intraclass-coefficient (ICC) of 0.72 (95%Cl: 0.65-0.78). Kappa coefficient was 0.40 when grouping the results into 6 categories (0-0.01, 0.02-0.10, 0.11-0.20, 0.21-0.30, 0.31-0.40, >0.41), increasing to 0.53 for 3 categories (0-0.10, 0.11-0.30, >0.31). A minority of tumours(21/991) showed high level of TAMs (> 0.31).
Correlation between TMAs vs. WS was highly significant by "eyeballing" as well as by DIA with Spearman correlation coefficients of 0.55 and 0.62 ($p<0.0001$), respectively. A strong significant correlation was found between DIA and "eye-balling" for both WS and TMAs ($p<0.0001$, Kruskal-Wallis test).
Conclusion: The interobserver agreement by "eye-balling" was moderate, whereas correlation between "eye-balling" and DIA was highly significant. The association between TMAs and WS by DIA and "eyeballing" was found to be highly significant indicating that CD68-assesment can be performed on, e.g., biopsies. This indicates that DIA may be a useful tool for estimating TAMs with the perspective of delivering a more reproducible and quantifiable estimate and securing the analytical validity of CD68 as a potential biomarker.

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PS-02-025

Molecular phenotype of breast cancer in women under 35 years old

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Background & objectives: Breast carcinoma is the most common malignant tumour in young women, with higher mortality rate compared with older population. The aim of present study was to reveal the peculiarities of breast cancer' molecular phenotype in patients under 35 years old.
Methods: We examined the pathologic features and molecular tumour' phenotype in 35 young women (aged ≤35years) with invasive breast cancer. Medical records were reviewed for clinical characteristics. Breast tissue histological slides H&E stained observed under a microscope. Hormonal status, Her2/neu status and Ki 67 were determined by

immunochemical (IHC) staining. Histologic grading of breast carcinoma was performed by Elston and Ellis method.
Results: Among 1009 cases of breast cancer 35 young women were selected for study group. The most frequent histological diagnosis was invasive carcinoma of a nonspecific type (91%), invasive lobular carcinoma was established in 8% of cases and 1 % -was mucous cancer. Analysis of IHC studies revealed the predominance of the molecular genetic subtype - luminal B HER2 positive with a high index of proliferative activity Ki-67 (52%). Luminal A was 32% of cases, triple negative subtype was established in 8% of cases and HER2-positive in 8% of cases. Most often, the molecular genetic subtype luminal B HER2-positive corresponded to invasive nonspecific cancer with a high index of proliferative activity.
Conclusion: Our findings have shown that the group of young women presented with a different variation of molecular phenotypes compared to the general population of women with breast carcinoma. The most common molecular genetic subtype of breast cancer in young women under 35 y.o. was luminal B HER2-positive molecular phenotype. These results are discussed with regard to the pathogenesis and prognosis of the neoplasia in young women. The data obtained should be taken into account when developing the adjuvant therapy algorithm.

PS-02-026
Immunohistochemistry alone may represent a cost-effective alternative for HER2 status assessment on biopsy
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Background & objectives: ASCO/CAP guidelines recommend HER2 status assessment on newly diagnosed breast cancer due to its prognostic and predictive impact. Currently, a combination of immunohistochemistry (IHC) and in-situ hybridization (ISH) is recommended. We evaluated the reproducibility of HER2 assessment with IHC alone.
Methods: At our Institution, 1654 patients underwent both bioptical and surgical procedure between January 2014 and December 2020. Patients with in situ, microinvasive or multicentric carcinomas, and patients treated with neoadjuvant therapy were excluded. The final cohort comprised 923 patients. ErbB2 IHC staining was performed with Dako AcP A0485 on OMNIS platform and scored according to 2018 guidelines.
Results: Overall concordance for ErbB2 IHC was 88.95% (821/923), in line with the literature-reported values for IHC alone. Revision of the 102 discordant cases revealed that only 7 (<1%) had the potential to significantly impact on the therapeutic choices for the patient (either negative/equivocal to positive or positive to negative changes between biopsy and surgical specimen). All other discordant results were between negative and equivocal status and, according to current guidelines for neoadjuvant treatment, would have not resulted in either over-treatment or under-treatment of the patient.
Conclusion: HER2 status has a tremendous impact on the prognosis and treatment of the patient and must be assessed in a timely and precise manner to ensure the best treatment is administered. Although the combination of IHC and ISH is to be preferred for its accuracy, our data suggests that IHC alone could be a valid alternative in settings in which cost or availability do not allow for ISH testing on all newly diagnosed cases, restricting ISH testing to equivocal cases.

PS-02-027
Semiquantitative evaluation of TILs in breast cancer shows differences among histotypes and tumour grade.
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Background & objectives: Current research in tumour microenvironment (TME) of breast cancer focuses mainly on molecular subtype and receptor status. In this work, we compare TME characteristics between no special type and lobular breast cancer to ascertain if a correlation with histotype exists.
Methods: At our Institution, 1724 patients underwent surgery for breast cancer (January 2012-December 2018). Patients who received neoadjuvant therapy were excluded. A final cohort of 1395 invasive breast cancer was considered; 1047 were diagnosed as no special type, 190 as lobular, and 158 as other histotypes. Stromal tumour-infiltrating lymphocytes (TILs) were assessed semi-quantitatively and grouped into a "brisk" or "non-brisk" category.
Results: Among the 1021 no-special type cases in which TILs were assessed, "brisk" TILs were found to be associated with histologic grade of the tumour: 7% in the G1 group (8/113), 19% of the G2 group (106/548), and 48% of the G3 group (171/360). In contrast, grade did not seem to impact the adaptive immune response in lobular carcinoma, and "brisk" infiltrate showed an analogous distribution: 17% in the G2 group (27/155) and 22% in the G3 group (7/32). This is not unexpected, as the no-special type histotype includes most of the triple-negative and HER2-enriched invasive breast cancer, which are found to be associated with increased TILs.
Conclusion: Our data suggest that in no-special type breast cancer TILs appear to parallel histologic grade and could reflect the increased genomic instability of high-grade cancers. In contrast, lobular carcinoma may represent a subtype of breast cancer in which adaptive immune response is underregulated, possibly underlying a low genomic instability and consequent low burden of neoantigens. As more therapies emerge for which TILs could represent a predictive factor, a more comprehensive understanding of its significance in breast cancer is needed.

PS-02-028
Copy number alteration influences tumour microenvironment in breast cancer
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Background & objectives: The introduction of therapies targeting genomic instability (e.g. PARP inhibitors) has made it crucial to gain a deeper understanding of the impact of genomic instability on breast cancer. Here we investigate the relationship of genomic instability with tumour microenvironment.
Methods: At our Institution, 1724 patients underwent surgery for invasive breast cancer (January 2012-December 2018). A cohort of 1003 patients was analysed by immunohistochemistry and grouped based on their molecular subtypes into three copy-number alterations (CNA) patterns identified by Kwei et al. ("simple", "amplifier", and "complex"). Stromal tumour-infiltrating lymphocytes (TILs) were assessed semi-quantitatively and grouped into a "brisk" or "non-brisk" category.
Results: In our cohort, "brisk" TILs were found to be significantly associated with the CNA-associated patterns defined by Kwei et al. Infiltrate was categorized as "brisk" in 15% in tumours belonging to the "simple" pattern (59/402), in 34% of the tumours belonging to the "amplified" pattern (184/534), and in 52% of the tumours belonging to the "complex" pattern (35/67). Although the use of molecular classification as a surrogate for CNAs is not as precise as the actual genetic analyses, the correspondence between these classes and the CNAs-associated pattern is supported in the literature.
Conclusion: Our data suggest that genetic instability could have a role in eliciting a strong stromal lymphocytic response in breast cancer, and we postulate this to be due to an increased number of neoantigens contributing to generate and maintain this response. In light of the current and upcoming therapies targeting genomic instability, the identification of

surrogate markers to evaluate this instability, including TILs, will become crucial in the understanding and management of breast cancer.

PS-02-029

Interobserver variability of breast grading in core biopsies

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Background & objectives: Nottingham histologic grading has become widely accepted as a powerful indicator of prognosis in breast cancer. The objective of this study was to evaluate the interobserver variability of this grade in scoring breast cancer in core biopsies among 2 pathologists.
Methods: This is a retrospective study of 65 cases of invasive ductal carcinoma that were independently evaluated by two pathologists and graded according to the Nottingham histologic system. A detailed histopathological assessment was carried out and analysed statistically using the Kappa agreement score.
Results: The mean size of biopsies was 15 mm. There was a substantial agreement among the 2 pathologists in scoring tubular formation, pleomorphism, and final grading (Kappa=0.7, 0.65 and 0.8 respectively). A fair agreement was noted in scoring mitosis (Kappa=0.35).
Conclusion: The interobserver variability of Nottingham grading in scoring breast cancer in core biopsies remains good. The relatively weak agreement in scoring mitosis is secondary to the small size of the micro-biopsies, not covering the 2 mm2 fields necessary to grade this parameter. This often leads to an extrapolation of the number of mitoses.

PS-02-030

High tumour-stroma ratio in oestrogen receptor-positive breast cancer is correlated to poor histopathological parameters

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Background & objectives: In breast cancer, attention has focused on the prognostic value of tumour- stroma ratio (TSR), mainly in the triple-negative subtype. The objective of this study was to determine the prognostic value of TSR in oestrogen receptor (ER) positive invasive breast carcinomas.
Methods: TSR was measured in hematoxylin and eosin-stained surgical specimens of 70 consecutive EP positive breast carcinomas. Scoring percentages were given per 10-fold per image field. Tumours with a low ratio had ≥50% of stroma and a high ratio had <50% of stroma. The relationship of TSR to routinely used prognostic histopathological parameters was analysed.
Results: All tumours were of no special type. The mean age of patients was of 65 years. There was no multifocality. Sixty percent of tumours had a high ratio and 40% a low ratio. High ratio tumours were significantly correlated with large size (p=0.02), grade 3 (p=0.045), presence of vascular invasion (p=0.0034) and lymph node metastasis (p=0.0012). No significant association was found with the mitotic activity index and HER2 status.
Conclusion: High TSR was related to poor histopathological parameters in EP positive breast carcinomas, contrasting data in triple-negative breast cancer, and highlighting the importance of considering ER status when interpreting the prognostic value of TSR.

PS-02-031

Breast cancer in young women: clinicopathological features of 27 cases

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Background & objectives: Breast cancer in young women has gained increased attention with an attempt to improve diagnosis and prognosis. The objectives of this study was to analyse the clinico-pathological features of breast cancer occurring in young women under 30 years.
Methods: We retrospectively studied 27 cases of histologically confirmed breast cancer, collected during 8 years, in gynaecology and pathology departments of our institution. All patients were under 30 years of age at diagnosis. Clinical data, pathological investigations and outcome statistics were analysed.
Results: The average age was 26.5 years. The tumour was T4 in 35% of cases and M1 in 3 patients. Treatment was radical in 60% of cases. Histological type was an invasive ductal carcinoma in all cases (grade III 35 %). Lymph node involvement was noted in 27.5%.Phenotype was:HER2 in 7 cases, triple negative in 8 cases, luminal A and B in 6 cases each. Chemo and radio therapies were performed in respectively 90 and 95% of cases, Hormone and targeted therapies were performed in 40% and 25% of cases respectively. Recurrences were noted in 25% of cases, distant metastases in 45% of cases and disease related dealth in 12% of cases. BRCA1 was positive in 5 patients.
Conclusion: Breast cancer in young women seems to be highly heterogeneous and has potentially aggressive and complex biological features.

PS-02-032

Association between positive lymph node ratio and prognostic clinicopathologic factors in breast cancer with axillary involvement

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Background & objectives: Recently, the ratio of the number of the metastatic lymph nodes (LNs) to the total number of examined LNs (LNR) has been suggested as a prognostic factor in breast cancer. Here, we investigated the association between clinicopathological parameters and LNR.
Methods: This study included 83 consecutive female patients with LN-positive breast cancer who underwent partial/radical mastectomy with axillary LN dissection. Clinicopathological parameters were retrospectively retrieved from patient records. LNR was defined as the ratio of positive nodes to total number of examined nodes. The relationship between LNR and clinicopathological parameters was statistically analysed.
Results: Median age was 51±1.7 years (range 30-82). The mean number of LNR and positive LNs was 0.3 (0.04-1) and 4.4 (range 1-27), respectively. More than half of the patients (51.8%, n=43) were pN1a. In univariate analysis, larger tumour size (advanced pT), presence of lymphovascular invasion (LVI), extranodal extension (ENE), and stage were significantly associated with higher LNR ($p<0.05$). A positive LN number of ≥4 was significantly associated with higher mitotic scores, advanced pT, presence of LVI and perineural invasion, and ENE ($p<0.05$). However, in multivariate logistic regression analysis, only ENE was significantly associated with LNR and positive LN number (p=0.011, OR=5.05, 95% CI=1.458–17.511, p=0.003, OR=7.135, 95% CI=1.942–26.216, respectively).
Conclusion: Unfavourable histopathological features were associated with LNR and the number of positive nodes but we could not verify most of these associations by multivariate analysis due to small number of patients. On the other hand, the significant association of ENE with LNR and the presence of ≥4 positive LNs was confirmed by multivariate analysis. We speculate that the presence of ENE in sentinel LNs may provide a clue in predicting pN but prospective studies are needed to test this hypothesis.

PS-02-033

Changing trends in hormone receptor and Her2 rates in breast cancer overtime

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Background & objectives: In 2006 we published our breast cancer oestrogen receptors (ER)/progesterone receptors (PgR)/Her2 rates in Jordan which were 50.8%/57.5%/17.5% respectively for ductal and 68%/90.9%/13.6% for lobular. An update of these rates is warranted in view of remarkable socioeconomic and technical changes.
Methods: 1185 breast cancer cases were accessioned in our department between January and December 2018. ER/PgR and HER-2/neu results were retrospectively collected from patients' pathology reports. They were originally evaluated by immunohistochemistry (IHC). In addition, evaluation of HER2/neu was done by fluorescent in-situ-hybridization in IHC equivocal cases. The testing was originally interpreted according to the 2013 CAP-ASCO guidelines.
Results: 867 (73.2%) cases were ductal, 669 (77.2%) of which were ER-positive, 663 (76.5%) PgR positive, 223 (25.7%) HER2/neu-positive and 86 (9.9%) were triple negative (TN). 86 (7.3%) were lobular carcinomas, 83 (96.5%) of which were ER-positive, 76 (88.4%) PgR positive, 5 (6.6%) were HER2/neu-positive and 2 cases (2.3%) were TN.
232 (19.6%) cases represented other variants, 32 (13.8%) of which were TN.
The total number of TN was 120 (10.1%). The number of low ER (1-9%) cases was 33 (2.8%), low PgR (1-9%) was 99 (8.4%). The number of cases with low both ER and PgR status was 4 (0.3%). The number of triple positive cases was 131 (11.1%).
Conclusion: There is a significant change in the rates of ER/PgR between 2006 and 2018 (p= 0.0001 and 0.0043 respectively for the ductal and <0.001 for ER in lobular). There is also a substantial difference although not statistically significant in HER2 rates. The reasons behind this change are not known but we may hypothesize that improved IHC quality and the accumulated experience of pathologists in addition to adoption of a more westernized lifestyle by patients as possible contributors.

PS-02-034
Analysis of prescribed adjuvant therapy for early triple-positive breast cancer
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Background & objectives: Adjuvant therapy - gold standard for BC therapy. It is based on the stage and the surrogate tumour subtype. For BC with HR expression and HER2 overexpression (TPBC) the NCCN protocols recommend a combination of chemotherapy, hormone and targeted therapy.
Methods: The aim of our study was to investigate the regimens of adjuvant therapy for TPBC that were prescribed to patients at our centre from 2012 to 2020. We selected patients with TPBC who received treatment at our centre from 2012 to 2020 and did not receive neoadjuvant therapy. Postoperative therapy (HT, TT and CT) appointments were monitored.
Results: The sample included 60 patients: pT1bN0 6.6%, pT1bN+ 3.3%, pT1cN0 35%, pT1cN+ 13.3%, pT2N0 25%, pT2N+ 15%, pT3N2 1.6%. Nobody received TT in the pT1b group, in the pT1c group - 51.7%, in the pT2 group - 54.1%. HT in the pT1b group received 66.6% of patients, pT1c group - 58.6%, pT2 group - 62.5%. Chemotherapy in the pT1b group received 50% of patients, pT1c group - 65.5%, pT2 group - 66.6%. The pT3N2 patient received a TT+CT. 36.6% of patients received a full combination of therapy, 30% - two types of therapy, 25% received one type of therapy, 1 patient didn't receive AT, 4 patients have no data.
Conclusion: Regardless of the pT category and the presence/absence of metastases in the regional lymph nodes of the patient with TPBC in the adjuvant mode, there are different treatment regimens. In only one third of the cases the patients were prescribed a combination of chemotherapy, hormone therapy, and targeted therapy. The presence of both hormonal receptors and HER2 expression in such patients and possible cross-talk between the signalling pathways of these receptors complicates the choice of therapy in this group.

PS-02-035
Intra- and inter-observer agreement in fibroepithelial lesions diagnosed with core needle biopsies in the breast
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Background & objectives: Fibroadenoma (FA) and phyllodes tumour (PT) create diagnostic difficulties with core needle biopsies (CNB). The aim of this study is to evaluate the accuracy of FA and PT diagnoses as well as inter and intraobserver variability in CNBs.
Methods: Sixty-one patients were included in the study. Five breast pathologists independently reviewed these in 3 rounds. Inter-observer κ statistics were assessed and they were interpreted as follows: Kappa(K) ≤ 0 as indicating no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.
Results: There was fair agreement between the pathologists with a κ value of 0.21 in round 1, and 0.28 in round 3. But there was none to slight agreement in round 2 (K =0.20). In the first round, the researchers were given only the age of the patients, while in the second round no information was given. The K values of stromal fragmentation, stromal cellularity, mitosis and atypia which were evaluated in the 3rd round were K = 0.73, 0.51, 0.47, and 0.40, respectively in the order of interobserver agreement. While intraobserver agreement was fair (K= 0.37, 0.37, 0.31) in 3 investigators, intraobserver agreement was moderate (K= 0.44,0.46) in 2 investigators.
Conclusion: The intraobserver agreement of the diagnosis of FEL in CNBs was found to be fair. To be able to diagnose FA and PT accurately there are no definite criteria however when the age, the defined histological criteria are given the agreement increases. The excisional biopsy is still gold standard in the diagnosis of FA and PT.

PS-03 | Cardiovascular Pathology Posters

PS-03-001
MMP9 expression and extracellular matrix remodelling in aortic diseases
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Background & objectives: Matrix metalloproteinases (MMPs) with roles in both physiological and pathological processes, are specialized for degrading various components of the extracellular matrix (ECM). Its synthesis and secretion may be affected by various endogenous or exogenous factors, including medications such as statins.
Methods: Aortic tissue of 40 patients with pathohistological diagnosis of dissection, mild and severe atherosclerosis, aortitis, mucoid degeneration and cystic medial necrosis was sampled. Tissue was stained with hematoxylin-eosin (HE) staining and immunohistochemically for MMP9. Epidemiological and clinically relevant data were obtained from patients records.
Results: Majority of patients were 60-69 years old, predominantly males. Most frequent diagnoses were atherosclerosis and dissection. MMP9 expression was noted rarely in mucoid degeneration and cystic medial necrosis, while number of cells were increasing in cases of mild atherosclerosis and aortitis, accompanied by mild to moderate ECM remodelling.

Most abundant immunopositivity for MMP9 was observed in inflammatory cells in severe atherosclerosis and aortic dissection, followed by intensive extracellular matrix remodelling. In cases of severe atherosclerosis MMP9 expression was most prominent in macrophages in proximity of plaque. Application of statins in therapy, in most cases reduced MMP9 expression in atherosclerosis.
Conclusion: MMP9 expression in aortic diseases is a major contributor to ECM remodelling, while statins up to some point led to reduced MMP9 expression.

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PS-03-002
Scanning electron microscopy in the diagnosis of complications of coronary artery stenting
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Background & objectives: Along with drug therapy and surgical treatment of coronary artery disease (CHD), interventional cardiology is actively being introduced into practice, where the most effective way is stenting of the affected segments of the coronary arteries.
Methods: A study of 45 stent coronary arteries (CA) with installed stents was carried out at various times (from one day to 3 years) in type 1 myocardial infarction (MI), using scanning electron microscopy (SEM).
Results: SEM helped to identify complications that developed during the installation of stents, and made it possible to see the processes of thrombus formation, as well as the formation of neointima. Thus, in 26.6%, type A dissection was observed, in 2% - CA perforation with the formation of pseudoaneurysm, in 8.2% - acute occlusion by a thrombus, in 4% - stent deformation.
Conclusion: Serial scans made it possible to determine the nature of the location of the stents in the affected areas of the coronary vessels. The magnification of the image of the object under study by several thousand times made it possible to objectively approach the issues of the quality of manufactured stents, possible damage during the installation of the latter into the lumen of coronary vessels, and the processes of thrombus formation on stents without medicinal coatings.

PS-03-003
Myocardium of children with congenital heart disease tetralogy of Fallot. Fibrosis, ploidy and ultrastructural features
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Background & objectives: The right ventricular (RV) myocardium of children with Tetralogy of Fallot (TF) undergoes hemodynamic overload immediately after birth, which results in significant morphological changes. This study aimed to investigate the myocardial morphology in children with TF and without cardiovascular pathology.
Methods: RV myocardium of patients with TF (n=51, 3-33 months) and without cardiovascular pathology (n=12, 1-36 months) were studied. Masson-trichrome and H&E-staining were used to assess the proportion of fibrosis and cardiomyocytes diameter. Cardiomyocyte ploidy was counted on DAPI-stained cell suspension obtained from paraffin-embedded tissue. Tissue fragments were also processed for electron microscopy. Significant correlations were revealed using nonparametric statistics.
Results: In TF children myocardial fibrosis didn't differ significantly from the control (5,5±2,1% vs 5,8±3,2%), didn't correlate with the age and cardiomyocyte diameters, but correlated with myofibrils assembly in cardiomyocytes. Fibrosis negatively correlated with low LVEF and O2 saturation. The cardiomyocyte diameter in TF children was significantly larger than in control (10,5±2,1μm vs 5,7±0,9μm) and correlated with the incidence of dyspnea-cyanotic attacks. The cardiomyocyte ploidy classes 2c:4c:8c:16c:32c in TF children was 22:49:24:4,5:0,5, in control - 71:2:6.2:0,8:0. In cardiomyocytes of TF children, ultrastructural signs of incomplete differentiation were revealed: foci of myofibril assembly, mitochondria, glycogen granules, centrioles in the sarcoplasm. The number of cardiomyocytes with areas without myofibrils decreased with age.
Conclusion: In RVOT myocardium of 1-2-year-old children with TF, fibrosis corresponded to age control, but increased with hemodynamic overload and hypoxemia. The diameter and ploidy of cardiomyocytes in children with TF exceeded the age norm, and the number of tetra- and octaploid cardiomyocytes was increased. Differentiation of cardiomyocytes with the assembly of myofibrils and other ultrastructural features was not only age-dependent but associated with hemodynamic parameters of the severity of congenital heart disease.

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PS-03-004
Gender differences in changes in the structure of the media of the ascending aorta in patients with its dilatation and/or dissection
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Background & objectives: Dilation and/or dissection of ascending aorta in women and men can be caused by various reasons, including connective tissue dysplasia, and, accordingly, can have different morphological manifestations, the study of which is the purpose of this work.
Methods: Ascending aorta biopsies of 24 women (35-84 years) and 20 men (31-74 years) with aorta dilatation and/or dissection were examined. The thickness of aortic media was measured, Masson-trichrome, alcian blue and Weigert stain were used. The smooth muscle cells presence, fibrosis, cystic media degeneration (CMD) and elastic fibres were determined using a 4-point scale. The results were processed statistically.
Results: The diameter of ascending aorta in women was 57±10mm, in men 53±6mm. Aortic media thickness in women (374-1597μm) and men (798-1810μm) did not differ statistically. Aortic dissection was detected in 6/24 women and 4/20 men. In women aorta, CMD occurred significantly more often than in men (13/24 vs 3/20), it correlated with an increase in the aorta diameter. Smooth muscle cells loss and elastic fragmentation were identified. In men, aortic media petrification was revealed significantly more often than in women, (11/20 vs 3/24), an increase in the ascending aorta diameter correlated with elastic fragmentation. Aortic dissection in all patients was associated with smooth muscle cells loss, and media fibrosis.
Conclusion: The remodelling of the aorta with its borderline enlargement in women and men was due to different changes in the aortic media morphology, which were possibly hormone-dependent. In women, changes in the structure of aortic media were characterized by more frequent development of CMD and the accumulation of acidic glycosaminoglycans, in men - with petrification of the aortic media. Aortic dissection in patients of both genders was due to focal necrosis, smooth muscle cells loss, and media fibrosis.

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PS-04 | Cytopathology Posters

PS-04-001
Endoscopic ultrasound-guided fine needle aspiration of intrapancreatic accessory spleen: a case series report and review of the literature

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Background & objectives: Intrapancreatic accessory spleen is a benign congenital anomaly that can pose a diagnostic challenge, both clinically and in cytopathology. Clinical suspicion in the differential of a hypoechoic tail lesion should include this possibility but cytomorphologic features allows for the diagnosis.
Methods: From two intrapancreatic accessory spleen (AS) diagnosed in the last year in our department, we retrospectively review the literature regarding the differential diagnosis of hypoechoic pancreatic tail lesions and the main clinicopathological findings of AS. The clinical, endoscopic and cytomorphologic features are described with the immunohistochemical stains performed onto cell block material (CD3, CD20, CD8, CD56, Synaptophysin).
Results: Two female patients, aged 61 and 67 years old, were diagnosed of pancreatic AS in the last year. Both were evaluated by endoscopic ultrasound fine needle aspiration cytology (EUS-FNA) with rapid on-site evaluation (ROSE). The cytological smears revealed the presence of a hematic background on which a lymphoid population with small cell morphology predominated. Additionally, the presence of intermixed vascular tracts and some groups of habitual pancreatic acinar morphology were observed. Immunostaining of the cell block material confirmed the described cytology consisting of B lymphoid aggregates (CD20+) together with mature T lymphoid cells (CD3+) intermixed with vascular tracts lined by endothelial cells of the splenic sinusoidal type (CD8+).
Conclusion: The diagnosis of pancreatic AS by EUS-FNA is infrequent and the series describe a similar distribution based on sex and wide age range presentation. They are usually small lesions (between 0.8 and up to 3 cm) of the pancreatic body or tail and the clinical differential diagnosis include neuroendocrine or solid pseudopapillary neoplastic tumours. Some cases show cystic changes and development of epidermoid cysts. Cytology allows a specific diagnosis of the entity based on cytomorphological evaluation, avoiding unnecessary surgical interventions.

PS-04-002
Investigation of HPV-positive ASC-US shows in every third case squamous intraepithelial lesions – results of the German combined screening

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Background & objectives: 2020 the combined screening with HPV test and cytology for the early detection of cervical cancer was introduced in Germany. With a cytology finding of atypical squamous cells and a positive HPV test a diagnostic colposcopy should be carried out.
Methods: In 2020 total of 62557 Pap smears were cytological examined and HPV test was performed by using the HPV Aptima Test, which discriminated HPV 16, HPV 18/45 and other types (16,18,31, 33,35,39,45,51,52,56,58,59,66,68). After diagnosis of atypical squamous cells of undetermined significance (ASC-US) and positive HPV test colposcopy in a specialized centre within 3 months were recommended.
Results: In 2352 women (3,8 %) ASC-US were diagnosed and in 1017 cases a HPV positivity was found. In 110 Cases (11 %) HPV 16 were detected, in 92 cases (9%) HPV 18/45 were detected and in 815 cases (80%) "other types" were detected. In 383 cases a colposcopy were performed and reported. In 272 cases (71 %) no essential lesion were detected and in 68 cases (18%) a low grade intraepithelial lesion (SIL) were diagnosed. In 43 cases (11%) a high grade SIL were diagnosed. No invasive cancer were found.
Conclusion: In the first year of the combined German screening we detected 1017 (1,6%) women with HPV positivity and atypical squamous cells of undetermined significance (ASC-US). After performing colposcopy 71 % of these women were inconspicuous and in 29 % intraepithelial neoplasia were detected. In 18 % LSIL and in 11 % HSIL were histological diagnosed. No invasive cancer was found. These data seems to be an expression of the importance of HPV positivity in ASC-US by detecting cervical lesions.

PS-04-003
Utility of Ki-67, p53 and PTEN biomarkers in endometrial carcinoma by imprint cytology

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Background & objectives: Worldwide, endometrial carcinoma is one of the most frequently diagnosed cancer among women and a considerable cause of death. Cytomorphology alone is not often sufficient to provide an accurate diagnosis, thus immunocytochemistry is required for aim assist.
Methods: Endometrial samples freshly resected from 168 women who underwent total abdominal hysterectomy were studied. The cytological diagnosis was confirmed by pathologists. Cytological imprint smears were obtained by touching the cut surface of fresh cancer tissues. The specimens were stained with Papanicolaou stain, Ki-67 (clone MIB-1, dilution 1:150), p53 (clone DO-7, dilution 1:50) and PTEN antibody (clone 6H2.1, dilution 1:80).
Results: Out of 168 cases, 123 were endometrioid and 45 non-endometrioid carcinomas. The rate of positive expression of Ki-67 (85.5%) and p53 (82.4%) was high in type II tumours ($P<0.001$), in cases of advanced and aggressive clinical stage and poor histologic differentiation and in cases with myometrial infiltration depth >1/2 ($P<0.001$). Also, high percentage of p53 (100%) positivity was found in all cases with positive lymph node involvement. High rate of positive expression of PTEN was observed in type I (43.4%) ($P=0.910$) and low-grade carcinomas (60.1%) ($P=0.03$), in unaffected by the disease lymph nodes ($P<0.001$) as well as in cases with myometrial infiltration depth <1/2 ($P<0.001$).
Conclusion: We believe that the use of Ki-67, p53 and PTEN antibodies in addition to cytomorphologic features, appeared to be useful for the diagnosis of endometrial carcinoma in endometrial cytology with imprint smears and may help identify tumours with high malignant potential and possible aggressive behaviour or ability to relapse offering valuable information, both in prognosis and treatment of patients with endometrial carcinoma.

PS-04-004
Role of endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of mediastinal disease in young patients

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Background & objectives: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) procedure is essential to diagnose diseases with mediastinal involvement. Cancer in younger patients comprises a distinct entity associated with poorer prognosis. This study aimed to review clinicopathological data in young patients who underwent EBUS-TBNA.
Methods: We retrospectively reviewed EBUS-TBNA results over two years (2019-2021) in patients aged under 55 years old. Rapid on-site evaluation (ROSE) was performed in all cases. Cytopathologists selected samples for ancillary studies. RT-PCR system (Therascreen/Idylla) was

used for EGFR, ALK and ROS1; after May 2020, Next Generation Sequencing 52 gene-panel-based method was carried out (Oncomine Focus Assay, Thermo Fisher Scientific l).
Results: We studied 60 patients (38M/22F) aged 30-54. Of total, 61.7% showed negative for malignancy diagnosis; the reason for testing was a suspected diagnosis of sarcoidosis in 12 cases. One bronchogenic cyst was observed. In the remaining 23 cases (38.3%), 60.8% corresponded to NSCLC (86.6% adenocarcinoma, 1 poorly differentiated carcinoma and 1 squamous carcinoma). Molecular testing on adenocarcinoma cases was performed: 1 patient carrying EGFR deletion, another with BRAF mutation and 2 more patients with KRAS mutation and ALK fusion, respectively. 4.3% presented as small cell carcinoma and 8.7% as Hodgkin's lymphoma. In addition, 1 NUT carcinoma, 3 metastases of renal cell carcinoma and 2 of breast carcinoma were found.
Conclusion: EBUS-TBNA combined with ROSE has a high yield in the diagnosis of both neoplastic and non-neoplastic diseases with mediastinal involvement. In younger patients, the former may present with nonspecific symptoms and often have advanced disease at the time of diagnosis. Molecular testing in lung cancer is mandatory, especially in young patients. Rare subtypes of lung carcinoma should be included in the differential diagnosis.

PS-05 | Dermatopathology Posters

PS-05-001
Young pathologist's nightmare: unexpected dermatopathology cases
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Background & objectives: Dermatopathology encompasses a wide group of neoplastic/non-neoplastic lesions. Accurate pathologic diagnosis may be difficult especially for young pathologists, as there are numerous overlapping features. Our aim was to demonstrate some extraordinary situations that we often encounter in daily routine.
Methods: Five patients with unexpected pathologic diagnosis were retrieved between May 2020 and March 2021. The gender, age, site/characteristics of the lesions, preliminary diagnosis were collected from clinical data. After the first histopathologic evaluation, connection with the clinical diagnosis was established for all lesions. The second biopsies were taken from three of the patients for confirmation.
Results: Three of the five patients were female and the age distribution was between 6 and 64. The biopsy sites were lower extremity (three biopsies), back(one biopsy), scalp(one biopsy). Two of the patients were children and the preliminary diagnosis were traumatic panniculitis and vitiligo. The pathological diagnosis were granuloma annulare and mycosis fungoides, respectively. While two of the patients' clinical diagnosis were basal cell carcinoma and necrobiosis lipoidica, the histomorphology was surprisingly compatible with lichen planus in both biopsies. The preliminary diagnosis of the other patient was squamous cell carcinoma. The biopsy demonstrated acantholytic disease with suprabasal clefting. The results of blood tests and immunofluorescence evaluation were also consistent with pemphigus vulgaris.
Conclusion: In the present case series, we evaluated the challenging spectrum of dermatopathology. Our cases suggested that the preliminary diagnosis is very important in skin lesions, but we should keep in mind the other possibilities. Clinical appearance sometimes can have overlapping features, and the experience of pathologist plays an important role in this situation. Therefore, the combination of good clinicopathologic communication and expert ideas is necessary in the management of challenging cases.

PS-05-002
Cutaneous metastases: a case series
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Background & objectives: Cutaneous metastases from a distant malignancy are a diagnostic challenge for pathologists. Secondary tumour deposits in the skin represent advanced malignancy and the skin is an uncommon site of metastatic disease when compared to other organs (0.5-2% through all malignancies).
Methods: The present study has analysed 41 cases of cutaneous metastases from internal malignant neoplasms. Patient characteristics, tumour localization, and clinical pre-diagnosis were evaluated.
Results: We evaluated 41 cutaneous metastases; the mean age of the patients was 62. Nine cases (23%) presented as primary manifestations of the tumour; biopsy evaluation in these cases suggested the possible primary tumour site and triggered further evaluation. The most common malignancy was breast carcinoma, and most common localization was anterior chest wall through all patients as well as for female patients. The most common malignancies were lung (n=5, 26%) and gastric carcinomas (n=5, 26%) for male patients, and the head and neck region was most common localization. In our cohort, 32 patients were clinically suspected of metastasis. However, 9 patients' clinical pre-diagnosis was primary skin malignancies without metastasis suspicion.
Conclusion: The classic presentation of cutaneous metastases was a firm, painless, flesh-coloured to an erythematous dermal nodule (or nodules). There is usually a long-time lag between the diagnosis of the primary malignancy and the recognition of the skin metastases. It is concluded that cutaneous metastases occur rarely and the presentation of internal malignancy with skin involvement is uncommon. Metastasis to the skin is often a pre-terminal event that heralds poor outcomes.

PS-05-003
Primary cutaneous gamma/delta T-cell lymphoma in Taiwan is more often solitary and not ugly-looking
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Background & objectives: Primary cutaneous gamma/delta T-cell lymphoma (PCGD-TCL) is a very rare and aggressive. Patients usually present with multiple plaques, tumours, and/or subcutaneous nodules primarily distributed over the extremities. We present the clinicopathological findings of a small cohort of cases from Taiwan.
Methods: We investigated the clinicopathological features of PCGD-TCL cases with chart review, extensive immunohistochemistry for phenotyping including T-cell receptor (TCR) βF1, TCR-γ, and TCR-δ, in situ hybridization for EBV-encoded small RNA (EBER), treatment modality, and follow-up information.
Results: We identified six patients with a median age of 57. The lesions presented in the head and neck regions (n=3) and extremities (n=3). In five patients, the lesions were solitary, including two ulcerative. The tumour cells expressed CD3, CD8 (4/5), TIA-1 (5/6), granzyme B (5/6), TCR-γ (3/3), and TCR-δ (4/6). In two cases, the neoplastic cells expressed TCR-γ but not TCR-δ. Three cases partially expressed βF1. All negative for EBER. Four cases were at stage IE, and two at IIE. Excluding one recent case under chemotherapy, one died of lymphoma in 7 months, the remaining four were in complete remission after radiotherapy, either alone or with chemotherapy, in 6-126 months.
Conclusion: In this small series of cases from Taiwan, we found that five of the six PCGD-TCL cases presented with a solitary lesion, clinically mimicking lipoma or epidermal inclusion cyst in two cases. The clinical presentation is distinct from the ugly-looking, frequently necrotic, multiple tumorous lesions as reported in the literature. It is important to include PCGD-TCL in the differential diagnosis of solitary cutaneous TCL and perform extensive immunohistochemical study including cytotoxic markers and TCR.

PS-05-004

Pathological assessment of sentinel nodes in patients with cutaneous melanoma in Russian cancer research centre

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Background & objectives: Evaluation of sentinel lymph node (SLN) is crucial for cutaneous melanoma staging and treatment in patients with clinically negative lymph nodes. We evaluated SLN of patients who underwent SLN biopsy (SLNB) for skin melanoma between 2018 and 2021.
Methods: SLNB was performed in 303 patients, an average age of 53,7 years. Grossing of SLN depended on the size: those less than 5 mm were taken entirely, 5-10 mm were bevalved and those larger than 10 mm were grossed in bread loaf technique. After evaluation of the hematoxylin- and eosin-stained sections (9 cut levels per block), immunohistochemistry was performed.
Results: The stage distribution was following: pT1 - 65 (21,5%), pT2 - 98 (32,3%), pT3 - 74 (24,4%), pT4 - 58 (19,1%), in 6 cases stage was unknown (pitfalls of primary tumour grossing). The average Breslow index was 2,85 mm.
Metastasis was detected in 42 cases (13,7%), in 2 cases (4,8%) the excised tissue did not contain lymph nodes. Among all positive SLNs, metastases up to 2 mm were detected in 11 cases (26,2%) by immunohistochemistry (S100, SOX10 or Tyrosinasa).
Conclusion: Pathological assessment of the sentinel lymph node for malignant melanoma is extremely important, but the process is unstandardized yet.

PS-05-005

Male patient with a primary apocrine sweat gland carcinoma of the axilla: A case report of a rare entity

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Background & objectives: Primary apocrine sweat gland carcinoma (PASGC) is a rare neoplasm with only 51 cases reported in the literature. It is often underrecognized, which can lead to undertreatment and enable disease progression.
Methods: A 74-year-old man with a recent history of adenocarcinoma of the lung, in remission for the past 6 years, presenting at our institution with a painless left axillary mass with 2cm, slowly growing for the past 3 years. On ultrasound examination, a diagnosis of epidermal keratinocytic cyst was suggested, and the patient remained on follow-up.
Results: As part of adenocarcinoma surveillance the patient was submitted to PET-CT, which showed the axillary mass was avid and suspicious for a metastatic neoplasm and was excised.
Macroscopic examination revealed a 2x2cm white nodule. Histologically, the tumour was well-circumscribed but infiltrative and centred in the dermis. Neoplastic cells showed an abundant, granular, eosinophilic cytoplasm, and large nuclei with prominent nucleoli. Immunohistochemically, they were positive for CK7, GCDFP-15, RA and negative for RE, RP, CK20, TTF-1, CDX2, P40 and PAX-8.
Based on these findings, a diagnosis of apocrine carcinoma was made. A full imagological workup of both breasts was performed, which found no suspicious masses/nodules, enabling a final diagnosis of PASGC.
Conclusion: PASGC are indolent but malignant tumours, with frequent local recurrence and lymph node metastasis. Due to their rarity, are often clinically misdiagnosed, leading to delayed therapy. Furthermore, a differential diagnosis with apocrine breast carcinoma cannot be made on immunohistochemistry or morphology alone, requiring a full imagological workup.
Surgical excision and lymph node dissection of clinically positive nodes are considered the treatment of choice. Further reporting and literature review are necessary to better understand the natural behaviour of this disease.

PS-05-006

The histopathological spectrum of inflammatory skin response to tattoo pigment

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Background & objectives: With the rising popularity of skin tattoos, it is expected that the rate of adverse reactions will rise. As newer inks are utilized. This study will describe both the clinical and histopathologic features of pathologic reactions to decorative tattoos.
Methods: There are six main categories of histopathologic reactions: allergic hypersensitivity, granulomatous, interface, pseudolymphomatous, tumoral and infectious.
We present a series of six cases of tattooed skin biopsies from 3 male and 3 female patients with ages between 29-77 years old, with clinical diagnoses of psoriasis/lichen planus, pseudolymphomatous reaction to tattoo, acral melanoma/blue nevus, dermatofibroma/dermal nevus, eczema, foreign body granuloma.
Results: Microscopic examination revealed three cases of granulomatous reaction(a foreign body granuloma with multinucleated giant cells and two sarcoidal granulomas); a case of superficial perivascular lymphocytic dermatitis; a case of dermatofibroma(with a dermal proliferation of fibroblasts and histiocytes, with storiform pattern) and a case of pseudolymphomatous reaction.
Common skin reactions to tattoo include acute inflammatory reaction due to the trauma caused by needles with/without superficial or deep local infections, systemic infections, allergic contact dermatitis, photodermatitis, granulomatous, lichenoid reactions and skin diseases localized on the tattooed area (eczema, psoriasis, lichen, and morphea). We also have to consider the possibility of the development of cutaneous pseudolymphomatous reactions, pseudoepitheliomatous hyperplasia, or even cutaneous neoplasms.
Conclusion: Knowing and understanding the histopathological spectrum of skin reaction to tattoo pigment will increase clinical detection of situations requiring additional evaluation, whether it is for underlying infection, systemic involvement of disease, or to rule out a cutaneous malignancy. In suspect cases, especially papulonodular lesions arising in tattooed skin, early histopathologic diagnosis followed by excision of the lesion is important.

PS-05-007

Multinucleated cell angiohistiocytoma: a series of 15 cases

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Background & objectives: Multinucleated cell angiohistiocytoma is a rare benign tumour with subtle histopathological features, making it an easy to miss diagnosis. The clinical appearance under the form of small red papules often leads to it being confused with an inflammatory disorder.
Methods: In this study, we reviewed a series of cases diagnosed over the course of 5 years (2017-2021) in one Dermatopathology unit. We examined the HE sections and clinical photos of 15 cases, aiming to identify common histopathological features that could aid in the diagnosis of this proliferation.
Results: MCAH is characterised by a histiocytic proliferation with multinucleated cells and dilated small blood vessels. In our cases, the histiocytic proliferation was distinct with frequent angulated and wavy cells, some with only a few scattered multinucleated cells present. There was a perivascular lymphocytic infiltrate, with half of our cases including frequent mastocytes. Thickened collagen bundles, randomly distributed in

the upper dermis were also common. Less common histological features were represented by the presence of neutrophils, sebaceous and basaloid induction and also an exophytic, sessile architecture.
Clinically seven of our cases presented on the face and scalp, localisations not frequently reported in literature for this tumour.
Conclusion: Multinucleated cell angiohistyocitoma is a proliferation that does not have striking features and thus requires a more thorough examination. Most of the cases we examined were clinically suspected of being inflammatory disorders, such as lupus erythematosus, lichen planus, sarcoidosis or even lymphoproliferative disorders. For these reasons, we find that this is an important diagnostic to be aware of.

PS-05-008
Cutaneous metastases: a series of 74 cases
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Background & objectives: Metastasis is the final stage in the evolution of malignant tumours and represents the main cause of cancer morbidity and mortality. Accurate histopathological diagnosis is urgent and essential for proper treatment.
Methods: This is a retrospective study including 74 cases diagnosed in our Pathology Department over a period of seven years (2015-2021). We thoroughly reviewed the HE slides, immunohistochemistry slides and the clinical information from the virtual database. Our aim was to observe histopathological features and make clinical correlations.
Results: Most cutaneous metastases were those of malignant melanomas (42%), followed by breast carcinoma (30%). The latter cases explain why most of the cutaneous metastases were diagnosed in women (68%).
Histopathologically, most of the cases did not present with ulceration (16%), epidermotropism (12%) or lympho-vascular invasion (19%). The typical clinical presentation was that of a nodule, with few cases of pigmented patches and dermatitis-like lesions.
The median age was 61 years, with one case of a 24-year-old without a prior history of melanoma.
Most of the cases presented on the trunk (44%), followed by head and neck (27%), extremities (14%), abdomen (11%), pelvis (4%).
Conclusion: Cutaneous metastases can be an important diagnosis to consider even in cases without clinical suggestion (one third of our cases) or without former history of neoplasms (one fourth of our patients). Although most metastases retain the histopathological features of the primary tumours, some can have a deceivingly bland appearance. Metastases of lobular breast carcinoma can mimic inflammatory disorders such as granuloma annulare, morphea or lupus.

PS-05-009
A breast lesion on the nape?
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Background & objectives: Endocrine mucin-producing sweat gland carcinoma (EMPSG) is a rare lesion, often underrecognized, mostly found in old women eyelid with heterogeneous growth pattern and considered the cutaneous analogue of solid papillary carcinoma of the breast.
Methods: We describe a case of a 75-years old woman complaining an asymptomatic skin coloured slightly raised lesion on the nape that underwent excisional biopsy. Gross examination revealed, in the dermis a seemingly cystic lesion of 0,6 cm of diameter. Specimen was processed according to routine procedure.
Results: Histological examination revealed, under a unremarkable epidermis, a cystic nodule composed of medium sized cells with round nuclei, sometimes prominent nucleoli, a discrete clear/eosinophilic cytoplasm and finely dispersed chromatin, organized in a predominant cribriform pattern and characterized by following immunohistochemical profile: EMA+, BerEp4+, CK7+/-, GCDFP15-/+, WT1-/+, CK20-, TTF1-, CEA-, Mammoglobin-, c-ErbB2-, positivity for oestrogen, progesterone receptors, and variable positivity for chromogranin, synaptophysin and androgen receptors. Moreover, PAS-Alcian stain revealed focal extracellular mucin deposits. Proliferation index assessed with Ki67 antibody, was low, about 5-10%. Provided the necessity to clinically exclude a metastasis, a diagnosis of Endocrine mucin-producing sweat gland carcinoma was made.
Conclusion: Only 22 EMPSG are described in literature, 50% initially misdiagnosed. Rare publications hypothesized the sequence carcinoma in situ-invasive carcinoma-mucinous carcinoma and parallelism with breast solid papillary carcinoma in situ-invasive solid papillary carcinoma-mucinous carcinoma, based on phenotypical and immunohistochemical similarities. Its outcome is favourable, with possible cutaneous recurrences and, because of its rarity, the molecular profile has not been studied yet. Therefore, investigating its molecular and chromosome abnormalities, could confirm breast-analogy and improve understanding the pathogenesis of both lesions.

PS-05-010
Cutaneous metastasis: a study of 58 cases diagnosed in our pathology unit
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Background & objectives: Cutaneous metastasis can arise in a variety of cancers, not infrequently being the first sign of malignancy. Patients most commonly present with flesh-coloured nodules or plaque and only a part of them are suspected of metastasis.
Methods: We retrospectively reviewed the clinical records of 58cases diagnosed with cutaneous metastasis in our service during a twelve-years period(2009-2020). Our objective was to collect data and establish clinico-pathological correlations regarding cutaneous metastases diagnosed at Colentina-University-Hospital. We collected information from our database(sex, age, clinical presentation, suggestion of metastasis, presence of malignancy in the past) and methodically re-examined hematoxylin-eosin and immunohistochemistry slides.
Results: The age distribution was 34-89 years(mean 65), the majority of the patients were females(55,17%), 67,92% had clinical history of malignancy, only 18,87% of cases were sent as cutaneous metastasis.76,36% of cases were clinically described as single nodules, 9,43% as carcinoma erysipeloides and 3,76% as alopecia neoplastica. Trunk was frequently involved(23 cases), followed by head and neck(9 cases) and extremities(8 cases). Breast carcinoma(43,4%) and melanoma(22,64%) were the most common tumours to present with cutaneous metastasis, followed by gastro-intestinal carcinomas(20,75%) and prostatic adenocarcinoma(7,55%). The vast majority of the tumours weren't ulcerated and didn't present necrosis(84,91%).81,13% tumours were associated with a significant reactive inflammatory process, 32,08% presented vascular invasion and 11,32% perineural invasion.
Conclusion: In our study, most cases consisted of single nodules on the trunk at patients who already had a diagnosis of a malignancy, the most frequent being breast carcinoma and melanoma, as expected, accuracy of the clinical diagnostic increased when dealing with patients with known malignancies. It's important to further maintain a high level of suspicion when dealing with patients who already had been diagnosed with a form of malignancy in the past.

PS-05-011
Histopathological features of COVID-19 cutaneous lesions: a clinico-pathological study of 5 patients

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Background & objectives: With the increase of the coronavirus disease, more extensive data has shared about the dermatological findings of the disease. We aimed to describe histological features of cutaneous eruptions of the Covid 19 patients in our hospital.
Methods: We evaluated all skin biopsies which performed in hospitalized Covid-19 infected patients presenting concomitant cutaneous manifestations since March 2020. We reviewed 3 male and 2 female patients with a mean age of 24 years (range from 3-52). All patients had a nasopharyngeal swab positive for Covid-19 before the occurrence of rash.
Results: Clinically, all five patients presented maculopapular rash of the trunk and extremities. The latency between rash and onset of extracutaneous Covid-19 symptoms ranged from 3 to 30 days. Histologically, patients showed spongiotic dermatitis, basal vacuolar degeneration, red blood cell extravasations, endothelial hyperplasia, perivascular lymphocytic infiltrate, scarce neutrophils and eosinophils in a variable degree. Fibrinoid necrosis of the vessel walls was not found. Histopathological features of cutaneous manifestations reported in our study were unspecific.
Conclusion: Spongiosis and perivascular inflammatory infiltrate can be observed in various eruptions such as viral rash and drug reaction. Histopathological features of these two types of eruptions can also overlapping. Therefore, further studies are needed to clarify the relationship between cutaneous rash and Covid-19 virus.

PS-05-012
Study of the use of imiquimod for psoriasis model formation
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Background & objectives: In connection with a significant decrease in the quality of life of patients suffering from psoriasis, it became necessary to study the formation of a psoriasis model to study the possibilities of therapy choosing.
Aims: to develop psoriasoform skin lesions in rats.
Methods: 20 female Wistar rats were used. A psoriasis model was formed by applying a 10% solution of imiquimod to the back for 10 minutes once a day. 5 rats made up the control group (1gr). In 2nd group the solution of imichimod was used for 1day, in 3rd group-3days, in 4th group-5days. Histological preparations were stained with hematoxylin&eosin.
Results: In 2gr, 2 animals showed an increase in cellularity in the dermis, mild hyperaemia in the papillary layer of the dermis, and no pathomorphological changes were found on the side of the epidermis. In 3gr, the following changes in the epidermis were revealed in 3animals: in one case-acanthosis, in two animals-a scab with the formation of intraepidermal polymorphic cell proliferation. 4 animals in the dermis had polymorphic cell infiltrates, diapedesic haemorrhages, oedema and hyperaemia. In 4gr, 4 rats showed changes in the epidermis and in the dermis. Acanthosis, spongiosis, and the formation of epidermal pustules with exudate containing inflammatory cells were observed. In 2cases in 4gr,epidermal exfoliation, erosions, pustules & plaques was revealed.
Conclusion: The application of a 10% solution of imiquimod induces changes in rats similar to those in the dermis and epidermis in human psoriasis. Thus, changes in the skin after using a 10% solution of imiquimod in rats can serve as a model for psoriasis.

PS-05-013
The impact of hyaluronic acid and trehalosa on histological parameters of the skin
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Background & objectives: To study the morphological effects of the skin biorevitalization to improve its quality and rejuvenation before and after exposure.
Methods: The study involved 20 women aged 51. Biorevitalization was carried out by using a single injection of hyaluronic acid and trehalose under local anaesthesia. The skin was taken by punch biopsy before and 6 weeks after face injection. Slides were stained with hematoxylin and eosin and Masson's trichrome.
Results: The average thickness of the epidermis was 70.21±3.38 μm before the procedure and 85.13±7.01 μm after 6 weeks ($p=0.05$). The average thickness of the papillary and reticular layer of the dermis was 97.62±7.98 μm and 667.88±48.16 μm before the procedure, respectively. After the procedure, thickness decreased by 30% ($p<0.05$) and amounted to 68,95±5.03 μm and 468.67±43.53 μm. Decreased dermis thickness occurred due to decreased tissue oedema. In Masson's stained samples, the bulk density of collagen fibres was 65.6±7.0% before the procedure and increased to 74.4±5.8% after the procedure ($p<0.01$).
Conclusion: Hyaluronic acid and trehalose injections show significant changes that include epidermis thickening, induration of the dermis, and decreased tissue oedema.

PS-05-014
H Syndrome, a rare autosomal recessive genodermatosis, a case presentation
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Background & objectives: This is a rare autosomal recessive genodermatosis with possible severe multisystem involvement. Its major cutaneous signs are hyperpigmentation, induration, and hypertrichosis. The cutaneous manifestations are very important as they are a pathognomonic clue for the diagnosis of this multisystemic syndrome.
Methods: A 13-year-old child presented with asymptomatic brown patches and hypertrichosis over his legs, inner thighs and the back, which appeared during infancy, associated with hearing loss since birth. He was diagnosed with insulin-dependent diabetes mellitus at the age of 7.
There was parental consanguinity and history of death of his sister from a cardiac problem and similar skin findings.
Results: On examination, the child was short for his age. He had indurated and hyperpigmented patches over the thighs, legs and the lower back with hypertrichosis and enlarged ambiguous genitalia. No hallux valgus was noted.
Abdominal examination revealed splenomegaly, but no hepatomegaly or lymphadenopathy was present.
Abdominal ultrasonography confirmed splenomegaly and echocardiography showed a pericardial mass.
Genetic study was not performed as it was not available to confirm the SLC29A3 gene on the long arm of chromosome 10 (10q22).
Histopathological examination of the involved skin showed mild acanthosis, increased melanin deposition in the basal keratinocytes, and nonspecific perivascular lymphocytic infiltrate in the superficial and mid dermis with mild dermal fibrosis.
Conclusion: We presented a case of H syndrome, a rare autosomal recessive genodermatosis.
Our diagnosis was based on the clinical and family history, clinical examination and investigations including a skin punch biopsy, and the patient was referred for the paediatrics department for further management and follow up.
It is important to recognize this syndrome which presents with a wide clinical variability and not to miss the characteristic skin findings which in most cases are good clues to the diagnosis.

PS-05-015

Lichenplanopilaris and telogen effluvium associated with severe dysaethesia and a lipedematous scalp, a case report of alopecia with multiple aetiological factors

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Background & objectives: A 47-year-old female who presented with a two-month history of diffuse scalp swelling which started after otitis media, associated with constant pain radiating to the face. Later she developed two patches of hair thinning in the vertex and occiput.
Methods: Clinical examination revealed a boggy and extremely tender scalp without erythema. There was reduced pin prick over V1 and V2 nerves. Other cranial nerves were normal on examination. CT scan and MRI of the head revealed thickened scalp fat up to 13.7mm.
Vitamin D, iron, zinc and thyroid levels were normal. Antinuclear antibodies(ANA) were borderline elevated. She had no anaemia.
Results: On microscopy, horizontal sections of the 4mm punch biopsy of the thinned vertex hair patch showed mild folliculocentric lymphocytic infiltrate with mild lamellar perifollicular fibrosis at the infundibulum, in keeping with lichen planopilaris (scarring alopecia), supported by the borderline elevated ANA levels.
Horizontal sections of the occipital hair loss patch biopsy showed seven telogen hair follicles without fibrosis or inflammation, supportive of telogen effluvium (nonscarring alopecia).
She was treated with gabapentin 400mg tablets TDS, greater occipital nerve block to control pain and topical betamethasone for alopecia.
One case of lichen planopilaris with androgenetic alopecia has been reported but such triple aetiology combination with lipedematous alopecia has not been described before.
Conclusion: We report a case of scarring alopecia; lichen planopilaris, associated with a nonscarring alopecia; telogen effulvium, in a background of severe hyperasthesia and lipedematous scalp, requiring gabapentin and nerve block to control the severe pain.
Hair loss due to multiple aetiological factors is reported, but not in a similar setting.
It is possible that severe occipital neuralgia together with the lipedematous scalp may have resulted in nonscarring alopecia.
A good clinicopathological correlation when reporting similar cases is very essential.

PS-05-016

Alopecia areata: is the recruitment of plasmacytoid dendritic cells time dependent? An immunohistochemical study

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Background & objectives: The expression of type 1 interferon-related proteins in alopecia areata (AA) lesions has been demonstrated and since plasmacytoid dendritic cells (pDCs) are premium producers of type I IFN their presence in acute, intermediate and chronic AA lesions was investigated.
Methods: Forty biopsy specimens, from a corresponding number of patients with AA lesions, were collected Twelve (30%) of them were categorized into acute, eleven (27.5%) into intermediate and 17 (42.5%) into chronic stage of the disease, according to the duration of the lesions. Immunohistochemical analysis with CD4, CD8, FOXP3 and CD123 antibodies was performed in formalin-fixed, paraffin-embedded tissue sections.
Results: The lymphocytic infiltration was perifollicular, and in 37.5% of the cases an intrafollicular distribution was identified, as well. Heterogeneity in lymphocytic density and distribution was present among hair follicles of the same specimen. CD123+ cells were identified in 33.3% of the cases in a perifollicular distribution. Their presence was associated with the chronologically determined stages of the disease ($p=0.022$) more often observed in the intermediate stage of AA, followed by the acute stage. Furthermore, an association of CD123+ cells and FOXP3+ cells in the immune infiltrate surrounding the hair follicle was found ($p=0.013$). No statistically significant association between CD123+ cells and CD4+ or CD8+ cells or their ratio was found.
Conclusion: This study suggests a role of pDCs in the pathogenesis of AA and a possible contribution in the initiation and in the early stages of the disease, but not in maintaining the chronic process. Coexistence and association of regulatory T cells and pDCs in a subset of AA lesions may reflect the biology of an impaired immune microenvironment.

PS-05-017

Audit of melanoma sentinel lymph node protocol pre- and post- updated EORTC protocol at a tertiary centre

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Background & objectives: The sentinel lymph node is an important prognostic marker in melanoma but approaches to pathological handling are varied. This study compares the positive detection rate and workload between the previous local protocol at Ninewells Hospital and updated EORTC protocol.
Methods: The records of 58 consecutive patients with primary cutaneous melanoma who underwent sentinel lymph node (SLN) biopsy at Ninewells Hospital and Medical School in East Scotland between 01/09/2017-01/11/2020 were reviewed. A positive detection rate of metastasis in SLN biopsy and the number of slides generated per case were compared between the previous local protocol and the updated EORTC protocol.
Results: SLN protocol was performed on a total of 108 sentinel lymph nodes (previous protocol n=45, new protocol n=63). With use of the previous local protocol, 8.89% of sentinel lymph nodes (4/45) demonstrated metastatic melanoma deposit. With implementation of the updated EORTC protocol, 12.69% of sentinel lymph nodes (8/63) showed metastatic deposit. The new protocol is associated with a higher detection rate (+3.81%) but this was not significant (Chi squared p=0.53). However, the average number of slides generated in the old protocol was 38 slides per lymph node but just 11 slides per lymph node on the new protocol ($p=<0.001$, Welch's t-test).
Conclusion: The new EORTC protocol is proven to be non-inferior in detection of positive nodes but generates significantly fewer slides than the previous local protocol. The findings add evidence to support the use of the updated EORTC protocol for evaluating SLN. Studies with greater power would clarify whether the new protocol also has increased sensitivity to nodal disease.

PS-05-018

The characteristics of primary cutaneous melanomas associated with sentinel lymph nodes metastases

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Background & objectives: The purpose of this study was to evaluate the clinical and histological features of the primary cutaneous melanomas associated with sentinel lymph node metastases.
Methods: From the database of our pathology department, we selected the cases diagnosed as primary cutaneous melanomas, followed by sentinel lymph nodes excision from 2018 to 2020. We evaluated 26 cases with positive sentinel lymph nodes and 31 cases with negative sentinel lymph nodes.

Results: The first group included 14 females and 12 males (median age: 63,1 years). For the second group (20 females and 11 males), the median age was 55 years (p=0.0162). In the group with positive sentinel lymph nodes we noticed more often the nodular subtype (50%; p=0.0145), a Breslow index >4 mm (69,2%; p<0.001), ≥5 mitosis/mm^2 (65,4%; p=0.0126), ulceration (77%; p=0.0275), lymphovascular invasion (19,2%; p=0.0106), satelites (27%; p=0.0103) and pT4 stage (69%; p<0.001). In the second group: superficial spreading type, vertical growth phase (67.7%), Breslow index >4 mm (13%), ≥5 mitosis/mm^2 (32,3%), ulceration (48,5%), satelites (only 3,2%), early stages (61,2%), lymphovascular invasion absent. In both groups, the Clark level IV predominated.
Conclusion: In our study, the most important factors that can predict metastases in sentinel lymph nodes are the Breslow index and the pathological stage. The clinicopathological characteristics that affect the outcome of the patients are an advanced age at diagnosis, satelitosis, lymphovascular invasion, mitotic rate, the nodular subtype, and ulceration.

PS-05-019
A 1-year retrospective study of PD-L1 and CD8 expressions in malignant melanoma in South-eastern Romania
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Background & objectives: Anti-programmed cell death protein 1(PD-1) therapy markedly improves prognosis in patients with the most aggressive tumours - melanomas. Our study is ongoing to better understand the role of PD-L1 as an immune-oncology marker, in combination with other prognostic features.
Methods: Retrospective evaluation of 31 cases of melanoma performed at our hospital in Constanta between 2018 to 2019. Data retrieved included clinical history and histological features such as Breslow tumour thickness, Clark level of invasion, greater dimension, pTNM stage, inflammatory infiltrate, lymphovascular and perineural invasion, number of mitoses. Histological and immunohistochemical studies (PD-L1 and CD8) were followed by statistical analysis.
Results: Of 31 cases, 57% were females, 43% were males, with anatomical sites such as posterior thorax 40%, followed by head and neck 23% of cases and less frequent in other sites. Between the four histologic types of melanoma encountered in our study we established some statistically significant differences of PD-L1 expression specially between invasive superficial spreading melanoma with vertical growth nodule/nodular melanoma and acral melanoma /in situ melanoma. The Breslow tumour thickness is the only reliable and recognized prognostic feature in melanoma, showing in this study a general negative correlation with the PD-L1 expression, with a rising percentage of negative expression cases in melanomas with higher values of Breslow.
Conclusion: An integrated analysis of both PD-L1, CD8 and TIL's are be useful elements for predicting prognosis in patients with melanoma. Our findings suggest that there is a high variation of PD-L1 expression in melanoma, depending on the morphology, but further studies are needed in a larger cohort of melanoma patients, in order to validate a predictive value of the immunohistochemical PD-L1 expression.

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PS-05-020
The intricate aspects of diagnosing a nevoid malignant micromelanoma: a case report
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Background & objectives: Micromelanomas, having a diameter under 5 mm, are a new topic of interest in dermatopathology, raising awareness around early detection of this potentially fatal cancer. A nevoid micromelanoma poses a triple threat, considering its benign-looking features, rarity and small size.
Methods: This study reports a 34-year old Caucasian female, who presented to the hospital with multiple cutaneous lesions, four on her right upper arm and two on her right lower leg. Examination reveals the lesions were varying in size (from 4 mm to 7 mm) and macroscopic appearance (some nodular, some polypoid and one white plaque, with a grey halo).
Results: On histopathological examination, the results were as follows: three of the lesions were compound nevi, two were intradermal nevi, one of which was associated with a basal cell carcinoma with multiple risk factors, and the white, 4 mm, plaque was diagnosed as MELTUMP. A second opinion was requested and the lesion was ruled out as a nevoid malignant melanoma (Breslow index 0.8 mm, pT1b). To support the diagnosis, immunohistochemical analysis was performed, which showed melanocytic proliferation positive for S100 and MelanA, mitoses present, diffuse positivity for HMB45, indicating absence of cell maturation, Ki67 proliferating index of 5%, CD 45 positivity for chronic inflammation and CD 34 not supporting vascular invasion.
Conclusion: This particular case emphasizes the attention that should be given to benign-appearing nevi, especially those under 5 mm, in view of the fact that micromelanomas can be easily disregarded as benign, because of their low advancement in evolution and small size. In order to achieve early diagnosis of skin neoplasms, the entire arsenal at the pathologist's disposal should be used, as it can help improve the patient's diagnosis and prognosis.

PS-05-021
Clinical and histopathological features of nodular melanoma: a retrospective study from a Romanian tertiary centre
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Background & objectives: Nodular melanoma (NM) is the most invasive melanoma subtype, often diagnosed in advanced stages, which causes a consistent proportion of deaths related to melanoma. This study aimed to identify the clinicopathologic features of NM diagnosed in a Romanian tertiary centre.
Methods: A retrospective study was conducted on all cases of NM diagnosed between 2017-2020 in the Department of Pathology of the Mureș County Clinical Hospital. The following variables were recorded: demographic data, tumour localization, Breslow thickness, Clark level of invasion, mitotic rate, presence of ulceration, tumour-infiltrating lymphocytes (TILs) and regression.
Results: The study group included 34 patients with NM (18 females and 16 males), with a mean age of 65.9±17.2 years. The most frequent tumour site was the trunk (47.1%), followed by the limbs (35.3%). Most of the tumours had a Breslow thickness >4.0 mm (55.9%) and a Clark level of IV (64.7%). The mean mitotic rate was 7.2±5.1 mitoses/mm2 (range 1-22) and there was a significant positive moderate correlation between mitotic rate and Breslow thickness, with Spearman correlation coefficient r=0.43 (0.098-0.677), p=0.01. Ulceration was present in 25 cases (73.5%). Most tumours presented brisk TILs (41.2%). Regression was observed in 2 cases (5.9%) and one NM was associated with nevus (2.9%).
Conclusion: The aggressive phenotype of NM is confirmed by the high Breslow thickness, frequent ulceration, increased mitotic rate and low association with regression and nevus remnants. Therefore, NM should

be regarded as a de novo malignancy with high metastatic potential and delayed diagnosis.

PS-05-022

Immunohistochemical expression of matrix-metallo-proteinases in melanocytic nevi with intravascular protrusions and intravascular nevus cell aggregates compared to common melanocytic nevi

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Background & objectives: Matrix-metallo-proteinases play a significant role in the progression of melanocytic lesions. The aim of this study is to evaluate MMP expression in common melanocytic nevi (CMN) with intravascular protrusions (IVNP) and intravascular nevus cell aggregates (IVNcA).
Methods: We performed a case control study including 30 CMN with IVNP and IVNcA and 30 paired CMN without IVNP and IVNcA and stained them for MMP-2, MMP-3, MMP-9, MMP-11 and MMP-13. Two investigators utilizing a modified Sinicrope's method scored the uptake of immunostains. Data was analysed using a paired Student's t test. The level of significance was set at $p<0.05$.
Results: We found that MMP-2, MMP-3, and MMP-11 were overexpressed in melanocytic nevi with IVNP and IVNcA compared to CMN ($p = 0.004$, 0.004 and 0.002, respectively). Interestingly, MMP-9 was overexpressed in common melanocytic nevi without intravascular protrusions and aggregates ($p = 0.002$). There was no statistically significant difference in the expression of MMP-13 in both study groups ($p = 0.2691$).
Conclusion: Our findings demonstrate that the majority of the analysed MMPs are differentially expressed in melanocytic nevi with intravascular protrusions and aggregates compared to CMN. This suggests that MMP-2, MMP-3 and MMP-11 play an important role in the pathogenesis of benign melanocytic lymph node deposits.

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PS-05-023

Tissue inhibitors of matrix-metallo-proteinases variation in melanocytic nevi with intravascular protrusions and/or aggregates versus common melanocytic nevi

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Background & objectives: We evaluated TIMPs expression as players in tumour progression in common melanocytic nevi (CMN) versus CMN with intravascular protrusions (IVNP) and intravascular nevus cell aggregates (IVNcA).
Methods: Our study (case control type) includes 60 cases of CMN, half of them with IVNP and IVNcA; TIMP-1, TIMP-2 and TIMP-3 expressions were investigated. All cases were seen by two investigators; a modified Sinicrope's score was used. Data was analysed using a paired Student's t test for a level of significance of $p<0.05$.
Results: TIMP-1 was overexpressed in CMN nevi without IVPN and IVNcA ($p = 0.002$). TIMP-3 has a tendency towards overexpression in CMN with IVNP and IVNcA ($p = 0.0106$). No statistically significant difference in the expression of TIMP-2 in both study groups ($p = 0.8249$) was present.
Conclusion: TIMP-3 is overexpressed in CMN with IVNP and IVNcA compared with CMN without IVNP and IVNcA, TIMP-1 has the opposite manifestation while TIMP-2 has no significant variation; the importance of this differences in the expression of TIMPs in the pathogenesis of vascular affinity of melanocytes needs further research.

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PS-05-024

Association between histopathological findings and the diagnosis of cutaneous leishmaniasis, confirmed by PCR, in an endemic region of the Brazilian countryside: a cross-sectional study

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Background & objectives: Leishmaniasis presents itself from small skin lesions to visceral disorders that can evolve to death. To evaluate the association of histopathological criteria with the results of polymerase chain reaction (PCR) of clinically suspected cases of cutaneous leishmaniasis (CL).
Methods: An observational, cross-sectional, and retrospective study that evaluated, by PCR and histological examination, skin samples received during 9 years of clinically suspected cases of CL.
Results: The data showed full agreement between histopathological results and PCR when amastigote structures were identified. Moreover, the evaluated histological variables did not show statistical significance with the result of the PCR when considered individually: ulceration ($P = 0.231$), epidermal hyperplasia ($P = 0.595$), hyperkeratosis ($P = 0.103$), presence of granuloma ($P = 0.280$), neutrophils ($P = 0.475$), histiocytes ($P = 0.241$), lymphocytes (0.543), plasmocytes (0.291), and necrosis (0.746).
Conclusion: The data from the present study highlight the high specificity of microscopy analysis with 100% agreement with the PCR result for clinically suspected cases in an endemic Brazilian region. However, a histopathological finding in isolation cannot predict PCR positive results.

PS-06 | Digestive Diseases Pathology - GI Posters

PS-06-001

Mast cell quantification in chronic dextran sulphate sodium induced colitis animal model of inflammatory bowel disease

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Background & objectives: Mast cell participate in inflammatory bowel disease pathogenesis by releasing various inflammatory mediators. Dextran sulphate sodium induced colitis in laboratory animals is commonly used IBD model. The aim of the study is mast cells quantification in chronic mouse/rat DSS model.
Methods: Animals were exposed to DSS in drinking water in three cycles of five-day duration. FFPE tissue sections were toluidine blue and PAS stained. Disease activity was evaluated using score (Int Pharmacol (2009) 9:1444). Mast cell number and percentage of degranulated mast cells was evaluated by digital image analysis (Calopix software, TRIBVN, France). Statistical evaluation was performed using GraphPadPrism software.
Results: Disease activity score was significantly higher in DSS groups of mice and rats in comparison to negative control groups.
In murine naïve and DSS-treated mice colon toluidine-stained mast cells were present in peri-intestinal fat tissue, mainly situated near vessels. In DSS-treated animals, number of mast cells slightly increased, while percentage of degranulated mast cells was not statistically higher than in naïve mice. In rat naïve colon toluidine-stained mast cells were found in submucosa and peri-intestinal fat tissue. In distal colon of naïve rats most mast cells

were degranulated. Percentage of degranulated mast cells in proximal colon submucosa significantly increased in DSS group compared to naïve animals.
Conclusion: In this study differences in mast cell number, distribution and degranulation status in naïve colon and DSS-colitis between mice and rats were highlighted. Also, most of the mast cells in naïve and DSS-colitis groups were degranulated (activated) in distal colon part.

PS-06-002
The impact of COVID-19 on colorectal cancer patients: where we are and what have we done?
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Background & objectives: The new coronavirus disease 2019 (COVID-19) is an ongoing pandemic, generating an unprecedented health crisis, especially among patients with colorectal cancer (CRC). To better manage the evolving crisis, a state of emergency was declared in Romania on March 16, 2020.
Methods: The state of emergency had profound effects on oncology patients, particularly for CRC patients. Briefly, this study evaluated the impact of the COVID-19 pandemic on CRC patients in the largest hospital in western Romania. We performed a cross-sectional analysis on colorectal (CR) resection specimens received in our pathology department between March 16, 2018 and March 16, 2021.
Results: In 3 years of study data, 1035 CR resection specimens were examined: 733 were CR adenocarcinomas, 14 malignant CR tumours other than adenocarcinomas, 46 tumour recurrences, 28 specimens with direct invasion/metastases from other cancer and 214 were benign or non-neoplastic specimens. Only CR adenocarcinomas were selected, analysing the distribution and clinico-morphological features over 3 time periods: March 16, 2018-15 March 2019, March 16, 2019-15 March 2020 and March 16, 2020-16 March 2021. A slight decrease in the number of specimens was noted in the last year of the pandemic compared to previous years with two exceptions: March 2020, before the announced lockdown and June 2020, after the lockdown ended.
Conclusion: A difference was noted regarding the surgical treatment when between 2018-2020 elective surgeries were more frequent, while between 2020-2021 emergency interventions were more frequent. Finally, regarding CRC and COVID-19 pathological overlap, 6 patients had COVID-19 before hospitalization, 2 were infected at the time of surgery and 7 presented nosocomial infection. No specific histological findings were identified.
In conclusion, the impact of COVID-19 on the management of CRC patients was noticed in our hospital, but the overall impact was minor.

PS-06-003
Secondary appendiceal tumours: clinico-pathological spectrum of 20 cases in a 30-year single centre retrospective study
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Background & objectives: Secondary appendiceal tumours (SATs) is an uncommon entity. It often causes acute appendicitis. In this study, we report the clinical and histopathologic features of secondary neoplasms involving the appendix.
Methods: We performed a single-centre, retrospective study of patients with confirmed SATs over a 30-year period of time. Direct extension of neoplasms originating in organs in proximity were excluded. The following parameters were recorded: patient clinical history, the appendiceal wall involvement, primary tumour site, and histologic type.
Results: The study consisted of 20 cases. The median age was 65 years.14 presented acute abdomen/appendicitis at diagnosis. Primary sites were gastrointestinal (n=6, 3 gastric signet-ring; 3 rectal adenocarcinomas), gynaecological (n=3, 1 ovarian clear cell carcinoma, 1 endometrial carcinoma; 1 leiomyosarcoma), pancreas-biliary tree (n=3), genito-urinary (n=2, 1 urothelial carcinoma; 1 seminoma), lung (n=1 small cell carcinoma), breast (n=1), mesothelioma (n=1), and 3 adenocarcinomas of unknown origin. The wall involvement was: subserosa only (n=7), subserosa-muscle layer (n=7), subserosa-submucosa (n=3) and subserosa- mucosa (n=3). 13 SATs were synchronous and 5 were metachronous. Follow-up was available in all patients: 16 died of disease (median:2,5 months), 2 were free of disease and 2 in progression.
Conclusion: Although appendiceal metastasis are rare, it often results in acute abdomen-appendicitis. Familiarity and awareness of SATs is vital for accurate pathological diagnosis. The most frequent primary site in or series is the gastrointestinal tract. The SATs were usually associated with widespread disease and poor prognosis.

PS-06-004
Anti-apoptotic markers - role in personalized surveillance of patients with chronic gastritis and extensive intestinal metaplasia
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Background & objectives: Gastric intestinal metaplasia (IM) is a pre-cancerous lesion, metaplastic areas expressing an impaired balance between apoptosis and proliferation. We aimed to investigate anti-apoptotic activity in areas of IM, trying to identify patients with higher risk of evolution towards malignancy.
Methods: Immunostaining for bcl-2, Ki67 and MUC4 was performed on 20 biopsies showing chronic gastritis with extensive IM, separated in two groups: 10 cases Helicobacter pylori positive (HP+) and 10 cases Helicobacter pylori negative (HP-). Bcl-2 and MUC4 positivity in metaplastic epithelium were scored as 0/1+/2+/3+/4+. Ki67 expression was quantified as the percentage of positive tumour nuclei.
Results: Analysing comparatively the two groups, HP+ cases had a higher degree of severity of gastritis (average score 2.4 compared to 0.6) and more important glandular atrophy (average score 0.4 compared to 0). The mean score of bcl-2 and MUC4 positivity in the metaplastic epithelium was more important in the HP+ group (1.3 versus 0.9 for bcl-2 and 1.6 versus 1.2 for MUC4, respectively). In the HP+ group, Ki67 expression in metaplastic epithelium was significantly higher than in HP- group. Practically, HP+ group had a high proliferation rate associated with a high anti-apoptotic activity.
Conclusion: The alteration of the balance between apoptosis and cell proliferation is crucial in the development of gastric cancer; following the dynamics of anti-apoptotic markers in gastritis with intestinal metaplasia we can ensure a good surveillance of patients at high risk for dysplasia and gastric cancer.

PS-06-005
Association of IL-10 -1082A/G polymorphism with colorectal cancer risk
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Background & objectives: Tumoral microenvironment can count many kinds of growth factors and cytokines including IL-10. Substantial evidence recognizes IL-10 as an anti-inflammatory cytokine. We aimed to evaluate the involvement of IL-10-1082A/G polymorphism in the occurrence of colorectal cancer (CRC) in a Tunisian population.

Methods: Forty-nine patients (males 67% and females 33%, Mean age=60 years) with CRC, matched by sex with eighty healthy controls (males 66% and females 34%, Mean age=58 years) were genotyped for the cited polymorphism using the refractory mutation amplification system (ARMS-PCR).
Results: The genotypic distribution of AG genotype was increased in patients (69%) compared to controls (49%) suggesting its linkage to CRC risk (p=0.022; OR=2.383; IC 95% [1.126- 5.041]). Gender stratification demonstrated the association of IL-10 -1082A/G polymorphism only in males (p=0.05, OR=2.417, IC 95% [0.979-5.966]). Stratifications according disease stage and metastases do not show significant differences between allele/genotype distribution in patients vs controls.
Conclusion: Although preliminary, our data demonstrated that IL-10 -1082A/G polymorphism was related to CRC susceptibility in overall population as well as for males.

PS-06-006
A study of HLA-G 14pb Ins/Del gene polymorphisms profiling in colorectal cancer among females
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Background & objectives: Some studies have focused on the involvement of HLA-G gene, mainly the 3'untranslated (3'UTR) region, in colorectal cancer(CRC) susceptibility. We aimed at exploring whether HLA-G 14pb Insertion/Deletion (Ins/Del) could affect the occurrence or the progression of colorectal cancer in Tunisian females.
Methods: Forty female patients diagnosed with colorectal cancer at the Salah Azaiz Institute in Tunis (mean age= 54.65 years) and fifty-four healthy donors (mean age: 55.36 years). Genotyping of HLA-G 14pb Ins/Del was performed by conventional PCR.
Results: Comparison of the distribution of alleles and genotypes of polymophism14pb Ins/Del of the HLA-G gene showed that patients with Del allele (61% vs. 52%; p=0.199, OR= 1.467, 95% CI: [0.815-2.640]) and homozygous genotype Del/Del (43% vs. 24%; p=0.058, OR= 2.331, 95% CI: [0.962-5.645]) are more likely to be associated with colorectal cancer risk. There was neither correlation with demographic parameters nor with prognostic parameters (stage, grade).
Conclusion: In summary, HLA-G gene appears to be crucially involved in the genetic predisposition to colorectal cancer in Tunisian population. Further studies with larger cohort are needed to consolidate these preliminary findings.

PS-06-007
Clinicopathological features and prognostic factors in resected gastric cancer: a 19-year experience in a single tertiary centre
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Background & objectives: In western countries, gastric cancer (GC) is diagnosed at advanced stages. Several prognostic factors apart from the TNM system have been reported. Our aim is to describe the outcomes and prognosticators of all patients with GC resected at our institution.
Methods: Retrospective study of all cases of GC surgically resected in a tertiary hospital from 2000 to 2019 (N=377). Clinical features were collected, histological features were independently assessed by two pathologists and statistical analyses were performed. Patients who received neoadjuvant therapy, metastatic tumours at diagnosis and patients with R1/R2 resections were excluded from the study. 315 patients were finally included.
Results: Tumours were intestinal (61%), diffuse (30.8%) and mixed (9.9%), according to Laurén's classification. Necrosis, vascular invasion, perineural infiltration, infiltrative pattern, high grade tumours, signet-ring cells and budding were observed in 22.1%, 37.3%, 37%, 64.3%, 50.2%, 32.8% and 22.4% of cases. Most tumours were T3 (49.2%), N+(59.6%). During follow-up, 36.7% of tumours recurred and 27.4% of patients died due to GC. Recurrence was significantly related to patient age, tumour size, presence of signet-ring cells, Laurén subtype, tumour grade, perineural infiltration, vascular invasion, T and N stage. Tumour death was significantly associated with presence of signet ring cells, Laurén subtype, tumour grade, necrosis, infiltrative pattern, vascular invasion, desmoplasia, T and N stage.
Conclusion: Most GC cases were diagnosed in elderly (mean: 72 years) and symptomatic (89.9%) patients, and GC was detected at advanced stages. Apart from the TNM stage, several histological features were correlated with patient outcomes, including the identification of signet-ring cells, perineural infiltration, vascular invasion, Laurén classification, tumour grade, presence of necrosis and desmoplasia. The assessment of histological features is cost-effective, easy to perform, and it may improve the prognostic stratification of GC patients.

PS-06-008
Predicting outcome in resected gastric cancer: development of lymph node ratio-based prognostic scores for progression and survival
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Background & objectives: The TNM staging system is the main prognostic tool in gastric cancer (GC). Lymph-node ratio (LNR) is a recently studied feature which could improve patient stratification. Our objective is to develop LNR-based prognostic scores for patients with resected GC.
Methods: Retrospective study of all cases of GC surgically resected in a tertiary hospital from 2000 to 2019 (N=377). 315 cases were included. Clinicopathological features were collected and univariate and multivariate analyses were performed. Prognostic scores for predicting tumour death and recurrence were constructed based on hazard ratios (HRs). Their prognostic role was analysed by receiver-operating characteristic (ROC) and Kaplan-Meier analyses.
Results: Most tumours were T3 (49.2%) N+ (59.6%), and mean LNR was 0.2. The recurrence score included LNR, T stage and Laurén subtypes, and classified our patients into 5 groups (S1-S5). Kaplan-Meier curves for disease-free survival (DFS) showed an excellent prognostic stratification, and p value (log-rank test) was <0.001. The score for tumour death included LNR and T stage. Kaplan-Meier curves for overall survival (OS) showed and excellent stratification into 5 prognostic groups (p <0.001). Mean OS for S1-S5 cases were 172, 140, 116, 84 and 22 months, respectively. The AUC values for recurrence and tumour death were 0.722 and 0.763. Both scores were independently related to OS and DFS.
Conclusion: Lymph node staging is a controversial issue in GC, and several alternative lymph node classifications have been proposed. According to previous studies, LNR may reflect the extent of lymph node dissection and overcome the limitations of the N stage. In our study, LNR-based prognostic scores showed good prognostic performance in GC patients. Thus, LNR-based scores may be helpful for patient stratification in GC, and they may serve as an alternative or an adjunct to the traditional TNM classification.

PS-06-009
Prognostic role of the log odds of positive lymph nodes in western patients with resected gastric cancer: a comparison with the 8th TNM staging system

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Background & objectives: Several alternative lymph node (LN) staging systems have been recently described in gastric cancer (GC). The log odds of positive LNs (LODDS) is calculated as "log [(positive LNs+ 0.5)/(negative LNs+0.5)]". We aim to evaluate the prognostic role of LODDS in GC.
Methods: Retrospective study of all cases of GC surgically resected in a tertiary hospital from 2000 to 2019 (N=377). Clinicopathological features were collected, LODDS was calculated and statistical analyses were performed. 315 patients were finally included. LODDS was categorized into 5 groups (S1-S5) for survival analysis. Cases were classified as S1 (25.6%), S2 (18.4%), S3 (21.3%), S4 (20.3%) and S5 (14.4%).
Results: The LODDS classification was significantly associated with tumour size, Laurén subtype, presence of signet-ring cells, tumour grade, perineural infiltration, lymphovascular invasion, growth pattern, tumour recurrence and death. Kaplan-Meier analysis of disease-free survival (DFS) according to the LODDS classification produced distinct, non-overlapping curves ($p<0.001$). Kaplan-Meier analysis of overall survival (OS) showed good patient stratification ($p<0.001$), but S1-S2 curves overlapped after 60 months. N stage showed worse prognostic performance for both OS and DFS by Kaplan-Meier analyses. AUC values for recurrence and death were similar between the two classifications. LODDS classification was independently related to both OS and DFS.
Conclusion: Some investigators have suggested that LODDS may be superior to the TNM stage in GC. In our study, the LODDS-based classification showed better prognostic performance than the N stage, and it was an independent predictor of OS and DFS. Based on these findings, LODDS-based staging systems can be used at least as complementary methods to predict patient outcomes in GC. Further research should evaluate the role of LODDS classifications in GC, and efforts should be taken to standardize cut-off values.

PS-06-010
Development of a simplified log odds of positive lymph nodes-tumour staging system for western patients with resected gastric cancer
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Background & objectives: The log odds of positive lymph nodes (LODDS) has been proposed as an alternative staging system for predicting patient outcomes in gastric cancer (GC). Our aim is to develop a simplified tumour-LODDS staging system for patients with resected GC.
Methods: Retrospective study of all cases of GC surgically resected in a tertiary hospital from 2000 to 2019 (N=377). Clinicopathological features were collected. Neoadjuvant, metastatic and R1/R2 cases were excluded, and 315 patients were finally included in the study. LODDS was calculated, and cases were categorized into 5 groups (L1-L5). A T-LODDS staging system was developed and statistical analyses were performed.
Results: GC cases were classified as L1 (25.6%), L2 (18.4%), L3 (21.3%), L4 (20.3%) and L5 (14.4%). The T-LODDS classification divided patients into 5 stages (S1-S5). Cases were S1 (8.3%), S2 (24.4%), S3 (17.5%), S4 (28.7%) and S5 (21.1%). The T-LODDS system was significantly associated with systemic symptoms, tumour size, depth, macroscopical type (Borrmann classification), Laurén subtype, presence of signet ring cells, tumour grade, lymphovascular invasion, perineural infiltration, infiltrative growth, tumour recurrence and death due to tumour. Kaplan-Meier curves for overall survival (OS) and disease-free survival (DFS) showed distinct non-overlapping curves, and p value according to log-rank test was <0.001. T-LODDS classification was an independent predictor of both OS and DFS.
Conclusion: The simplified T-LODDS classification showed an excellent prognostic performance in our study, and it was an independent predictor of OS and DFS. Based on these results, the T-LODDS staging system can be useful for predicting prognosis of patients with resected GC, and it can at least complement the traditional TNM system. More studies should be performed in larger populations to validate its prognostic value.

PS-06-011
Prognostic value of a new staging system based on the location of metastatic lymph nodes in patients with gastric cancer
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Background & objectives: In 2016, Choi et al. published a hybrid topographical and numerical lymph node (LN) staging system for gastric cancer (GC). Our objective is to develop a T-LN staging system based on the Choi classification for patients with resected GC.
Methods: Retrospective study of all cases of GC resected in a tertiary hospital from 2000 to 2019 (N=377). Clinicopathological features were collected. Neoadjuvant, metastatic and R1/R2 cases were excluded. 315 patients were included. Choi classification was applied, and tumours were classified as N0 (49%), N1 (22.9%), N2 (17.4%) and N3 (107%). A T-LN classification was constructed, and statistical analyses were performed.
Results: Patients were categorized into 6 groups according to the T-LN classification: S1 (15.9%), S2 (15.5%), S3 (19.9%), S4 (19.1%), S5 (25.1%) and S6 (4.4%). This classification was significantly related to systemic symptoms, tumour size, depth, Laurén classification, signet-ring cells, tumour grade, necrosis, perineural infiltration, lymphovascular invasion, recurrence and tumour death. Kaplan-Meier curves for OS showed good stratification into 6 prognostic groups ($p<0.001$). The TNM system showed poorer discriminatory ability (IA-IB, IIA-IIB and IIIB-IIIC curves overlapped). In respect of disease-free survival (DFS), both the TNM and T-LN systems showed good prognostic stratification. AUC values for recurrence and tumour death were similar. The T-LN classification was independently related to OS and DFS.
Conclusion: Previous research has shown that novel LN classifications based on the anatomical extent of the disease can successfully predict the prognosis of GC patients. In our study, a T-LN staging system based on the Choi classification showed slightly better prognostic performance than the TNM system. Thus, alternative T-LN classifications may help to overcome the limitations of the current TNM system. Further studies in larger populations should be performed to confirm the prognostic value of alternative staging systems in GC.

PS-06-012
Assessment of immunohistochemical expression of MMP9 and EGFR in colorectal carcinomas with tumour budding – immunohistochemical expression as prognosis tool and potential therapeutical target
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Background & objectives: Tumour budding (TB) is an adverse prognostic factor in colorectal carcinomas (CRC), involved in local invasion and distant metastasis.
The purpose of our study is evaluation of MMP9 and EGFR immunohistochemical expression in peritumoral budding (pTB) and intratumoral budding (iTB).

Methods: We conducted a retrospective, comparative study including 20 cases of colorectal adenocarcinomas (10 with pTB and 10 with iTB) recording the type, stage, grade of anaplasia and grade of TB. We analysed expression of MMP9 and EGFR in tumour, tumour budding and peritumoral stroma and we correlated the results with clinicopathological data.
Results: MMP9 showed strong positivity in tumour in 17 cases (8 with iTB, 9 with pTB), and in TB in 14 cases (8 with iTB, 6 with pTB); it was moderately positive in peritumoral stroma in 15 cases (10 with iTB, 5 with pTB). EGFR was positive in tumour in 7 cases (4 with iTB, 3 with pTB), in TB in 12 cases (5 with iTB, 7 with pTB), and in peritumoral stroma in 4 cases with pTB. EGFR expression was statistically significant higher in peritumoral stroma of tumours with pTB than of tumours with iTB. MMP9 expression in peri-budding stroma was stronger that in peritumoral stroma (p=0.0029, two tailed t-test)
Conclusion: MMP9, a gelatinase involved in degradation of extracellular matrix and of the basement membranes, two essential steps in tumour invasion and migration, is strongly positive in tumour cells and has and enhanced expression in stroma around TB areas. EGFR expression is high in tumour stroma, especially in tumours with pTB. As potential therapeutical targets and markers of poor prognosis, MMP9 and EGFR can be used in establishing sub-groups of CRC patients to include in clinical trials.

PS-06-013
Immunohistochemical expression of Silent information Regulator 2 Homologue1 (SIRT1) in colonic inflammation dysplasia carcinoma sequence
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Background & objectives: Colorectal carcinoma (CRC) is the seventh most common lethal cancer in Egypt. SIRT1 as histone deacetylase has supposed protective role in colorectal inflammation and carcinogenesis. To compare immunohistochemical expression of SIRT1 in control group, inflammatory bowel disease, adenoma and CRC.
Methods: This retrospective study was carried out on 78 cases, divided into four groups; 30 cases of CRC (colectomy specimens), 22 cases of adenoma, 15 cases of IBD and 11 cases of control group. Immunohistochemical expression of SIRT1 was evaluated by H-score in using microarray technique.
Results: SIRT1 showed nuclear staining in all cases of the control and IBD groups. Adenoma and CRC cases showed also SIRT1 expression in 95.5% and 77.4 % respectively. There was a significant progressive reduction of H-score values of SIRT1 from normal colonic specimens (Mean=185) compared to IBD (Mean=78), adenoma (Mean=84) and carcinoma (Mean=63). On the other hand, there was no statistical differences between adenoma and carcinoma groups regarding SIRT1 expression
Conclusion: SIRT1 has a protective suppressor role against intestinal inflammatory and neoplastic processes. Its defective expression is associated with promotion of inflammatory, dysplastic and carcinogenesis sequence.

PS-06-014
Prognostic significance of microsatellite instability in gastric adenocarcinoma
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Background & objectives: Gastric cancer (GC) is one of the most aggressive malignancies. Several associations between microsatellite instability (MSI) and other clinicopathological factors have been reported in GC. In this study we investigated the correlation between MSI and prognostic factors of GC.
Methods: The study included 37 patients with gastric adenocarcinoma. MSI deficiency was assessed by immunohistochemical analysis using MLH1, PMS2, MSH2 and MSH6 and confirmed by polymerase chain reaction (PCR) using a panel of five microsatellite markers specific for two mononucléotide loci (BAT25, BAT26) and three dinucleotide loci (D5S346,D17S250 and D2S123).
Results: Out of 37 total cases of gastric cancer, 29 (78,5%), 3 (8%), and 5 (13,5%) were microsatellite stable (MSS), low-level MSI (MSI-L), and high-level MSI (MSI-H), respectively. Compared to MSS/MSI-L, MSI-H gastric cancers were significantly associated with female gender (P=0,021) and inflammatory stromal reaction (p=0,03). There was no statistically significant association between MSI-H and other selected clinical parameters: age, tumour location, who histotype, lymph node status, vascular invasion, perineural invasion and pTNM status.
The 5-year overall survival of patients with MSI-H tumours was 80% versus 44% for MSS/MSI-L tumours (p=0,37).
Conclusion: The MSI status should be incorporated in routine pathological report because it defines a different pathological entity with a better outcome. Also, by its correlation with inflammatory stromal reaction, it can be considered as a useful biomarker to identify patients who will respond to immune checkpoint blockade inhibitors.

PS-06-015
Clinicopathological characteristics of Epstein-Barr virus-associated gastric carcinoma in 108 Tunisian cohort
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Background & objectives: The Cancer Genome Atlas, in 2014, provided a new molecular classification defining EBV-associated-gastric carcinoma (EBVaGC) as a distinct subtype.
We analysed clinicopathological characteristics of EBVaGC.
Methods: One-hundred and eight gastric cancer patients treated by gastrectomy between 2001 and 2018 were enrolled. Clinical and pathological features were recorded from the database. All diagnoses were confirmed histologically. Tissue cores were sampled from the paraffin embedded tumours after marking the most representative tumour regions and prepared as tissue microarrays. EBER in-situ hybridization was performed by an automated method.
Results: The tumour was EBER-negative if staining was only expressed in benign lymphoid cells, and EBER-positive if the malignant epithelial cells showed a nuclear staining. There were 108 gastric cancer patients of which 62 were men. EBV positivity was present in 39 cases. EBVaGC was associated with age at diagnosis (45-84years;P =0.009).EBVaGC involved the proximal parts in 20 cases. EBV-positivity was most detected in poorly cohesive adenocarcinomas (53.8%;P=0.003). Seven cases were lymphoepithelial-like carcinomas. There was no correlation of EBER-positivity with the tumour stage or metastatic lymph nodes. Median as well as 1, 3, and 5-year survivals among EBER-positive tumours were shorter. The difference wasn't shown to reach statistical significance (P = 0.19).
Conclusion: We found tumour EBV positivity more frequently in male than female gastric carcinomas patients, similar to several other studies. We also found higher EBV positivity in poorly cohesive adenocarcinoma in contrast to other studies who showed predominance of intestinal type. EBVaGC is a distinct subtype of gastric carcinoma with regard to its clinicopathological features. It must be diagnosed in every resected specimen as it can become a predictive biomarker for response to immune checkpoint inhibitors.

PS-06-016
Prognostic value of tumour-stroma ratio in colorectal carcinomas

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Background & objectives: Tumour-Stroma Ratio (TSR) is currently considered as a prognostic factor in several cancers. The objective of our study was to assess the prognostic value of TSR in colorectal carcinomas (CRC).
Methods: The study was retrospective in a period of one-year. We included all cases of CRC stade II and III, diagnosed in the Pathology department of Habib-Thameur Hospital, and for which tumour excision was performed. Tumours were classified into two groups: Tumours rich in stroma (TSR ≤50%) and tumours poor in stroma (TSR>50%), following a methodology widely used in the literature.
Results: A total of 33 cases of CRC were included (16 males and 17 females). The mean age was 61.8 years. The TSR value was between 10% and 80% with an average of 39%. The TSR was > 50% in 17 cases (51.5%) and ≤ 50% in 16 cases (48.5%). The overall survival was significantly reduced in cases of Tumours rich in stroma (p=0.005). We found a correlation between a TSR ≤50% and tumour size (p= 0.028). Correlations between TSR and lymph node status, tumour stage, and lymphovascular invasion were not statistically significant.
Conclusion: Our study demonstrated that a high stroma proportion or an exaggerated desmoplastic response would be associated with an unfavourable outcome in patients with CRC. TSR is an important prognostic and predictive factor for CRC. Its easy assessment and reliability allow it to be used in clinical practice, particularly to identify high-risk patients who can justify adjuvant chemotherapy.

PS-06-017
Gastric MALT lymphoma: a report of 42 cases in a Tunisian health care centre

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Background & objectives: Gastric MALT lymphoma (GML) is a rare pathology with a low potential for malignancy. However, this lymphoma can be easily under-diagnosed due to clinical and endoscopic polymorphism. Our study's aim was to assess clinical, endoscopic, and anatomopathological features of GML.
Methods: This was a retrospective descriptive study that included all cases of GML, collected from the Pathology Department of Habib Thameur Hospital over a period of 23 years (from 1997 to 2020).
Results: We collected 42 cases of GML. These were 24 men and 18 women (sex ratio = 1.3). The mean age was 53.7 years. The disease was revealed in the majority of cases by abdominal pain. The endoscopic appearance was nonspecific, dominated by ulcerations (42%), an ulcerative tumour (18.4%), congestive gastropathy (15.8%), nodular gastropathy (10.5%) or rarely an infiltrated appearance. These lesions were in the antrum in the majority of cases. Helicobacter Pylori (HP) was present in 44.5%. HP status was uncertain in 14% of cases. The transformation of GML into large B cell lymphoma was noted in 24% of cases. Immunohistochemistry confirmed the B phenotype in all cases.
Conclusion: Inconsistent with our results, GML is more common in males. Its incidence increases significantly from the age of 40. It is a lymphoma with a low potential for malignancy. This lymphoma progresses slowly and may resolve completely after eradication of HP. Its transformation into LBDGC is possible and due to the accumulation of new genetic alterations, especially, involving the bcl6 and p53 genes. The immunological phenotype is CD20 +, CD79a +, CD5-, CD10-, CD23-, CD43-, bcl2 +.

PS-06-018
Isolated germline MSH6 mutation associated with Muir-Torre syndrome: a case report and review of the literature

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Background & objectives: Muir-Torre syndrome (MTS) is a phenotypic variant of hereditary nonpolyposis colon cancer (HNPCC) associated with germline mutation in mismatch repair gene MSH2 (90%) or MLH1 (10%). We describe a rare case of MTS harbouring an isolated MSH6 mutation.
Methods: Clinicopathologic features including phenotypic, histologic and molecular characteristics of a recently diagnosed patient with MTS and isolated germline MSH6 mutation are described. A literature review is carried out identifying similar reported cases. Included cases meet criteria of MTS (visceral malignancy associated with sebaceous epithelioma, adenoma or carcinoma) while demonstrating an isolated MSH6 mutation upon germline mismatch repair gene analysis.
Results: A male with a history of multiple sebaceous neoplasms and colorectal carcinoma (CRC) at age 54 was found to have a germline point mutation in exon 4 of MSH6. Seven additional similar cases were identified in the literature making a total of eight cases meeting inclusion criteria: 7/8 cases (87%) were male and 6/8 cases (75%) developed CRC, with an average age of presentation of 58.8 years. 60% of CRC occurred in distal (rectosigmoid) colon. 5/8 cases (62%) developed extracolonic cancer. The majority of mutations involved exon 4 of the MSH6 gene.
Conclusion: Despite scarce data, preliminary characterisation of MSH6 mutation-associated MTS suggests a male predominance, a relatively older age of CRC presentation (58.8 years in our series versus 50 years, the median age of presentation of CRC previously reported in MTS) and high risk of both colonic (especially of the distal colon) and extracolonic malignancies. This peculiar phenotype may contribute to these patients frequently being missed when screening for HNPCC using Amsterdam criteria.

PS-06-019
Tumour-associated M2 macrophages in stage I-II gastric adenocarcinomas

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Background & objectives: Macrophages are cellular protagonists of tumour microenvironment in many tumours. In order to clarify the clinico-pathological significance of intratumoral macrophages, we have compared clinico-pathological features of two cohorts, analysing stage I-II gastric adenocarcinomas containing macrophages with pT- and stage-matched controls.
Methods: Twenty-four cases of stage I-II gastric adenocarcinomas with intra-glandular foamy macrophages were identified; their clinico-pathological features were firstly compared with 72 pT-matched as well as stage-matched control cases of adenocarcinomas with case-control ratio of 1:3. The immunohistochemical procedure against prediluted antibodies: CD68, CD 80 and CD163 on a Ventana BenchMark Ultra. Univariate and multivariate analysis have been applied.
Results: Macrophages showed immunoreactivity for CD68 and CD163 and were organized in mature granulomas. Immunohistochemical features were reminiscent of M(Hb) macrophages, a specific phenotype within M2 macrophages. In any case of our cohort, M1 macrophages was documented by CD 80 immunostaining. There were no significant differences in age, gender, tumour location, size, lymphovascular and perineural invasion between case group with M(Hb) macrophages and pT- as well as stage-matched controls; furthermore, case group showed lower frequency of lymph node metastasis (p=0.02). A significant different clinical course and overall survival rate were also observed in gastric adenocarcinomas with macrophages (p=0.02) in comparison to controls.

Conclusion: We suggest that tumour-associated M(Hb) macrophages are related with a quite indolent growth and a better prognosis of patients with this peculiar variant of gastric adenocarcinomas.

PS-06-020

Novel immunohistochemical markers for gastrointestinal stromal tumours with potential prognostic and therapeutical value

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Background & objectives: Gastrointestinal stromal tumours (GISTs) are the most frequent mesenchymal neoplasms of the digestive tract and are characterized by variable histopathological features and clinical outcomes. The aim of this study is to evaluate Her2 and p16 expression in GISTs.
Methods: We present a retrospective study including 16 cases of GISTs. Immunohistochemical analysis for c-kit, DOG1, CD34, Her2 and p16 was performed. For all specimens we registered location, morphology, mitotic count, tumour size and tumour risk (based on recent WHO guide: low risk - 1, 2, 3a, 3b; high risk - 4, 5, 6a, 6b).
Results: The stomach location demonstrated predominant spindle morphology (5/6 cases) and a smaller medium size (4.6 cm) compared to the colon (7 cm). Her2 positivity correlated with a higher risk (71.42% of high risk-GIST showed Her2 overexpression vs. 33.33% of low risk-GIST), but also with a mixt morphology and a gastric location. There was no relationship found between p16 expression and any of the histopathological features.
Conclusion: Our results suggest a strong correlation between Her2 overexpression and risk grade, tumour extension and mitotic index. Despite literature data, our research could not correlate p16 levels with any of the high-risk features. These interesting findings demonstrate the necessity for larger studies that can further characterize from a molecular point of view this peculiar type of stromal tumours. A better understanding of GISTs can lead to the discovery of new therapeutical options.

PS-06-021

Proximal gastrointestinal lesions in Crohn disease in paediatric patients – a single centre experience

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Background & objectives: Precise diagnosis of Crohn disease (CD) in children and adolescents and lesion distribution are crucial for therapy choice in CD. The aim of study is to determine frequency of lesions in proximal segments of gastrointestinal tract in paediatric CD patients.
Methods: All biopsies taken at the University Children's Hospital, Belgrade over the 4-year period (2017-2019) were reviewed using histopathology reports from the files of the Institute of Pathology, Faculty of Medicine, University of Belgrade. Selected histological slides were re-examined.
Results: A total of 49 cases of CD were identified with similar frequency in both gender (M:F=1.04). The average age of patients was 14.5 ± 2.61 years. Median of symptoms duration before histopathological diagnoses of CD was 5 months (3 weeks - 5 years). One quarter of patients (13/49) had specific histopathological findings related to CD in proximal segments of gastrointestinal tract. Chronic granulomatous inflammation was found in the oesophagus (3), stomach (5) and duodenum (1). Focally enhanced gastritis was found in 10.2% of patients with CD of ileum and colon. More than half of patients with characteristic CD lesions (7/13) in proximal gastrointestinal tract had normal findings at proximal endoscopy.
Conclusion: A significant proportion of paediatric CD patients have proximal gastrointestinal lesions. Multiple biopsies are crucial for CD diagnosis in proximal gastrointestinal tract in children because poor endoscopic detection of characteristic lesions.

PS-06-022

Hepatoid adenocarcinoma of the gallbladder: a diagnostic pitfall with hepatocellular carcinoma

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Background & objectives: Hepatoid adenocarcinoma is a variant of adenocarcinoma with histopathological features that resemble hepatocellular carcinoma, its main differential diagnosis. It most commonly arises in the stomach and less frequently in the lung, kidney, pancreas and gallbladder, the latter being exceedingly rare.
Methods: We report the case of 59-year-old male followed in the infectious diseases department due to hepatitis C infection. An ultrasonography study revealed a polypoid lesion of the gallbladder, initially suspected as a metastasis of hepatocellular carcinoma. However, computed tomography and magnetic resonance imaging detected no lesions in the liver besides hepatic cirrhosis. The patient was then submitted to a cholecystectomy.
Results: Microscopically, a malignant epithelial neoplasm was found, with muscular layer invasion. The tumour was composed of cords and sheets of large polygonal cells with enlarged nuclei, evident nucleoli and abundant cytoplasm, resembling hepatocytes. There was neither lymphovascular nor perineural invasion and no hepatic tissue was identified. Immunostaining was diffusively positive for CAM5.2, Glipican-3 and AFP, with multifocal arginase positivity. No immunoreaction was found for CK7 and CK19. Thus, the patient was diagnosed with primary hepatoid adenocarcinoma of the gallbladder. The patient's serum AFP values returned to normal range after the surgery. Only 15 other cases have been reported in English published literature during the last 20 years, which were reviewed.
Conclusion: This rare entity is thought to derive either from hepatic differentiation of conventional adenocarcinoma during tumour progression or from bipotential neoplastic cells that differentiate into cells with either hepatoid or glandular features. Hepatoid adenocarcinoma may or may not produce AFP and seems to have a more aggressive course than adenocarcinomas without hepatoid features, regardless of AFP production. Due to location and morphologic similarities to hepatocellular carcinoma it should be taken into account as a differential diagnosis, as treatment is distinct.

PS-06-023

Histological grading of mucinous colorectal carcinoma - an ongoing challenge

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Background & objectives: The pathological grading of mucinous carcinoma (MC) is still unreliable, with successive amendments in the 2000/2010/2019 WHO colorectal carcinoma (CRC) classifications. We aimed to investigate whether the histological grade based on glandular differentiation has prognostic significance in MC.
Methods: We performed a retrospective study on a group of 191 patients with MC who underwent surgery at the "Pius Brînzeu" County Emergency Hospital from Timişoara, Romania. All tumours were staged and graded according to the AJCC 2017 and WHO 2019 CRC classifications. In multivariable analyses, we assessed the associations between the histological grades and the other prognostic factors in CRC.

Results: Based on the degree of glandular differentiation, 17 cases (8.9%) were well differentiated (G1) MC, showing >95% glandular formation, 115 (60.2%) moderately differentiated (G2) - 50-95% glandular formation, and 59 cases (30.89%) poorly differentiated (G3) with glandular structures in <50% of the tumour. Regarding the associations of histological grade with the prognostic parameters, we observed positive correlations between MC grade and patients' age (p=0.0332), tumour extension - pT (p=0.059), lymph node status - pN (p=0.0168), lymphovascular invasion – LVI (p=0.0005) and tumour site – right colon/left colon/rectum (p=0.0477). All G3 MCs cases were diagnosed in the pT3-pT4 stage and the vast majority was associated with right side, pN+ and LVI+.
Conclusion: In our hands, the conventional classification based on the degree of glandular differentiation seems to have prognostic significance. Due to the ease of evaluation on usual stained slides, histological grade appears to be a promising prognostic factor in MC, but still requires establishing of the cut-offs between grade classes, therefore standardization of the assessment method and its validation in large prospective cohort studies.

PS-06-024
Clinicopathological analysis of prognostic factors in colorectal carcinoma: a large retrospective study
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Background & objectives: The tumour stage remains the strongest and most reliable prognostic factor in colorectal cancer (CRC). We evaluated the clinicopathological parameters in early vs. deeply invasive NOS adenocarcinomas, variables that could better predict the adverse outcome in patients with CRC.
Methods: We performed a ten-year retrospective study on 1612 patients with NOS adenocarcinomas who underwent surgical resections in Timişoara County Hospital. Associations between the pT parameter (pT1-pT2 vs. pT3-pT4) and the following prognostic factors: age, sex, tumour location, histological grade (G), lymph node status (pN), lymphovascular invasion (LVI) and distant metastasis were statistically analysed using Chi square/Fisher's exact test.
Results: Regarding the tumour extension in the intestinal wall, we observed 240 (15%) pT1-pT2 and 1372 (85%) pT3-pT4 adenocarcinomas. In terms of tumour differentiation: 107 adenocarcinomas were well differentiated (7%) (G1), 1280 (79%) moderately differentiated (G2), 207 (13%) poorly differentiated (G3) and 18 cases (1%) undifferentiated carcinomas (G4). From the category of pT1-pT2 tumours, only 2 cases (0.8%) were pM1, 42 (17.5%) pN+, 27 (11.25%) LVI and 105 tumours (43.75%) were diagnosed in the rectum. In the multivariate analysis, right localization (p<0.0001), poor differentiation (p = 0.0005), pN+ (p<0.0001), LVI+ (p<0.0001) and distant metastasis (p<0.0003) were significantly associated with the depth of tumour invasion.
Conclusion: In our study, we showed that clinicopathological parameters could provide solutions for risk stratification in patients with CRC. Although the analysis of certain molecular factors are useful and attractive from the perspective of prognostic significance for these patients, the risk of aggressive tumour behaviour in CRC with early invasion of the intestinal wall can be predicted easier and more cost-effective by evaluating histological parameters on HE stained slides.

PS-06-025
Clinicopathologic and prognostic differences between mucinous and non-mucinous adenocarcinoma
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Background & objectives: Mucinous adenocarcinoma (MAC) is a histological subtype of colorectal cancer. The principal aim of this study was to evaluate whether the biological behaviour of MACs differs from that of non-mucinous adenocarcinoma (NMAC) in patients undergoing surgery for colorectal cancer.
Methods: The relationship between clinicopathologic parameters and tumour histology was investigated in 180 consecutive patients who underwent surgical resection for colorectal carcinoma.18 out of 180(10%) tumours were MAC,162 out of 180(90%) were NMAC. The patients' clinicopathological parameters and follow-up and survival data were obtained. The log rank test was used for univariate survival analysis, and the multivariate Cox regression for overall survival (OS) and disease-free survival (DFS).
Results: On multivariate analysis, larger tumour size and lymph node involvement were more frequently observed in patients with MAC than NMAC (odds ratio (OR) = 10.411,95% confidence interval (CI)=2.436-44.498, p=0.002, OR=6.402, 95%CI=1. 380-29.696, p=0.018, respectively) The majority of the MAC were located on the right side (OR=7.539, 95%CI=1.575-36.074, p = 0.11). The median follow-up period was 46 months. We observed a statistically significant difference between MAC (81.3%) and NMAC (94.9%) for five-year DFS (OR=4.518,95%CI=1.130-18.072,p=0.033). We did not observe a statistically significant difference for five-year OS between MAC (72.2%) and NMAC (84.6%).The multivariate Cox proportional hazards model revealed that larger tumour size, older age and presence of lymphovascular invasion were significantly associated with decreased OS (OR= 2.070, 95%CI=0.991-4.321, p=0.053, OR =3.712 95CI =1.655-8.326, p=0.003 and OR=3.652, 95%CI=1.676-7.956, p=0.002, respectively).
Conclusion: Patients with MAC have worse outcomes compared to patients with NMAC. On multivariate analysis, mucinous histology was an independent predictor for DFS with an odds ratio of 4.518.

PS-06-026
Role of microvessels in predicting risk of distant metastasis in localised colorectal cancer
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Background & objectives: Colorectal cancer can recur within five years as distant metastasis in about 25% of cases. Our study aimed to identify the role of microvascular density (MVD) and pericyte impaired microvessels (MPI) in the risk of metastasis.
Methods: We undertake a retrospective study of lymph node-negative colorectal cancer with synchronous distant metastases (n=53), metachronous metastasis (n=45), and without metastases (n=53). The mean follow-up was five years. Triple immunohistochemical staining was made: ERG, α-SMA, podoplanin. In the highest neovessel density area, individual microvessels are counted in an area 1.0 mm2. The index of microvessel immaturity MPI/MVD was calculated (Index-V).
Results: Normal blood vessels have shown ERG expression and α-SMA immunoreactivity anywhere around the vessel perimeter, whereas immature tumour microvessels lacked α-SMA immunoreactivity. The difference of MVD in groups was insignificant, mean 10/mm2 in non-metastasizing and 11/mm2 in metastasizing. Metastasizing tumours demonstrate significantly higher MPI (mean 8/mm2 versus 2/mm2) and higher Index-V (mean 0.69 versus 0.21). Both showed a significant correlation with distant metastasis (p<0.0001).
Conclusion: These findings demonstrate that immature neovascularization correlates with metastasis, resulting in a poorer prognosis. Taken together, not only microvessel density but also vascular maturation is crucial factors for colorectal cancer patients. The evaluation of tumour angiogenesis from the viewpoint of its maturation and its quantity helps predict the tumour's malignant potential.

PS-06-027

Interobserver agreement in classification of dysplasia in colorectal adenomas; a multicentre study

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Background & objectives: Grading of dysplasia in colorectal adenomas (CRA) is important given the huge impact on post-polypectomy surveillance. Two-tiered grading system low-grade dysplasia (LGD) and high-grade dysplasia (HGD) is suggested and terms such as adenocarcinoma in-situ or intramucosal carcinoma are discouraged.
Methods: To assess the usage of current dysplasia grading guidelines in routine daily practice and the interobserver variability in CRAs, pathologists are provided by current detailed dysplasia grading guidelines. Six gastrointestinal, 3 routine pathologists independently evaluated 40 CRA-biopsies, first-as in their routine practice and after (min 30 days washout) current guidelines were provided. Inter-observer κ statistics was assessed using multi-rater Kappa.
Results: All observers preferred to use variable terminology including adenocarcinoma in-situ and/or intramucosal adenocarcinoma for HGD in routine practice; these cases are grouped as HGD for statistics. The interrater agreement was fair (K=0.371;95%CI 0.369-0.372) among all observers. However, it was higher among routine pathologists in comparison to GI pathologists; moderate (K=0,600;95%CI 0.594-0.606) versus fair (K=0,261; 95%CI 0.258-0.263) respectively. In the second review, interrater agreement increase to moderate among all observers (K=0,509;95%CI 0.508-0.511). The increase-rate was intense among GI-pathologists (K=0.523;95% CI 0.520-0.525) but was slight, reaching to substantial among routine pathologists (K=0,630;95%CI 0.624-0.635). The diagnostic rate of LGD increased by 1,1 to 10 times among GI pathologists in the second review.
Conclusion: Current dysplasia grading guidelines are not widely used even amongst in GI pathologists. Variable terminologies for HGD are still common in practice. Implementation of current guidelines to practice increases interobserver agreement and helps to avoid overdiagnose of LGD as HGD. Strategies should be developed to ensure the usage of current guidelines in routine practice.

PS-06-028

Incidence and clinicopathological features of mismatch repair deficient (MMR-d) colorectal carcinomas (CRC): a tertiary single-centre data from Turkey

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Background & objectives: Mismatch repair immunohistochemistry (MMR-IHC) is a widely used method to detect microsatellite instability (MSI). Reflex testing to all newly diagnosed colorectal carcinomas (CRCs) is suggested. The study aims to investigate the incidence of MMR-d CRCs and clinicopathological features.
Methods: Consecutive CRC resections from a total of 455 patients in between March 2017- May 2020 were included in the study. The data were recorded from database including MMR-IHC results. Suboptimal stainings were reviewed and 24 patients were excluded for various reasons.
Results: MMR-d tumours constituted 10% (44/431) of all CRCs, the mean age of the patients among MMR-d tumours 63,14 (min34-max94); MMR-stable tumours 64,2 (min 30-max90). MMR-d and MMR-stable tumours female/male ratio was 21 (47,7%)/23 (52.3%); 165 (42.6%) /222 (57,3%) respectively.
The rate of MMR-deficiency among multiple CRC tumours was higher (25%) than unifocal tumours (10,7%). Right colon was the most common location in MMR-d tumours in comparison to MMR-intact tumours (72%, 30,6%). The rate of mucinous adenocarcinoma was also higher in MMR-d tumours 11,3% (5/44) than MMR-intact tumours 6,3% (25/395).
Among MMR-d tumours, 72,7% (n=32), 25% (n=11), %2,2 (n=1) showed MLH1&PMS2, MSH2&MSH6 and PMS2 deficiency respectively.
Conclusion: According to our single-centre data, the incidence and clinicopathological features of MMR-d tumours seem to be in line with the literature in Turkish population. It is noteworthy that multiple tumours tend to have a higher rate of MMR deficiency in comparison to unifocal tumours.

PS-06-029

Tumour infiltrating lymphocytes in microsatellite-unstable gastric adenocarcinoma

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Background & objectives: Microsatellite instability (MSI) is a major molecular subtype in gastric adenocarcinoma characterised by high lymphoid infiltration.
The aim of this work was to assess tumour-infiltrating lymphocytes (TILs) in gastric cancer with MSI status.
Methods: TILs density was scored on haematoxylin-eosin staining slides in thirty-seven gastric adenocarcinoma cases. Score ranged from no staining (0), weak staining (1), moderate staining (2) to strong staining (3).
Gastric adenocarcinoma microsatellite status was classified as MSI-high, MSI-low and microsatellite stable (MSS) after performing immunohistochemistry and genotyping.
Fisher exact test was used for statistical analysis.
Results: Among the thirty-seven cases, eight cases had MSI status: five were MSI-high and three MSI-low.
In the twenty-nine MSS cases, TILs were absent in ten and present in nineteen cases. Among these latter, TILs level was high in three cases, moderate in five cases and low in eleven cases. In gastric adenocarcinoma with MSS status, the number of cases with absent TILs and low-density TILs was significant ($P<0.05$).
In the five cases of MSI-high, TILs level was the highest in three cases and moderate in two cases.
In the three cases of MSI-low, TILs level was the highest in one case only and moderate in two cases.
Conclusion: Tumour infiltrating lymphocytes were present in all gastric adenocarcinoma MSI cases and in 19/29 cases with MSS status. However, the absence and the low density of TILs in gastric adenocarcinoma MSS cases were significant.

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PS-06-030

A double CD4/CD8α-β immunohistochemistry in duodenal biopsy with intraepithelial lymphocytes – could be that a first diagnostic step in celiac disease suspected cases?

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Background & objectives: People who suffer from celiac disease present HLA II DQ2 or DQ8 which binds to gliadin and then activates CD4 T-cells in the intestinal mucosa. This autoimmune activation produces chronic inflammation of the small bowel mucosa, leading to gradual malabsorption.

Methods: A double immunohistochemistry was constructed using CD4 antibodies matched by DAB on brown and CD8(Ventana CP57 clone) antibody matched by RED. We applied CD8 α-β subunit because of their specificity and 80% sensitivity to celiac disease. This approach allowed us a full insight into CD4+ and CD8+ lymphocytes distribution. All CD8+ cases were serologically tested according to celiac disease guidelines.
Results: In group of 20 patients with chronic active gastritis caused by Helicobacter pylori and also in group of 12 patients with active ulcerative colitis we found IEL above 40/100. The double CD4/CD8 assay presented stromal dominance CD4+ lymphocytes and IEL CD8+ were detected in non-typical way. Unsurprisingly, celiac independent mucosal lymphocytosis was observed in 60% cases, but in 7 *H. pylori* cases and 3 among ulcerative colitis, anti-transamidase antibodies were detected. These cases were re-diagnosed as a principal entity with concurrent silent celiac disease.
Conclusion: In our opinion double CD4/CD8 staining provides more information then CD3 plus CD8 or the recommended singular test of CD3.

PS-06-031
The newly developed SP70 is a specific marker for gastric adenocarcinoma of fundic gland type
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Background & objectives: GA-FG is a novel and rare entity with low-grade malignancy. SP70,as a newly developed monoclonal antibody (McAb), was found to be sensitive in many tumours. This study aims to explore the diagnostic value and potential role of SP70 in GA-FGs.
Methods: A total of 33 cases were obtained from our institution (including 16 fundic gland polyps (FGPs), 9 oxyntic gland polyps/adenomas (OGPs), and 8 GA-FGs). We performed immunostaining for SP70 in different groups. SPSS 21.0 was used for statistical analysis.
Results: Immunohistochemically, 16/16 (100%) FGPs were diffusely positive for SP70, and some scattered SP70 positive cells were observed in OGPs (5/9, 55.6%); however, expression of SP70 was completely missing in GA-FGs (2/8, 25.0%), with statistical significant differences between groups ($P < 0.001$). In light to this significant finding, we are now carrying out further studies with large sample to confirm our results.
Conclusion: SP70 could serve as a potential biomarker to identify GA-FGs and hold. A diagnosis of GA-FG should be considered with the depletion of SP70 expression.

PS-06-032
Immunohistochemical evaluation in dysplastic and non-dysplastic Barrett's oesophagus
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Background & objectives: Morphological diagnosis of dysplasia in Barrett's oesophagus (BE) is demanding and requires huge experience in gastrointestinal pathology. Despite using similar guidelines agreement between pathologists on presence and grade of dysplasia remains unsatisfactory. Immunohistochemical evaluation may improve diagnostics of dysplastic BE.
Methods: Morphological diagnosis of dysplasia in Barrett's oesophagus (BE) is demanding and requires huge experience in gastrointestinal pathology. Despite using similar guidelines agreement between pathologists on presence and grade of dysplasia remains unsatisfactory. Immunohistochemical evaluation may improve diagnostics of dysplastic BE.
Results: DBE was presented in 17 patients (15,2%): 15 patients with low-grade dysplasia (LGD) and 2 with high-grade dysplasia (HGD). Hyperexpression of p53 was recognized in 15 (88,23%) cases of DBE (13 LGD, 2 HGD), staining in non-dysplastic BE (NDBE) was scattered. Expression of p16 was cytoplasmic in 9 (52,94%) cases of DBE (focal in 7 LGD, diffuse in 2 HGD), but scattered nuclear in NDBE. Immunostaining of Ki67 and cyclin D1 was marked in DBE and focal in NDBE. Expression of β-catenin changed pattern from membranous in NDBE and LGD to cytoplasmic and nuclear in HGD. Expression of AMACR was scattered in NDBE, focal in LGD and diffuse in HGD.
Conclusion: Immunohistochemical evaluation with p53, Ki67, cyclin D1, β-catenin and AMACR is a promising tool for precise diagnosis of dysplasia in patients with BE. It is helpful for distinguishing between NDBE, LGD and HGD. Further research is needed to assess prognostic value of these immunohistochemical markers in progression to oesophageal adenocarcinoma in patients with BE.

PS-06-033
Poorly differentiated clusters in colorectal cancer: a novel predictive factor associated with other relevant poor prognostic factors
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Background & objectives: Colorectal cancer (CRC) is currently the third most-commonly diagnosed cancer. Recently, poorly differentiated clusters (PDC) - small groups of ≥5 cells without glandular differentiation – had been proposed as a novel prognostic factor associated with other adverse histopathological findings.
Methods: In a cohort of 84 patients with surgically resected stage I-IV CRC -without neoadjuvant or adjuvant treatment-, we assessed retrospectively the prognostic value of several clinical-pathological variables, including PDC, tumour budding (TB), grade (G1-G3), lymphovascular (LVI) and perineural (PI) invasion, lymph node metastases, survival time and clinical stage. Statistical analysis was performed with SPSS.
Results: The cohort included 54 men and 30 women (40-90 years). 25 patients died from the disease, with a survival time between 0-50 months, and 7 patients died from causes other than disease. G2 (85.7%) was the prevailing histological grade and stage III (33,3%) was the predominant clinical stage. A 50% of the cases had metastasis to lymph nodes, 66.7% LVI and 28.6% PI. Regarding TB, 52.4% had a low score, 27.4% moderate and 20.2% high. PDC evaluation resulted in a low score in 58.3%, moderate in 21.4% and high in 20.2%. Histological grade ($p < 0.016$), TB ($p < 0.0001$), LVI ($p < 0.007$) and PI ($p < 0.031$) were significantly associated with PDC.
Conclusion: PDC grade seems to be a prognostic factor in CRC, as high PDC score in peritumoral regions were associated with other relevant poor prognostic factors, like grade, TB, LVI and PI. Given its easy identification, it may be included in the histological report. However, before it can be introduced in clinical practice, more studies should be performed in order to establish the optimal cut-off for each grade and give it broader validation.

PS-06-034
PRGS and in-situ immunophenotype as a combined „tool" for monitoring the therapeutical efficiency of PIPAC in different peritoneal cancer diseases: a single centre experience
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Background & objectives: Pressurized intraperitoneal aerosol chemotherapy (PIPAC) is able to induce regression of peritoneal metastasis (PM). The Peritoneal Regression Grading Score (PRGS) is used for assessment of therapy response. Nevertheless, the role of the related immune phenotype is still unknown.
Methods: We investigate retrospectively the PRGS of patients with peritoneal metastases in a single and reference centre for PIPAC in Austria. The PRGS was judged on four peritoneal biopsies with HE-staining and tumour-entity related immunostainings to quantify infiltrating tumour cells. Additionally, the effect of localized immune response was analysed by additional immunohistochemical staining for CD3, CD4, CD8, CD25 and TIA, too.

Results: Overall, peritoneal metastasis of the enrolled 48 patients (female/male: 26/22 with a mean age of 60.3 +/- 11.6 years) derived mainly of gastric cancer, malignant mesothelioma and ovary cancer. Based on a total sum of 134 PIPACs and 532 PRGS the mean [with confidence interval]/median PRGS after the first and after the last PIPAC were 2.6 [2.4-2.7]/3.0 and 2.0 [1.9-2.2]/2.0 with the lowest value of 1.1 [0.8-1.4]/1.0 at the fourth PIPAC. Additionally, we were able to link the PRGS and associated fibrosis to a specific regulative immune response. The PRGS and the observed immune phenotype were associated to intraperitoneal status and clinico-pathological parameters.
Conclusion: We demonstrated that the standardized applied PRGS is adequate to monitor the therapy response and outcome in cases with enhanced PM. The related in-situ immune phenotype supported this notion. In the future, the definitive predictive and prognostic role of the PIPAC induced immune reaction needs to be evaluated in prospective and international clinical trials.

PS-06-035
Liquid-based anal cytology in patients with HIV/AIDS: case series
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Background & objectives: Anorectal cytology (ARC) screening programs can allow the detection of small lesions for treatment and eradication of high-grade intraepithelial lesions and careful monitoring to detect early invasive cancer. Demonstrate the importance of ARC in HPV-induced lesions.
Methods: It was performed the liquid-based anal cytology in 219 HIV-positive patients, aged 18 to 75 years, 188 men and 31 women, with a mean age of 40 years.
Results: Among the 219 participants cytologically evaluated, we identified 12 people (5.47%) presenting atypical squamous cells of undetermined significance (ASCUS), a marker for a possible anal neoplasm. About this result, it is notable the higher prevalence of ASCUS in men (83.3%) compared to women (16.6%) in the survey. The average age of the patients was 43 years. Subsequently, it will be necessary to perform an anoscopy to explore other possible clinical findings in the examination.
Conclusion: Over the past 50–60 years the incidence of invasive squamous cell carcinoma of the cervix has decreased around 80% in countries which have implemented cervical screening program with quality, coverage, treatment and follow-up of the women. Likewise, anal screening programs may generate comparable success, since anal cytology sampling of the anal–rectal transformation zone can detect squamous intraepithelial lesions. Therewith, patients with ASC-US) or worse should be referred for anoscopy.

PS-06-036
Application of immunohistochemistry for gastritis staging assessment
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Background & objectives: Chronic gastritis (CG) staging is useful way to estimate the risk of gastric cancer. However, compliance with the international recommendations (the number and orientation of gastric biopsy specimens) is crucial. The usage of immunohistochemistry (IHC) techniques may improve staging assessment.
Methods: The study included antral mucosa specimens with absolute and metaplastic atrophy (n=465) from 155 patients with CG. IHC markers CDX2, MUC2, CD10, MUC5AC, MUC6 were used. MUC5AC, MUC6, MUC2 staining intensity was estimated on the basis of semiquantitative scale (from 0-absent to 3-marked). CD10 expression was assessed binary (presence/absence). CDX-2 staining was evaluated according to intensity: absent-0, weak/moderate-1, marked-2.
Results: In the samples with absolute atrophy MUC5AC and MUC6 were strongly expressed in the gastric surface/pits region and glands cells cytoplasm, respectively. The more was atrophy severity, the less was length of MUC6 expression zone. In intestinal metaplasia (IM) there was a nuclear CDX-2 staining in all cells, intensity varied from 1 in incomplete IM to 2 in complete IM. There was also strong cytoplasmic MUC2 expression in goblet cells, and brush border-associated CD10 expression in complete IM. Weak CDX-2 nuclear staining in the gastric epithelium had also been the most interesting. Focal complete IM was found in 75% of such specimens after additional histological sections.
Conclusion: The obtained data of the markers expression revealed CDX-2 protein as the most valid for atrophy assessment with sensitivity=86% [73.26-94.1] and specificity=74% [57.51-83.77]. Moreover, CDX-2 was expressed throughout the gland, which would be extremely helpful in absence of proper specimen orientation. This position gives us ground for thinking about CDX-2 as a possible surrogate marker of the gastric mucosal atrophy.

PS-06-037
CDX2 as a surrogate marker of gastritis staging
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Background & objectives: The usage of immunohistochemistry (IHC) may improve of chronic gastritis (CG) stage assessment in cases of potential non-compliance with the investigation protocol (fewer number of biopsy specimens). Marker of intestinal differentiation CDX-2 might be used for such approach.
Methods: CDX-2 expression parameters were evaluated in 155 CG cases assessed with OLGA system. The following parameters were analysed: expression pattern (EP, ≤3 cells – 1, >3 cells – 2, the whole gland – 3), CDX2-positive cells (PC, 0%-0, <5%-1, 5-25%-2, 25-50%-3, >50%-4), staining intensity (IS, none-0, weak-1, strong-2). CDX-2 expression indexes (EI) were calculated according by formula: EP+PC×IS.
Results: Correlations between CDX-2 index and CG stage were calculated according to artificial model of taking biopsies from one, two or three points of gastric mucosa. The highest r-Spearman's values were recorded for point 3 (stomach angle, r=0.673, p<0.01); 3 and 5 (greater curvature of the corpus, r=0.624, p<0.01); 1 (greater curvature of the antrum, r=0.592, p<0.01), respectively. Logistic regression models of CG staging based on CDX-2 index were constructed. The highest Se=80.4%, Sp=82.8% and Ac=83.9% were demonstrated by a model based on EI in biopsy specimens from points 1+3+5. EI less than 7 indicated CG stages I-II and greater than 7 for stages III-IV.
Conclusion: The adapted approach for CG stage assessment based on CDX-2 expression evaluation can be used if OLGA-system protocols are violated, number of specimens is low or samples are damaged (fragmentated, not oriented, etc). In such cases, CG staging with the usage of CDX-2 (EI) would be helpful approach to estimate CG stage in a particular patient and stratify the risk of gastric adenocarcinoma development.

PS-06-038
Gastric carcinoma with lymphoid stroma: a case report and literature review, with emphasis on different classification systems, including ISH/IHC classification as a molecular surrogate
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Background & objectives: Gastric cancer (GC) is the 3rd-cause of cancer-related mortality worldwide. The various current classification systems reflect its morphological, prognostic and molecular heterogeneity. Aim: Critically review/discuss the usefulness of different classification systems, applied to a rare case of GC with lymphoid stroma.
Methods: Case:62-year-old male with an infiltrative lesion in the incisura angularis/small curvature, which on resection measured 9x7cm and invaded the serosa. Microscopy showed a poorly differentiated neoplasm composed of polygonal cells with indistinct borders, arranged in irregular nests and permeated by abundant lymphocytes. EBER-ISH was positive. MLH-1, E-cadherin and P53 showed physiological expression. PD-L1 was positive in >50% of tumour cells.
Results: According to current GC classifications, our case would be included in the indeterminate-type (Lauren), infiltrative-type (Ming) and GC with lymphoid stroma (WHO) groups. These "morphological" classifications fail to reflect the driver tumorigenic mechanisms, and mostly lack clinical relevance or predictive/therapeutic value. The TCGA/ACRG molecular classifications partly answer these issues but are too expensive for routine use. Thus, a recent IHC/ISH based classification (mostly based on TCGA data) which divides GC in five clusters has emerged, which relies on the sequential evaluation of 4-markers: EBER-ISH, MLH1-IHC, E-cadherin-IHC and P53-IHC. The present case would be included in cluster-1 (EBV-associated). These tumours are frequently associated with PD-L1 expression, as seen in our case.
Conclusion: GC stratification based on IHC/ISH is widely accessible, reproducible, inexpensive and may represent a valuable tool in prognostic and therapeutic decisions. Regarding our case, GC with lymphoid stroma is a rare subtype, which is classically EBV-positive. Thus, it is often included in the EBV-positive cluster of the proposed IHC/ISH classification. These patients are mostly male, with poorly differentiated tumours, located in the body and have a better prognosis. Importantly, they frequently present PD-L1 and PD-L2 amplification, with potential therapeutic implications.

PS-06-039
The value of two sections on lymph nodes from patients with colorectal cancer in a routine setting
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Background & objectives: Staging of patients with colorectal cancer depends on identifying an accurate number of lymph node metastases (LNMs). This study aimed to investigate if two sections of each lymph node would contribute to detect more metastases compared with a single section.
Methods: Surgical specimens from patients diagnosed with colorectal adenocarcinoma in our department during a three-month period were included. Two sections were cut from each macroscopically identified lymph node. A resident and a pathologist evaluated all slides for presence of LNMs and consequent staging due to one versus two sections. A third pathologist confirmed all cases of LNMs.
Results: In total 3218 lymph nodes with two sections from 121 patients were available. A metastasis was identified in 158 lymph nodes (4.91%). In six of these a LNM were present in only one of the sections (3.80%). Each of the six lymph nodes originated from six individual patients. In two of six patients the presence of an extra LNMs was crucial for the stage. In one patient the pN category was changed from N0 to N0(i+) and in the other patient from pN1 to pN2.
Conclusion: The histological assessment of lymph nodes from patients with colorectal cancer with two sections instead of a single section resulted in a small increase in number of detected metastases. However, the stage was changed in two patients, which might influence the choice of oncological treatment. A single extra HE-stained slide results in a minor extra workload at a limited expense and is thus a feasible method in most laboratories.

PS-06-040
Dysplasia in Barrett's oesophagus - immunohistochemical features with potential prognosis value
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Background & objectives: In Barrett's oesophagus (BE) normal squamous mucosa is replaced by metaplastic columnar epithelium. BE predisposes to dysplasia and adenocarcinoma. We aimed to investigate immunohistochemistry features that could reinforce the diagnosis of dysplasia or predict higher risk for malignancy.
Methods: Immunostaining for p53, Cyclin D1, and BCL2 was performed on 16 biopsies showing Barrett's oesophagus separated in two groups: 8 cases with dysplasia and 8 cases without dysplasia, paired by sex and age. Expression was quantified in percentage of positive metaplastic mucosal cells. In the dysplasia group positivity was measured in dysplastic tissue and separately in non-dysplastic tissue.
Results: p53 was positive in all dysplasia cases and in just 3 non-dysplasia cases. Cyclin D1 was positive in all 16 cases, while BCL2 was light positive in 4 cases overall. Analysing comparatively the positivity percentages between the dysplastic tissue and the surrounding metaplastic tissue in 7 cases from group A (in 1 case dysplastic tissue was unfortunately depleted), we found a statistically significant (p=0.0482, t-test) mean difference (30.14%) in p53 staining. We also tested for differences in expression grades between the two groups, first comparing only non-dysplastic tissue and second comparing dysplastic epithelium from group A with metaplastic epithelium from group B, but found no statistically significant differences.
Conclusion: There is a significant degree of intraobserver and interobserver variability in the diagnosis of dysplasia in BE. Because finding of dysplasia in BE involves higher risk for malignant transformation and more extensive follow-up, there is a need for consistent methods of diagnosis. p53 positivity overall is proof for "field mutation" of metaplastic cells, while overexpression of p53 in dysplastic cells could be used for confirmation when in doubt and as a marker of poorer prognosis.

PS-06-041
Deeper sections reveal residual tumour cells in rectal cancer specimens diagnosed with complete pathological regression following neoadjuvant treatment
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Background & objectives: Guidelines and requirements for diagnosing complete pathological regression in rectal cancer after neoadjuvant treatment vary, and there is currently no consensus on best practice. We examined the consequences of this inconsistency for diagnostic accuracy and prognosis.
Methods: All patients diagnosed with ypT0 rectal cancer from 2015 to 2020 in our department were included (n = 23). In accordance with current British guidelines, three additional sections were cut from each FFPE block and stained with H&E. The distance between levels was 200 μm. Slides were reviewed by two pathologists for presence of residual tumour cells.
Results: Additional sections revealed residual viable tumour cells in seven patients (30.4 %) originally diagnosed with complete pathological regression. Of these, three patients (42.9 %) later had local recurrence or distant metastasis during the follow-up period, compared with two patients (12.5 %) in the group with no residual tumour cells in deeper sections (p = 0.14). In four of the seven patients with residual tumour cells, careful examination of the original slides revealed minute foci of tumour cells or areas suspicious for residual tumour. These areas were interpreted as non-malignant or overlooked at the time of diagnosis. The residual tumour was more obvious and easily recognized in the deeper sections.

Conclusion: Our results show that systematic use of deeper sections in evaluation of tumour regression in rectal cancer reveals the presence of residual tumour cells in a subset of patients originally diagnosed with complete pathological regression based on a single section per FFPE block. Furthermore, additional levels probably reduce the risk of overlooking small foci of tumour. Our results indicate that residual tumour increases the risk of recurrence, but due to the small sample size, the result is not statistically significant.

PS-06-042

IGF1 expression in gastrointestinal stromal tumours

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Background & objectives: Gastrointestinal stromal tumours (GISTs) are the most frequent mesenchymal digestive tumours, characterized by activating mutation involving KIT. They present with a spectrum of biological behaviours, from benign to malignant, but little is known about the factors that influence these transformations.
Methods: We evaluated the immunohistochemical profile and expression of IGF1 in 46 cases of gastric GIST from adult patients. A panel of three markers (CD117, CD34 and DOG-1) were used for diagnosis. IGF1 expression was identified in the cytoplasm of tumour cells, displaying a finely granular pattern, and was scored into 3 classes of intensity: negative, weak and strong.
Results: On histopathological examination, the most frequent subtype of GIST was spindle cell (50%), followed by the mixed and epithelioid subtype. Most tumours were diagnosed pT2 and pT3, with over half of them having increased mitotic activity. IGF1 was expressed in the vast majority of cases (97.82%). Most GISTs had uniform granular cytoplasmic expression, while some had scattered areas of accentuated staining in the tumour cells (17.39%). Strong IGF1 expression was correlated with larger tumour size ($p<0.001$), while no statistical association with other clinicopathological factors such as histological subtype, pleomorphism, mitotic activity, gross characteristics or sex of the patients was observed.
Conclusion: The IGF axis plays a significant role in some malignancies, being actively involved in carcinogenesis and cancer proliferation. Our study highlights the increased expression of IGF1 in the tumour cells of most GISTs, a feature suggestive of a secretory profile. Whether these tumours are governed by an autocrine/paracrine mechanism or not, the association with tumour size could indicate the active role of IGF1 in tumour growth and development and possible involvement in their biological profile.

PS-06-043

Role of RORα In epithelial mesenchymal transition and carcinogenic pathways of gastric carcinoma, an immunohistochemical study

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Background & objectives: Retinoid-related orphan receptor alpha (RORα) is a potent tumour suppressor gene. Epithelial mesenchymal transition(EMT) is involved in cancer invasion and metastasis. The aim is studying the role of RORα in EMT by immunohistochemical expression of RORα &E-cadherin in gastric carcinoma(GC).
Methods: Retrospective study of 73 surgically resected GC specimens with available corresponding adjacent non-tumour tissue and 167 cases of chronic gastritis collected from 2015 to 2020 at the archive of pathology department at faculty of medicine and National liver institute, Menoufia university. Tissue microarrays were constructed, RORα and E-cadherin immunohistochemical expression were assessed and then correlation with clinicopathological parameters and survival.
Results: RORα showed low expression in GC compared with adjacent non tumour and chronic gastritis($p=0.001$). Low expression of RORα was associated with diffuse type GC($p>0.001$), high grade tumours ($p=0.017$), positive nodal metastasis($p=0.013$) and high tumour budding($p=0.010$). E-cadherin showed low expression in GC compared with adjacent non-tumour and chronic gastritis($p>0.001$). Most GC exhibited heterogeneous and negative expression of E-cadherin (69.9%&21.9%). Negative and heterogeneous expression of E-cadherin were significantly associated with high tumour budding($p=0.021$), lymphovascular invasion($p=0.01$), diffuse type GC ($p=0.009$) and advanced tumour pathological stage ($p=0.005$). RORα showed co-parallel correlation with percent of E-cadherin membranous positivity($p=0.040$). Low RORα expression had a significant association to cancer-related death($p=0.036$) when compared with high RORα expression.
Conclusion: RORα reduction in both GC and adjacent non tumour tissue indicate that it is a multistep carcinogenic factor. Co-parallel correlation between RORα and E-cadherin expression suggest its role in inhibition of epithelial mesenchymal transition in GC. RORα may be a potential therapeutic target for GC by utilization of RORα agonist or activator.

PS-06-044

Her2 testing of gastric cancer patients in Albania: results from a retrospective study

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Background & objectives: Gastric cancer (GC) is the fourth most common cancer in Albania. HER2-positivity rates in GC are reported with a wide range. There is no data for it in Albania.
Methods: A total of 192 patients, with primary GCs was retrospectively analysed for HER2 overexpression by IHC. Dual SISH, was used in only 20 GCs with equivocal results. We dispersed HER2 results by: gender and age, histopathological diagnosis and stage, type of the specimen. The results were compared.
Results: We examined by IHC 73.4% (141 cases) surgical and 26.5% endoscopic biopsies: 18.4% (26 cases) and 15.7% (8 cases) HER2 3+, respectively. HER2 overexpression (3+) was detected in 17.7% (34 cases). HER2 equivocal (2+) was detected in 24.5% (47 cases). 17.8% , 14%, 4.7% were respectively intestinal type, diffuse, signet ring and the rest adenocarcinoma NOS. GC prevailed in the group age of 61-70 yrs (31.70%;), followed by 51-60 yrs (25%), 22.9% in 71-80-yrs. 20 cases analysed by SISH, showed Her2 amplification in 40% (8 cases). Economical restrictions and problems with preanalytical phase made it impossible to evaluate by SISH all 20 cases.
Conclusion: 17.7%of Albanian patients with primary GC were HER2-positive on IHC. There is no difference in biopsy and surgical specimen results. Economical restrictions can influence the results.

PS-07 | Digestive Diseases Pathology - Liver/Pancreas Posters

PS-07-001

The Role of STIM1 in Primary and Metastatic Pancreatic Ductal Adenocarcinoma

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Background & objectives: Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal malignancies. Therefore, we aimed to evaluate the role of STIM1 in the pathogenesis of primary and metastatic PDAC.
Methods: This immunohistochemical study was carried out on 73 PDAC cases; 48 primary cases and 25 cases of PDAC metastatic to the liver or

omentum. In addition, 23 cases from non-tumour pancreatic tissue and 10 normal pancreatic tissues as a control group were included. Tissue microarray (TMA) was prepared. Both epithelial and stromal STIM1 expression were evaluated in the studied groups.
Results: Both epithelial and stromal STIM1 were significantly overexpressed in primary PDAC cases compared to the adjacent non-tumour pancreatic tissue and normal pancreatic tissue groups (P<0.001, for all). High epithelial STIM1 expression was significantly associated with primary PDAC (81.3%) in comparison to metastatic group (60%) (P=0.049). However, there was no significant difference regarding stromal STIM1 expression between primary and metastatic PDAC (P=0.113). Epithelial STIM1 was significantly associated with the presence of significant intratumoral desmoplastic stroma (P=0.036).
Conclusion: Both epithelial and stromal STIM1 may have a role in the early development of PDAC. Targeting STIM1 may be effective in primary and metastatic PDAC patients. The significant epithelial STIM1 expression and its association with presence of desmoplastic stroma may indicate epithelial mesenchymal transition.

PS-07-002
Solid pseudopapillary neoplasm of the pancreas: a series of 11 cases
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Background & objectives: Solid-pseudopapillary neoplasms (SPN) of the pancreas are relatively rare epithelial tumours of low-grade malignancy that have no specific clinical or radiological features. Throughout this series we aim to focus on the clinical, microscopic and immunohistochemical characteristics of SPN.
Methods: We conducted a retrospective data analysis of 11 cases of patients diagnosed with SPN in our departments between January 2009 and March 2021.
Results: 1 out of the 11patients was male. Patients' age ranged from19 to78 years with an average of 29.
4 patients complained of abdominal pain. Only 2 showed portal-hypertension symptoms. In 2cases, SPN was an incidental discovery. The most common location was the pancreatic body. All-but-one patient underwent curative surgery, the remaining case was only biopsied. Grossly, the tumours were encapsulated brownish haemorrhagic friable nodules with an average size of 8.2cm (4–12cm). Only 4 were macroscopically cystic. Histologically, the common architecture alternates pseudopapillary and solid areas. Mitotic figures were rare to absent. Other features include cytoplasmic vacuolization(1case), hyaline globules(4case), degenerative changes such as necrosis(2cases) and calcifications(1case). All SPN stained with beta-catenin and CD10.
Conclusion: Familiarizing pathologists with SPN is important since complete surgical excision is usually curative. The overall prognosis remains good despite possible recurrences. When clinico-radiological signs are of no help ultrasound-guided fine-needle aspiration and histopathologic evaluation should do the deed.

PS-07-003
Alpha-smooth muscle actin positive stromal cells relates with stemness/cholangiocytic features in primary liver carcinomas
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Background & objectives: Alpha-smooth muscle actin (ASMA) expression in stroma suggests a crosstalk between epithelial and stromal cells through epithelial-mesenchymal transition. Primary liver carcinomas (PLCs) with stem/progenitor phenotype present worse prognosis. Expression of ASMA/progenitor cell/cholangiocytic immunomarkers in a series of PLCs was evaluated.
Methods: In a series of 94 epithelial malignant liver tumours, concerning 51 consecutive patients undergoing hepatic resection/liver transplantation (2012-2016), classified according with 2019 World Health Organization (WHO) histopathological criteria, CK7/CK19, EpCAM (BerEp4) and ASMA immunoexpression in single or clusters of tumour cells were searched. Eighty-six tumours were hepatocellular carcinomas (HCCs); 3 were combined hepatocellular-cholangiocarcinomas (cHCC-CCs) and 5 were intrahepatic cholangiocarcinomas (iCCs).
Results: Thirty-eight HCCs expressed ASMA in stroma fusiform cells, 14 also in surrounding hepatocytes; 4 had discrete immunoexpression in tumour cells; 22 HCCs were CK7+, 4 CK7+/CK19+,6 EpCAM +, where 3 CK7+/CK19+.
The cHCC-CCs presented ASMA positive fusiform stroma cells and 1 case showed positive peritumoral hepatocytes; 2 CK7+, 2 CK19+, 3 EpCAM+ and 2 CK7+/CK19+/EpCAM+.
In the 5 iCCs, 4 had ASMA+ stroma fusiform cells and 2 ASMA+ peritumoral hepatocytes; all cases were CK7+/CK19+ and 3 EpCAM+.
Forty-one of the 45 tumours (28 patients) showing ASMA positive fusiform stroma cells had F3/F4 (METAVIR score) peritumoral fibrosis. In 6 patients tumour recurred within 6 years after curative surgery.
Conclusion: Then significant association (p<0,05) was observed between tumour stroma expression for ASMA and CK7, CK19 and EpCAM tumour cells expression. ASMA expression seems to be associated with stem/cholangiocytic cells in liver carcinomas. These preliminary results deserve interpretation for treatment definition in order to effectively modulate the malignant epithelial/stroma cooperation, beyond searching serological biomarkers.

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PS-07-004
Histological abnormalities of intra-hepatic vasculature in chronic viral Hepatitis B
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Background & objectives: Chronic viral Hepatitis B (CVHB) is defined by chronic necrotizing and inflammatory lesions of the hepatic parenchyma.
The aim of study was to determine the abnormalities of intrahepatic vasculature in CVHB and their correlation with inflammatory activity and fibrosis stage.
Methods: Our study was retrospective on 30 cases of CVHB confirmed by the pathological examination of the liver biopsy over a period of 5 years (January 2013- April 2018) in La Rabta Hospital. For activity and fibrosis, the Metavir score was used. A statistical analysis was performed and the significance level was set at 0.05.
Results: This study included 13 males and 17 females with CVHB. The average age was 41 years. On histological examination, hepatitis activity was score 1 (N=7), 2 (N=19) and 3 (N= 4). The fibrosis was stage 1 (N= 10), 2 (N= 10) and 3 (N= 10). All cases showed vascular lesions. They were represented by portal angiomatosis (N=23), thrombosis of portal veins (N=7), sinusoidal dilatation (N=16), abnormal parenchymal draining veins (N=18), phlebosclerosis (N=14) and aberrant portal vessels (N= 24). Analytic study showed that activity is significantly associated with thrombosis of portal veins (p=0.02) and there is no significant association between vascular changes and fibrosis.
Conclusion: The vascular changes observed in chronic hepatitis involve angiogenesis lesions.
Two mechanisms explain the development of this angiogenesis:

First, it is part of the response to inflammation and the process of scarring that is triggered with chronic liver injury. Secondly, it is stimulated by hypoxia associated with fibrosis.
This angiogenesis has two consequences: the aggravation of fibrosis and the genesis of portal hypertension.
These lesions represent a sign of a progression of the disease.

PS-07-005
Colorectal cancer in patients with Inflammatory Bowel Disease and Primary Sclerosing Cholangitis
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Background & objectives: The increasing incidence of Inflammatory Bowel Disease (IBD) in Latin-America enables us to explore extra-intestinal manifestations and complications of the disease. This study aims to describe IBD patients and PSC who developed colorectal cancer at a reference centre in Colombia.
Methods: A chart review study of patients with IBD between 1996 and 2019 at Hospital Universitario Fundación Santa Fe de Bogota. Patients diagnosed with PSC and colorectal cancer were reviewed and analysed.
Results: From a total of 327 patients with IBD, 16 patients with colorectal cancer were identified. 13 had UC and 3 CD, 10 patients were female and 6 male. Mean age of diagnosis of IBD was 56.28 years old. 9 patients had pancolitis. 11 patients (68.75%) had previous hospitalizations compared to cancer-free patients (31.25% n=5). 4.3 % (n=14) of all patients with IBD developed PSC and among these 14.3% developed colorectal cancer. Compared with patients without PSC 3.8% developed colorectal neoplasia. A positive association between PSC and colorectal cancer was obtained in patients with IBD (OR= 4.18, p= 0.008). Low-grade dysplasia was found in 6/327 patients (2.2%) and one high-grade dysplasia.
Conclusion: IBD increases the risk of PSC and colorectal cancer. These diseases share an underlying predisposition and a PSC-IBD phenotype has been described. This study reinforces a positive association between PSC-IBD and the increased risk of colorectal cancer. This increased risk is greatest with pancolitis and with higher degrees of endoscopic and histological inflammation. Chronic inflammation with cytotoxic and carcinogenic effects of bile acids in the colon are proposed mechanisms. PSC is underdiagnosed in IBD. Follow-up magnetic resonance cholangiography is recommended.

PS-07-006
Prognostic and therapeutic role of IgG4 liver infiltrate in patients with autoimmune hepatitis and overlap syndrome.
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Background & objectives: Some autoimmune hepatitis (AIH) have elevated serum IgG4 levels, and clinical characteristics of such patients are currently incompletely characterized. The aim of this study is to correlate IgG4 expression in patients with AIH and overlap syndrome (OS), with clinical data.
Methods: Retrospective single-centre study that includes 109 patients, 77% with AIH and 23% with OS. Liver biopsies were submitted for pathological study and IgG4 and IgG immunohistochemical techniques were performed in all cases. The presence of >10 IgG4 plasma cells per high magnification field was considered significant. A comparison of those biopsies with some clinical, analytical and therapeutic parameters was performed.
Results: 61% women, average age: 51. At diagnosis, 19% presented severe acute hepatitis, 15% liver cirrhosis, 83% ANAs ≥1/80 and 18% ANCAs. 18% presented significant IgG4 infiltrate, 24% with OS and 17% with AIH (p=0.29) and was associated with higher age, advanced liver disease, 32% having cirrhosis (p=0.01), and analytically with higher IgG, lower albumin and higher ANCAs; 95% had ANAs ≥1/80 compared to 84% among those without IgG4 infiltrate (p=0.19). Patients with significant IgG4 infiltrate required second-line drug use less frequently (6% vs 34%, p=0.02), but longer time to discontinuation of corticosteroid therapy (22 vs 14 months, p=0.04). Complete response and time to complete response was similar (p=0.49 and p=0.65).
Conclusion: Hepatic IgG4 significant expression in patients with AIH and OS was associated with more advanced liver disease, 32% having cirrhosis at diagnosis. Corticosteroid tapering was slower, although the need for second-line drug treatment was lower in these patients. The study of IgG4 in liver biopsies of AIH and OS may be a useful parameter to understand evolution and management of these patients.

PS-07-007
The real life of precision medicine in biliary tract cancers: a tertiary referral centre experience
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Background & objectives: Biliary tract cancer (BTC) is the second most common malignant liver tumour with high aggressiveness and mortality. Intrahepatic and extrahepatic subtypes show different morphology, immunophenotype and molecular alterations, which should be investigated in the routine practice for precision therapy.
Methods: We performed a retrospective analyses of the molecular tests performed in our laboratory since July 2020 on a consecutive series of BTCs regarding the molecular alterations that have an impact on clinical decisions such as mutation of IDH1 and IDH2, FGFR2 fusions, mismatch repair proteins status, NTRK, ERBB2 and BRAF (as recommended by guidelines, immunohistochemistry, FISH and next generation sequencing).
Results: 27 patients affected by BTC were investigated after multidisciplinary meetings in the Liver Unit. We evaluated intrahepatic (85%) or extrahepatic cholangiocarcinoma (15%) on bioptic or surgical material. Targetable genetic alterations were found in 13 patients (48%), all affected by intrahepatic cholangiocarcinoma (ICC): 7 cases had IDH1 mutation (p.Arg132Cys, c.394C>T) and were poorly differentiated (G3) ICC "small duct type", 1 IDH2 mutation (p.Arg172Gly c.514A>G) in ICC undergone neoadjuvant chemotherapy, 3 FGFR2 fusions ICC large duct type (2/3 G3), one had loss of PMS2 confirmed by genetic testing (and IDH1 mutation) and 2 large duct type ICC with loss of both MLH1 and PMS2. No NTRK fusion neither BRAF mutation were found.
Conclusion: Biliary tract cancer has recently gained attention thanks to targetable molecular alterations allowing for personalization of therapies in clinical practice. The detection of these alterations is routinely performed and is highly reliable both on bioptic and surgical material. The significant incidence of these alterations in our routine practice strongly support the real need of searching for them in clinical practice to establish the correct therapy for our patients and deeply understand the complex biology of biliary tract cancers.

PS-07-008
Incidence of gallbladder carcinoma in patients submitted to cholecystectomy: experience of the Centro Hospitalar e Universitário de Coimbra
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Background & objectives: Malignant neoplasm of the gallbladder is uncommon with a poor long-term survival. Our aim is to identify the clinicopathological prognostic factors for survival in patients with Gallbladder cancer (GBC) submitted to surgery in our institution – a tertiary centre.
Methods: Forty-one patients underwent surgical treatment for GBC between 2008-2019 at our centre. The majority of the tumours (85.4%) were gallbladder adenocarcinomas; 41.5% of GBC were diagnosed incidentally, 65.9% of the patients had symptoms and 26.8% presented with acute cholecystitis. 46.3% of patients were stage III (AJCC) or higher. Analysis was conducted using SPSS.
Results: Median follow-up was 20.5 months (IQR 8.8-53.8) and median overall survival (OS) was 23 months. 3-year and 5-year survival rates were of 43.2% and 39.6%, respectively. On immunohistochemistry analysis, 6 patients (14.6%) were HER2+, but the HER2 status did not show influence on OS (median OS 18 vs 20 months, p=0.649); all had microsatellite stability. There was no association between HER2 expression and staging (p=0.35).
Conclusion: This study on GBC is, as far as the authors know, the first in Portugal. Surgery is still the gold standard for curative treatment and some patients with favourable prognosis may be identified. The over expression of HER2 could select patients for targeted treatment and prompt tissue sampling in unresectable patients.

PS-07-009
Clinicopathological study on morphological subtypes of hepatocellular carcinoma: a single-institution experience
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Background & objectives: The WHO 2019 recognized several morphologic subtypes of hepatocellular carcinoma (HCC) with different pathological features, immune profiles, and clinical relevance of diagnosis. We aimed to analyse HCC subtypes in our population and assess the histological parameters.
Methods: The resection specimens of 56 cases, received between 2007 and 2021 at the Maastricht University Medical Center+, were revised according to the current WHO 2019 classification and the ICCR guidelines. The data on age, sex, surgical specimen, morphological subtypes, tumour grade, growth pattern, tumour extension, margins, vascular and perineural invasion, regional lymph nodes and distant metastasis were collected.
Results: 56 resection specimens from 20 women and 36 men with the median age of 64 years [range 26 to 88 years] were obtained. The two most common morphologic subtypes were steatohepatitic and clear cell HCC. However, 36 cases (64.3%) demonstrated multiple morphological patterns. One tumour (1.7%) revealed a prominent lymphocytic infiltrate, suggestive of a lymphocyte-rich HCC. The syncytial cell-like giant cells were found in 15 cases, usually in less than 5% of the total tumour volume. The solid growth pattern was most common, yet we often observed concurrent heterogeneous growth patterns. Forty cases (71.4%) showed satellitosis. Perineural growth was an infrequent feature, identified only in two cases (3.5%).
Conclusion: While steatohepatitic and clear cell HCC were the most common morphologic subtypes, the majority of cases demonstrated multiple morphological patterns and heterogeneous growth patterns. Clear diagnostic criteria for the different morphological subtypes are necessary for tumours with heterogeneous morphology. Precise subclassification of HCC, particularly in cases with distinct morphologies and diverse tumour growth patterns, may facilitate an accurate prognostication, follow-up and treatment.

PS-07-010
Role of CD44/RhoA in the regulation of oncogenic YAP in hepatic carcinogenesis
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Background & objectives: Activation of oncogenic YAP is an early event in hepatocellular carcinoma (HCC). However, it remains unclear how YAP is activated in HCC. Several mechanisms, including control by Hippo signalling, beta-catenin signalling, or a CD44/RhoA- dependent pathway have been described.
Methods: YAP and CD44 expression were assessed by histopathology in human and mouse HCC. Human HCC cell lines HepG2, HuH7 and Mahalavu were treated with the CD44 antibody IM7 and Rho inhibitor rhosin. Treatment was evaluated via MTT proliferation assay. Protein and mRNA expression were quantified by western blot, immunofluorescence staining and quantitative real-time PCR, respectively.
Results: Immunohistochemistry staining in mouse and human HCC showed a correlation of the expression of CD44_v6 and active, nuclear YAP. Additionally, the expression of YAP target genes correlated with the expression of CD44 by mRNA in mouse and human HCC. While the CD44 antibody IM7 didn´t exert any effect on cell proliferation, rhosin – an inhibitor of downstream RhoA – decreased the proliferation in HCC cell lines significantly. By western blot, only slightly reduced YAP and P-YAP protein levels were observed, but immunofluorescence staining of HepG2 and Mahalavu demonstrated a significant increase in inactive, cytoplasmic YAP upon Rhosin treatment. In HepG2 cells, rhosin treatment decreased the expression of YAP target genes.
Conclusion: Correlation of YAP and CD44 staining in human and mouse HCC indicates that a previously described CD44/RhoA axis could regulate the activation of oncogenic YAP in HCC. Inhibition of RhoA in human hepatoma cells reduced proliferation and correlated with inactivation of YAP. If targeting of RhoA could therefore present a promising treatment strategy in human hepatocellular carcinoma is subject to further investigation.

PS-07-011
ESM1 as a predictive marker of tumour recurrence in patients who underwent liver transplantation for hepatocellular carcinoma
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Background & objectives: Angiogenesis participates in cancer pathogenesis and metastasis. Endothelial-cell-specific molecule-1 (ESM-1) is overexpressed in tumour endothelial cells in hepatocellular carcinoma (HCC). This study aimed to investigate ESM1 as a marker of tumour recurrence in patients who underwent liver transplantation for HCC.
Methods: This retrospective study included 52 patients who had undergone liver transplantation for HCC during period from March 2010 to March 2021. Clinical, laboratory and histopathological data were collected from medical records of Pathology Department, National Liver Institute, Menoufia University. Sections from tumour and non-tumour liver tissue were prepared for Immunohistochemical staining with ESM1 antibody.
Results: In the present study, 34.6% of HCC cases showed positive ESM1 expression in tumour, while all non-tumorous tissue showed negative ESM1 expression. Most cases (71.4%) with HCC recurrence were positive for ESM1 expression. ESM1 expression was significantly associated with age ≥ 55 years. Univariate analysis showed that ESM1 positivity (p= 0.043), Alpha-fetoprotein (p=0.021), tumour size ≥3cm (p=0.001), advanced tumour pathologic staging (p=0.002) and

microscopic lymphovascular invasion (p=0.019) were significantly associated with tumour recurrence after liver transplantation for HCC. Value of ESM1 expression as a predictor of HCC recurrence after liver transplantation was evaluated and showed 71.43% sensitivity, 71.11% specificity, 27.78% positive predictive value, 94.12% negative predictive value and 71.15% accuracy.
Conclusion: Immunohistochemical expression of ESM1 could be used as a marker of poor prognosis that predicts tumour recurrence in patients planning for liver transplantation in HCC cases. ESM1 might be used to predict outcomes in patients with HCC diagnosed through percutaneous biopsy or hepatic resection.
Key words: Endothelial-cell-specific molecule-1, Hepatocellular carcinoma, liver transplantation, Recurrence.

PS-08 | Endocrine Pathology Posters

PS-08-001
Injuries associated with papillary carcinoma in thyroid surgical parts in the department of pathology of the federal university of Ceará, Brazil, in the period from July 2016 to December 2020
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Background & objectives: Papillary thyroid carcinoma (PTC) is the most common malignancy of the thyroid. The verification of coexistence with associated findings is important for the monitoring and prognosis. The article aims evaluate the association between coexisting lesions in patients diagnosed with PTC.
Methods: Realized through the analysis of an institutional historical series involving all cases submitted to partial or total thyroidectomy for papillary carcinoma, performed in the department of pathology of the federal university of Ceará, Brazil, in the period from July 2016 to December 2020.
Results: A total of 110 patients were included in the study, with 69 (63%) associated with some finding, the most common being: lymphocytic thyroiditis (17%) and follicular adenoma (17%), in addition, 32% of patients had more than one finding. We observed a preponderance of women, representing a total of 101 (92%) among the cases, with a mean age of 55.2 years. Of the total, 2 (2%) patients had perineural invasion, 15 (16%) angiolymphatic invasion and 24.2 (22%) extraglandular extension. Regarding anatomopathological staging, 54% of pT1 cases, 14% pT2, 21% pT3 and 3% pT4.
Conclusion: In literature are few studies that analyse the presence of lesions associated with PTC and its implications. In our study, 65% of the cases of PTC were associated with one or more findings and their presence was associated with the presentation of disease at an earlier stage. It is possible that the search for medical treatment in the face of benign thyroid lesions favoured the finding of PTC at an earlier stage and influenced the prognosis and recurrence.

PS-08-002
Predictive Factors of Lymph Node Metastasis in Thyroid Papillary carcinoma
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Background & objectives: Papillary thyroid carcinoma (PTC) is associated to lymph node metastases (LNM), in up to30 to 80%. However, pathological predictors of LNM have yet to be established. We aim to determine clinicopathological predictive factors for LNM in PTC.
Methods: We retrospectively analysed 81 patients who were diagnosed with PTC in the Department of pathology of Habib Thameur's Hospital between January 2016 and December 2020. Univariate and multivariate logistic regression was used to analyse the correlation between clinicopathological characteristics and the LLNM of PTC.
Results: A total of 81 patients was included. They were 11 men and 70 women, with a mean age of 42,8±12,6 years. Thyroidectomy and loboisthmectomy were performed in 70 and 11 patients respectively. Mean tumour size was> 2cm in 38 patients. The tumour was in the lower third in 24 cases. Vascular invasions were diagnosed in 20 cases and capsular effraction in 35 cases. Perithyroid involvement was noted in 14cases.The mean number of nodes dissected was 11,5. In 43 cases the number of nodes dissected was>5. Correlation between lymph node status and different clinico-pathological predictives revealed a statistically significant correlation with number of nodes dissected>5 (p=0,004). There was not statistically signification correlation with the other predictive factors.
Conclusion: Management of lymph node dissection in PTC is still controversial. The factors that predict LNM in PTC are important for treatment assessment. The results of this study identified only one statistically significant independent predictive factor for LNM in PTC: number of lymph nodes dissected. Therefore, lymph node dissection should be as complete and exhaustive as possible in case of PTC. However, the morbidity of thyroid surgery is increased when neck dissection is performed.

PS-08-003
Temporal changes in the epidemiological profile of well-differentiated follicular cell-derived thyroid carcinomas in our institution over a 15-year period: a retrospective, transversal study of 722 cases
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Background & objectives: Our study aimed to document the time trend evolution of papillary (PTC) and follicular (FTC) thyroid carcinomas in our institution over a 15-year period and to assess the impact of 2017 WHO classification of thyroid tumours on their epidemiological tendency.
Methods: All PTCs and FTCs registered in our department between 2001 and 2015 were re-evaluated. The histological diagnosis was established according to both 2004 and 2017 WHO diagnostic criteria. Non-invasive encapsulated follicular variant of PTCs were reclassified as NIFTPs (non-invasive follicular thyroid neoplasms with papillary-like nuclear features). Tumours' time trend evolution (according to 2004/2017 WHO classifications) was analysed and compared.
Results: Our study included 701 PTCs and 21 FTCs. Irrespective of whether the WHO 2017 or 2004 diagnostic criteria were applied, we noticed a statistically significant increasing annual rate of PTC (from 81.6% in 2001-2003 to 97.8% in 2013-2015, p=0.001 and from 85.7% in 2001-2003 to 98.2% in 2013-2015, p=0.001, respectively). However, application of 2017 WHO diagnostic criteria (excluding NIFTP from the PTCs) resulted in a significant decrease of follicular variant of PTC cases (n=190/701, versus n=65/701, dif. 17.82%, IC: 13.7-21.8%, p< 0.0001). FTCs revealed a significant decreasing trend in the annual rate only at the beginning of the study period (from 14.3% in 2001-2003 to 1.8% in 2013-2015, p<0.0001).
Conclusion: Our data revealed a significant increasing trend of PTCs treated in our institution over a 15-years period, irrespective of whether the WHO 2017 or 2004 diagnostic criteria were applied. However, the introduction of the NIFTP category resulted in a significant reduction in the number of PTCs. FTC remains rare.

PS-08-004

Predicting biological behavior of parathyroid neoplasms by morphological and immunohistochemical features

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Background & objectives: Parathyroid neoplasms show a wide spectrum of morphology (adenoma-carcinoma), which is difficult to predict biological behaviour by histomorphology. The aim of this study is to evaluate morphological and immunohistochemical predictors of biological behaviour of parathyroid neoplasms in a wide study-set.
Methods: We re-evaluated 888 parathyroidectomy specimens between 2000-2020. We re-evaluated the H&E slides of recurrent and atypical adenomas besides the carcinomas, using morphological criteria such as mitotic activity, necrosis, fibrous bands, growth pattern, perineural/vascular/capsular invasion, and metastasis. We also reassessed recurrent cases (first and the second biopsy). Then we correlated the morphological data with the follow-up data to predict biological behaviour.
Results: In 20 years' time, 656 cases were reported as parathyroid adenomas (F/M: 509/147, avg. 53,2 yrs) including 7 recurrent adenomas (avg. 41,3 yrs), 22 atypical adenomas (F/M: 10/12 and avg. 52,7 yrs), one of which was recurrent, and 12 of the adenomas were located ectopically (9 intra/juxta-thymic and 3 intra-thyroidal). There was 15 carcinomas (F/M: 5/10, avg. 47 yrs), two of which were recurrent, revealing ki-67 in a range of 1%-10%, in the contrary ki-67 was up to 30% in atypical adenomas. Both neoplasms revealed fibrous bands and variable mitotic activity but only carcinomas showed lymphovascular & capsular invasion besides higher p53 expression.
Conclusion: Parathyroid neoplasms are a difficult group of neuroendocrine tumours because markers such as ki-67 and morphological findings such as fibrous bands, growth patterns and mitotic activity are not always helpful to predict the biological behaviour or to distinguish an adenoma from a carcinoma. However, known immunohistochemical markers ,such as p53, may help more to the pathologist as well as the other markers (cyclin D1, p27 etc) and clinical & radiological correlation of the case.

PS-08-005

Carcinomas of the thyroid with Ewing family tumour element (CEFTEs): a case report

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Background & objectives: Few cases of "Carcinoma of the Thyroid with Ewing Family Tumour Element (CEFTEs)" were reported recently, as a small-cell, non-neuroendocrine thyroid tumour displaying expression of p63, CD99 and cytokeratins associating a ESWR1-FLI1 rearrangement. Thyroglobulin and Calcitonin are typically negative.
Methods: We present the case of a 75-year-old female, who had a history of mucinous lung adenocarcinoma and presented with a large infiltrative thyroid mass associating pulmonary and cervical lesions. Total thyroidectomy with lymph node dissection was performed and chemotherapy was started for suspicion of lung adenocarcinoma relapse. Histological examination with subsequent immunohistochemical and molecular studies were realised.
Results: The tumour has a solid architecture with a very focal follicular pattern without papillary nuclear features. Tumour cells exhibited loss of follicular markers such as TTF1 and TG (except for a few zones), were negative for Calcitonin and CEA as well as neuroendocrine markers. P63 and CD99 expression was strong and diffuse. Ki67 was overall low with an average of 5%. Lymph node metastases showed very focal expression of CT and CGA. Molecular study showed a rearrangement of the ESWR1 gene with a ESWR1-FLI1 fusion transcript and no Ret mutation was found. The diagnosis of CEFTE was proposed. The patient was stable under simple surveillance after 56 months of follow-up.
Conclusion: We report a case of CEFTE which is a rare and newly described entity. It is believed to arise from either solid cell nests or a pre-existing papillary thyroid carcinoma. Since they present a small cell cytology and ESWR1 rearrangement, the distinction from a typical Ewing tumour is challenging. Most studies describe this entity as having a good prognosis, as was the case for our patient, and, unlike our case, occurring in young patients.

PS-08-006

Primary bilateral macronodular adrenal hyperplasia in a familial cluster with a novel ARMC5 mutation

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Background & objectives: Primary bilateral macronodular adrenal hyperplasia (PBMAH) is a rare cause of Cushing syndrome (CS). ARMC5 is the most frequently mutated gene in PBMAH. We report the clinicopathologic features of two cases within a familial cluster with a novel ARMC5 mutation.
Methods: A 58-year-old man with CS and bilateral nodular formations of the adrenal gland was diagnosed with PBMAH. ARMC5 sequencing analysis was performed and he underwent bilateral adrenalectomy. His 31-year-old son had mild CS symptoms and unilateral increase in volume and nodularity of the adrenal gland. He was found to have the same genetic alteration and was submitted to unilateral adrenalectomy.
Results: The adrenal gland was multinodular in both cases, the largest nodule measured 28 mm in the son and 25 mm in the father. Histologically, the nodules were mainly comprised of fasciculata zone-like cells, with varied degrees of lipid depletion. The permeated adrenal cortex was scarce and atrophic. ARMC5 sequencing analysis revealed a heterozygous mutation c.152G>T(p.Gly152) on exon 1 in both cases. After surgery, there was an improvement in metabolic control, blood pressure, proximal muscle strength and weight loss in both patients.
Conclusion: Mutations associated with ARMC5 and PBMAH are still being discovered. In patients presenting with CS and multinodular adrenal glands with macronodules, it is important to be aware of PBMAH, and test for it, even in cases with unilateral enlargement of the gland and indolent clinical behaviour, as in the son's case. Also, unilateral adrenalectomy may be effective, at least initially, in patients with mild PBMAH.

PS-08-007

Can histomorphological features predict lymph node metastasis in papillary thyroid microcarcinoma?

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Background & objectives: Papillary thyroid microcarcinomas (PTMC), despite their favourable outcome, metastasise to lymph nodes occasionally. Our purpose is to define histomorphological features that are associated with lymph node metastasis (LNM) in PTMCs.
Methods: 248 cases, diagnosed as unicentric PTMC, that have at least 2 years follow up or that were metastatic at the time of diagnosis, were reviewed. Age, gender, tumour diameter, tumour borders, histologic subtype, nuclear score, tumour infiltrating lymphocytes, desmoplasia, psammoma bodies, presence of papillary structures, capsule, lymphatic, vascular and perineural invasion status were noted.
Results: Mean follow up time was 79 months (18-155 months). Among 248 cases, 20 cases (8,1%) had LNM, of which 2 also had distant metastases (to the mediastinal lymph node). In univariate analysis, LNM was significantly more frequent in males, under the age of 50, and in tumours that are >7 mm and classical type, also in tumours that have lymphatic

invasion, nuclear score 3, psammoma bodies, papillary structures and infiltrative borders (p<0,01). Presence of desmoplasia was also correlated with LNM (p<0,05). Other features evaluated were not relevant with LNM. Lymphatic invasion and male gender were found to be independent variables in multivariate analysis.
Conclusion: Despite their favourable outcome, PMCs metastasise to lymph nodes occasionally. Lymphatic invasion and male gender were found to be independent predictors of LNM. Besides, patients harbouring high risk histology such as classical type histology, high nuclear score, infiltrative tumour borders, desmoplasia and psammoma bodies should be carefully followed-up.

PS-08-008
Features of Oct4 expression in neuroendocrine tumours of different types
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Background & objectives: The transcription factor Oct4 plays a decisive role in embryogenesis, as well as in the survival of tumour cells of poorly differentiated tumours, which is the reason for their progression and resistance to chemotherapy.
Methods: Immunohistochemistry was used to study 85 NET: lung -21 (3 typical, TC, 6 atypical, ATC, carcinoids, 7 SC-NEC, 3 LC-NEC), 6 thymus (ATK - 5, LC-NEC -1), 18 stomach, 17 intestines (10 small, G1, 4 intestine, 3 rectum, G1), 23 pancreas, 3 Merkel carcinomas. The expression of Oct4 in the cytoplasm of cells was assessed in points (0-3+).
Results: Of 64 low grade NETs of all localizations, expression was detected in 62.5% (40/64), in 100% NET in the stomach and small intestine. From 21 NEC to 1 LC-NEC stomach. The most intense expression (3+), was characteristic of NET small intestine and stomach (90%, 92.3%), and in 2 ACTH-positive ATCs of the thymus. Moderate expression of Oct4 (2+) was detected in 19.8% NET: 50% ATC lung, 39,1% NET pancreas, 2 NET small intestine and stomach. Oct4 expression was absent in all NEC lung, stomach (except 1 LC-NEC), large intestine, Merkel carcinomas, NET rectum, 35,8% (5/13) TC/ATC lung/thymus, 60,9.8% (14/23) NET pancreas.
Conclusion: ECL-cell NETs of the stomach and small intestine are characterized by intense cytoplasmic expression of Oct4, which can be used as an additional diagnostic and prognostic criterion, as well as a cellular target for the development of new approaches to their treatment.

PS-08-009
Thyroid nodules: confrontation of echographic and histological data
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Background & objectives: The Thyroid Imaging-Reporting And Database System (TI-RADS) classification is sensitive but not very specific, leading sometimes to abusive cytological and histological explorations. Our study aimed to evaluate the sensitivity and specificity of the TI-RADS classification by reference to histological results.
Methods: A cross-sectional, retrospective and descriptive study was conducted at Pathology department of Habib Thameur Hospital between January 2016 and December 2017. The nodules were classified according to the TI-RADS. The diagnostic value of this score by reference to histology data was evaluated by calculating sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV).
Results: Eighty-one nodules have been identified. The mean age was 46,7 years and the sex ratio (M/F) was 0.07. Fifty nodules were classified as suspect (TI-RADS IV and V) and 31 non-suspect (TI-RADS I, II and III). The histological study revealed 56 benign lesions and 25 carcinomas which 96% were papillary carcinomas. Statistical analysis of these results showed a significant relationship between TI-RADS classification and histological data with a Se of 88%, a Sp of 48,21%, a NPV of 9,7% and a VPN of 98%.
Conclusion: Our study confirmed the good sensitivity of the TI-RADS system (88%) with excellent VPN (98%). However, its low specificity (48,21%) prompted us to propose the generalization of other evaluation systems (EU-TIRADS and ACR TI-RADS) with a simpler and more precise notation, allowing better management of thyroid nodules.

PS-08-010
Cribriform-morular variant of papillary thyroid carcinoma– a case series
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Background & objectives: Cribriform-morular variant of papillary thyroid carcinoma (CMV-PTC) is among the rarest of all variants of Papillary thyroid carcinoma(PTC). Distinct female predominance and association with familial adenomatous polyposis (FAP) characterize this unique variant of PTC.
Methods: Retrospective clinic-pathological review of nine cases of CMV-PTC diagnosed over a period of 5 years (2017-2021) was undertaken. The clinical findings were recorded from the electronic record system, and imaging details were obtained from the picture archiving and communication system (PACS). There were 8 women, and one male patient. The mean age was 27.7 years (age range;16-38 years).
Results: Multifocality in 22.2%, Left lobe involvement in 77.8%, size range of 2.8-7.5cm, and clinically negative nodes in all were the most notable clinic-radiological findings. All cases, on histology, resembled columnar cell variant of PTC. Solid areas in 22.2%, non-squamous morules in 55.6% cases(highlighted by Bcl2 and CD10), mitosis >5/10hpf in 11.1%, microscopic extrathyroidal extension in 22.2%, lack of necrosis or nodal metastases were other salient findings. Immunohistochemistry showed diffuse nuclear positivity for Beta-catenin(100%), ER, PR, and TTF1. Endoscopy revealed asymptomatic colonic polyposis in 3 patients (including the male patient), which on histology were tubular adenomas indicating associated FAP. All patients are alive without disease at last follow-up (range: 3-48 months).
Conclusion: CMV-PTC is rare and underdiagnosed; 4 out of 9 cases with an outside histology were misdiagnosed as classical PTC, and not CMV-PTC. Lack of morules in all cases, and rarity and lack of awareness especially occurrence in male gender being possible causes. CMV-PTC preceded FAP in all our cases, and as early detection and treatment of FAP is life-saving; the importance of recognizing CMV-PTC cannot be overemphasized.

PS-08-011
Clinico-pathological and molecular characterization of 9 cases of tall cell variant of papillary thyroid carcinoma
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Background & objectives: Tall cell variant of papillary thyroid carcinoma (TCPTC) is a rare, but more aggressive variant of PTC. We aimed to investigate the clinico-pathological and molecular characteristics of 9 cases of TCPTC registered in our Department over an 8-years period.
Methods: All PTC cases registered in our department between 2008-2015 were reviewed. Nine cases of TCPTC with available follow-up data and well-preserved formalin-fixed and paraffin embedded tumour blocks for molecular analysis were identified and included in the study. All TCPTCs were subjected to RT-PCR amplification targeting the BRAFV600E and RAS (KRAS, NRAS, HRAS) somatic mutations.
Results: The mean age of the patients was 52.48±14.84 years-old; all but one were females. The mean tumour size was 24.95±11.34 mm and 3 cases were multifocal. Extrathyroidal extension, with tumour invasion into the strap muscles of the neck was documented in 5 cases. Lymph

node dissection was performed in 4 cases; of these, three displayed lymph node involvement. All patients were treated by total thyroidectomy and received radioactive iodine therapy. During the follow-up period, one case (staged pT1bN1) developed lung metastasis 65 months after the initial diagnosis. With regard to the molecular profile, six (66.7%) TCPTCs were BRAFV600E positive, whereas none of the cases was associated with RAS mutations.
Conclusion: Tall cell histology represents a poor prognostic factor in PTCs. Our results emphasize the importance of recognizing and reporting TCPTC because of its more pejorative prognosis, with an increased risk of local invasion, lymph node and distant metastasis, as well as high frequency of BRAFV600E mutation.

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PS-08-012
A rare parathyroid neoplasm as a mimic of hyperplastic goitre: a case report
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Background & objectives: Parathyroid carcinoma is a rare tumour with a typical clinical presentation of parathyroid hormone excess signs and hypercalcemia, but may rarely be indolent, producing only mass effect symptoms. Herein, we present a non-functioning parathyroid carcinoma case mimicking a hyperplastic goitre.
Methods: A 55-year-old woman with a diagnosis of hyperplastic goitre 8 years prior, revealed a slowly expanding neck mass that had recently induced dysphagia. Biochemical analysis revealed normal serum calcium and parathyroid hormone levels; anti–thyroid peroxidase and anti-thyroglobulin antibodies were both negative. Nonetheless, the fine-needle biopsy of the mass suggested a lymphocytic thyroiditis and a thyroidectomy was performed.
Results: Grossly, the thyroidectomy specimen weighted 148 g and was almost totally replaced by a multinodular tumour with 12 cm in largest axis, with a tan cross-section and focal haemorrhage. Histologically, the tumour showed a solid nodular pattern, subdivided by broad fibrous bands and was composed of mildly pleomorphic chief cells with round to ovoid nuclei, some with dense chromatin and prominent nucleoli. There was capsule invasion and angioinvasion. These cells demonstrated immunoreactivity for cytokeratins 8/18, chromogranin-A and parathyroid hormone (multifocal) and negativity for calcitonin, thyroglobulin and TTF-1. The tumour was diagnosed as a parathyroid carcinoma, clinically non-functioning, stage pT2.
Conclusion: Rarely, parathyroid carcinoma may present as a non-functioning cervical mass and remain clinically unsuspected, making it a diagnostic challenge by mimicking thyroid carcinomas or hyperplastic goitre, as our case was. Save for a surgery-related left vocal cord paralysis, the patient remains disease-free 11 months after the surgery, maintaining close follow-up without current need for further oncologic treatment.

PS-08-013
Anaplastic thyroid cancer: PD-1 and PD-L1 expression in a series of 13 cases
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Background & objectives: Immunotherapy targeting the programmed cell death-1 (PD-1) receptor and its cognate ligand (PD-L1) have shown promising results in several tumours. Our objective is to evaluate the expression of PD1 and PD-L1 in a series of anaplastic thyroid carcinomas (ATC).
Methods: PD1 (Cell Marque-NAT105) and PD-L1 (Ventana-SP142 and DAKO-22C3) immunohistochemical expression was assessed in 13 ATC. PD-1 staining was evaluated in inflammatory cells and PD-L1 in tumour cells and categorized according to the percentage of positive cells into: negative <1%, focal 1-25%, moderate 25-50%, diffuse >50%. The staining pattern (membranous, cytoplasmic and both) was also recorded in tumour cells.
Results: PD1 stained inflammatory cells in 9 cases (69%): 8 cases (89%) focally and 1 case (11%) diffusely. Membranous expression in tumour cells with PD-L1 (DAKO) was found in 11 cases (85%): 2 (18%) focally, 1 (9%) moderately and 8 (73%) diffusely. Conversely, PD-L1 (Ventana) staining in tumour cells was evidenced in 7 cases (54%): 6 cases (86%) focally and 1 case (14%) diffusely. Cytoplasmic stain was observed in 2 cases (28,5%), membranous in 2 cases (28,5%) and both in 3 cases (43%).
Conclusion: In our series a subset of ATC cases showed expression for PD-1 and PD-L1 in inflammatory and tumour cells respectively. The percentage of cases with tumour cell expression of PD-L1 differs among both clones. DAKO stained 85% of cases, most of them diffusely whereas Ventana 54% of cases with a predominant focal positivity. Finally, treatment options are lacking for ATC. Therefore, the use of PD1 and PD-L1 immunostaining as potential biomarker for immunotherapy in ATC deserve further research.

PS-08-014
Participation of proteins (Hsp90α) in the adaptive rearrangement of the pituitary-adrenal system of rats after long-term exposure to heavy metal salts
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Background & objectives: Pituitary-adrenal system takes an active part in regulating the body's adaptive capacity under the influence of exogenous factors. The morphological and immunohistochemical features of pituitary endocrinocytes and adrenal cortex under the adaptation to long-term exposure to heavy metals were studied.
Methods: The experiment was performed on 48 rats aged 5-6 months (2 control and 2 experimental groups). Experimental group animals received a combination of heavy metal salts: zinc/copper/iron/manganese/lead/chromium. Determination of heat shock protein marker 90 (Hsp90α) expression was performed using rabbit polyclonal antibodies to Hsp90α protein. The result was expressed as a percentage and evaluated on an accepted scale.
Results: Adaptive changes in the adenohypophyseal-adrenal system were characterized by an increase in the level of Hsp90α expression in the cytoplasm of 72-81% of adenohypophysis cells to moderate (2 points) and strongly positive (3 points) levels. Particularly high levels of expression to Hsp90α were found in the cytoplasm of cells located paravascularly. In contrast to the central link, in the adrenal cortex the areactivity of both the cytoplasm and the nuclei of corticocytes of all zones to Hsp90α has been established. In the glomerular and reticular zones, a moderately positive level of Hsp90α expression was found in vascular endotheliocytes, with special expression in the cortex's glomerular zone.
Conclusion: The pituitary gland showed a high level of expression to Hsp90α, which indicated a fairly high level of general restorative mechanisms of antistress protection. The reactivity of corticocytes of all adrenal zones to Hsp90α revealed a significant weakening of antiapoptotic and antistress protection in glandulocytes, weakening of control in cells regarding folding processes. Therefore, a 30-day adaptation period to a 90-day exposure to a combination of heavy metal salts is insufficient to fully restore homeostasis in the pituitary-adrenal system.

PS-08-015

Neuroendocrine neoplasia – relevant and interesting topics – a case-report and literature review

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Background & objectives: Neuroendocrine neoplasms (NENs) are heterogeneous and ubiquitous. Globally their nomenclature is inconsistent and biological behaviour may be confusing.
Different treatment options can reduce grade and tumour load.
We aim to report a case and review the literature emphasizing these issues.
Methods: A 29-year-old woman was referred to our Institution (Feb/2019) after a Grade 2 (Ki-67: 4.6%) Neuroendocrine tumour (NET) hepatic metastasis was diagnosed. 68Ga-DOTA-NOC-PET revealed multiple foci of somatostatin receptor overexpression consistent with stage IV disease originating in the terminal ileum. Somatostatin analogues (SSAs) and shortly after lutetium-177 therapy were started. Re-evaluation showed a partial imagiologic response and surgical treatment was decided.
Results: Terminal ileocolectomy, hepatic metastasectomies and peritoneal implants removal was performed.
Ileocolectomy revealed a well-differentiated NET, Grade 1, based on the findings of less than 2 mitoses/2mm2 and a Ki-67 labelling of less than 3%, with lymphovascular and extensive perineural invasion. Liver and peritoneal specimens revealed metastasis of the neoplasia just described. Thereby, a downgrade of the tumour was verified, assumed to be related with the neoadjuvant therapy used.
Conclusion: Our case showed that even a well-differentiated NET can behave very aggressively. In particular, small intestine NETs often present with stage IV disease.
The 2018 WHO/IARC expert consensus proposal for NENs classification may reduce the inconsistencies and confusions across these neoplasms.
Several trials revealed an effect of SSAs and lutetium-177 (specially in combination) on tumour cell proliferation in somatostatin receptor-positive advanced NETs, enabling surgery, as in our case. Pathologists must be aware of the possibility of tumour downgrading following these therapies.

PS-08-016

"Plump pink" cells: an important morphological feature predictive of high-risk papillary thyroid microcarcinomas

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Background & objectives: In this study we aimed to investigate the importance of reporting high-risk morphological features, such as the presence of "plump pink" cells (PPCs), in a series of papillary thyroid microcarcinoma (PTMC) cases.
Methods: We re-analysed all consecutive PTMC cases, registered at the Department of Pathology, Târgu-Mureş Emergency County Hospital from 2003 to 2014. The following morphological features were noted, apart from the presence of PPC: tumour size, histological variant, tumour borders, stromal reaction, calcifications and intratumoral multinucleated giant cells. We also quantified the PPC component as diffuse (up to ≥20%) or focal (<20%).
Results: Our study included 206 PTMCs of which, 91 were ≥5mm and 115 <5mm PTMC. Polygonal, PPCs, characterized by abundant eosinophilic cytoplasm were found in 48/206 PTMCs, of which 34 presented a diffuse pattern and 14 focal plump cell component. The diffuse pattern was seen rather in large (≥5mm) (p=0.002) than in small (<5mm) PTMC, in which PPC were focally distributed. We have also shown that large PTMCs were significantly associated with other morphological features, predictive of high risk in PTMC: subcapsular location (p=0.0001), infiltrative tumour border (p=0.011), positive resection margins (p=0.022), tumour associated stromal reaction (fibrosis/desmoplasia/sclerosis) (p=0.0001), calcifications (p=0.007) and intratumoral multinucleated giant cells (p=0.0001).
Conclusion: In this study we have shown that PPCs, especially when diffusely distributed, are significantly associated with morphological features predictive of high-risk like in PTMC. This pattern is important to be mentioned in the histopathological report, as it could have an impact in predicting the tumour biological behaviour and could help the clinician in better guiding the patient's management.

PS-08-017

Distribution of neuroendocrine neoplasms in a tertiary referral hospital in the Philippines

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Background & objectives: Neuroendocrine neoplasms ("NENs") have diverse presentations and outcomes. In Southeast Asia, the distribution of NENs is not yet studied. This study aims to describe the distribution and clinical features of NENs among patients at a tertiary hospital in the Philippines.
Methods: The study was an observational, cross-sectional study with retrospective review of patient records. Surgical pathology files from 2015 to 2020 were reviewed, and all histologically diagnosed neuroendocrine neoplasms were tallied and categorized by diagnosis, grade, stage, age, sex, primary tumour location, and hormone secretion. Statistical analysis was then performed using Microsoft Excel and R version 3.2.1.
Results: A total of 398 NEN cases were identified, accounting for approximately 0.5% of specimens received at the institution. NENs were most commonly diagnosed in the 60-79 year old age group, with a male:female ratio of 1.08.
Of the cases studied, 41.2% were well-differentiated neuroendocrine tumours ("NETs"), while 58.8% were malignant NENs.
The majority of cases were from the gastrointestinal tract (22.4%) and thoracic organs (20.1%). The individual organs in which NENs were most commonly diagnosed were the lungs (17.6%), followed by the rectum (11.8%), pituitary gland (8.8%), pancreas (6.5%) and uterine cervix (4.8%).
Abnormal hormone secretion was detected in NENs of the pituitary (71.4%), parathyroid (18.8%) and pancreas (15.4%).
Conclusion: The study revealed that the Philippine population demonstrates a distribution of neuroendocrine neoplasms by tumour site similar that seen in previous studies of East Asian and Pacific Islander populations. It remains to be seen if this is due to genetic similarities, environmental factors, screening and diagnosis practices, or some combination of the three.
We recommend further studies on the clinical presentation, staging, management and outcomes of local patients with neuroendocrine neoplasms.

PS-08-018

A cautionary tale of neuroendocrine differentiation in metastatic deposits – a two-case report

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Background & objectives: A metastatic deposit with neuroendocrine phenotype in a patient with a previous diagnosis of carcinoma will not always correspond to an unknown primary. We present two such cases and the necessary additional workup.
Methods: Case1: a 68year-old male with a diagnosis of epidermoid carcinoma of the palatine tonsil in 2015 underwent biopsy for one of several hepatic nodules 3 months after. Case2: a 56year-old male underwent biopsy of a suspected recurrence/persistence of a previous cerebellar

metastasis, 3 years after the initial diagnosis of stage IV lung adenocarcinoma with no EGFR-mutations nor ALK or ROS1 translocations.
Results: Both patients´ biopsies showed occupation by a small-cell phenotype carcinoma with neuroendocrine positivity. Clinical histories and slides of previous diagnosis were reviewed.
Case1: The patient underwent an hepatic metastasectomy, showing a small-cell neuroendocrine carcinoma. Upon revision, the previous tonsil biopsy presented an area with crushing artifacts and positivity for synaptophysin/p16, which was considered the primary origin of the metastasis.
Case2: the first cerebellar metastasis was consistent with non-small cell carcinoma, with solid and glandular areas. The patient had been submitted to multiple chemotherapy regimens and cranial radiotherapy prior to the last cerebellar biopsy showing small cell morphology.
Conclusion: We present two cases of neuroendocrine differentiation in metastasis. Case1 revealed to be from a combined neuroendocrine and non-neuroendocrine carcinoma of the tonsil. Case2 was explained as an histological transformation of non-small to small cell lung carcinoma; this has been reported in EGFR-mutated and, occasionally, non-mutated lung carcinomas. These illustrate possible scenarios in which the pathologist must consider the existence of an underdiagnosed neuroendocrine component in the primary tumour or the cytotoxic induction of a neuroendocrine clone after therapy.

PS-08-019
Determination of the management of neuroendocrine tumours in pathological anatomy services in Spain. Multicentre study
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Background & objectives: Neuroendocrine tumours (NETs) are a group of neoplasms that require a precise pathological assessment to be able to classify and adequately treat these patients.
Methods: An anonymous survey in digital format was designed in collaboration with the GETNE (Spanish Group of Neuroendocrine and Endocrine Tumours) Academy working group, made up of a multidisciplinary group that includes surgeons, nuclear physicians, endocrinologists, oncologists and pathologists. The survey included aspects related to clinical practice, and key elements in the anatomopathological diagnosis.
Results: 204 physicians responded to the surveys (45.6% surgery, 29.9% pathology, 8.8% oncology, 7.9% endocrinology, and 7.8% nuclear medicine). Some specialties had a higher prevalence of a reference person specialized in the management of NETs (p value <0.05). Regarding the assessment by pathological anatomy, 63.9% consider that the study of NETs sometimes represents a great diagnostic difficulty. In most centres, 51.2% do not have digital means to determine KI67 in a complementary way and 27.9% do not have IHC techniques to classify functioning NETs. 33.3% of pathological anatomy services always have the possibility of consulting cases with other centres and maintain correct communication with oncologists and surgeons (63.9% and 62.3% respectively)
Conclusion: The questions reflect that NETs are neoplasms that require specialized management since their diagnosis and classification is often not easy. A large part of the pathological anatomy services in Spain do not have some techniques that can serve as a complement in the diagnosis of NETs, but a large part have the possibility of consulting cases in other centres that have more experience as well as having the support from other specialties to improve the management of these neoplasms.

PS-08-020
A new pancreatic entity? Two novel cases of a intraductal papillary mucinous neoplasm (IPMN) mixed with a well-differentiated neuroendocrine tumour of the pancreas
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Background & objectives: The neoplasms known as mixed neuroendocrine- nonneuroendocrine neoplasms (MiNENs), the non-neuroendocrine component of MiNENs is usually represented by an invasive carcinoma, but has not been describe the association with a intraductal papillary mucinous neoplasm
Methods: We find two patients; one of those is a 51-year-old male. Magnetic resonance of the abdomen, which was performed for the suspicion of hemochromatosis, discovered a 3 cm cystic lesion with septa in the body region of the pancreas and the other is a 56-year old female with an incidental cystic pancreatic lesion of 4,5 cm in an ultrasound image
Results: The both lesions were characterized by cystically dilated ducts lined by flat foveolar gastric-type epithelium, without relevant cytoarchitectural atypia but focally forming microscopic folds and subtle micropapillary projections. Therefore and accordingly with these features, the lesions were fundamentally a mixed-type IPMN with low-grade displasia, gastric foveolar subtype. Additionally, there were an underlying proliferation of round, monotonous cells with clear/foamy cytoplasm, stippled chromatin and single nucleoli. Immunohistochemically, these cells were positive for chromogranin and synaptophysin, supporting a neuroendocrine phenotype. The ki-67 was 2%. The mitotic rate in the neuroendocrine component was <1/10 high power fields. The findings in the neuroendocrine component supported a well-differentiated neuroendocrine tumour grade 1
Conclusion: The finding of a well differentiated neuroendocrine tumour associated with an IPMN is unusual and has not been described before. The association of an IPMN with a poorly differentiated neuroendocrine carcinoma has been described. This lesion may be conceptually considered a part of same spectrum of neoplasms known as MiNENs, but we do not regard MiNEN as a proper diagnostic term but rather a conceptual categorization to relate a somewhat diverse group neoplasms of with mixed differentiation.

PS-08-021
A glance over the clinicopathological features of parathyroid adenomas
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Background & objectives: Parathyroid adenomas are benign neoplasms derived from parathyroid parenchymal cells and are the most common cause for primary hyperparathyroidism. In some cases, these tumours are a challenge for the pathologist. We aimed to assess clinicopathological profile of these tumours.
Methods: We performed a retrospective study on surgical resection specimens from patients with parathyroid adenomas operated at the "Pius Brinzeu" County Emergency Hospital Timişoara, Romania. Clinicopathological, serological - serum parathyroid hormone (PTH) and immunohistochemical data (antibodies anti-Ki67 and anti-Chromogranin A) were assessed.
Results: We identified 39 cases of parathyroid adenomas (32 women and 7 men, mean age 53). The most common site was in the inferior parathyroid glands (16 adenomas in right inferior gland, 10 adenomas in left inferior gland). A double adenoma was identified in the right thyroid lobe (RTL) and left inferior parathyroid gland, while an ectopic one in RTL was recorded. Morphologically, we identified 31/39 conventional adenomas, 2/39 water clear cell adenomas, 1/39 oxyphilic adenoma, 2/39 lipoadenomas and 3/39 atypical adenomas. 10/39 cases presented focal cytological atypia. Ki67 assay values were below 2% (higher value in atypical adenomas, but did not exceed 5%). All cases presented moderately elevated serum PTH.

Conclusion: Most parathyroid adenomas are solitary lesions with an easily recognizable, conventional morphology. The extent of increased mitotic activity raise the problem of differentiating adenomas from carcinomas, but the absence of vascular/capsular invasion certifies the benign nature of the lesion. Parathyroid adenomas arising in the thyroid gland can be difficult to differentiate from a thyroid neoplasms with follicular pattern. Elevated PTH levels are a supporting serological diagnostic element, while neuroendocrine differentiation markers are useful for the histological diagnosis of parathyroid adenomas.

PS-09 | Gynaecological Pathology Posters

PS-09-001

awareness of placental pathologic examination criteria and utilization of pathology reports among obstetricians

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Background & objectives: Studies demonstrated low rates of placentas submitted to pathologic examination and poor utilization of pathology reports.Assess obstetricians' awareness and utilization of the College of American Pathologists guidelines for placental pathologic examination and their understanding of reports terminology.
Methods: An anonymous survey was distributed to obstetricians working in different health institutes who are registered in Saudi Commission for Health Specialties' (SCFHS) database. Statistical Package for Social Science (SPSS) software was used to examine the association between the level of training/practice and the surveyed elements as well as types of the institute and the surveyed elements.
Results: 288 responses were received. 34.4% of respondents were aware of CAP guidelines, most of which were practicing in governmental hospitals. While 18% of respondents routinely sent placentas for pathological examination, about 70% of them routinely review the pathology report and understand the used nomenclature; this was significantly higher in university hospital practitioners. Out of the three groups, the residents' group was the least aware of the CAP guidelines and the least to review and understand pathology reports. In absence of CAP guidelines awareness, foetal anomalies were the most common indication used to send placentas for examination followed by medicolegal reasons and infections.
Conclusion: Placental pathologic examination was uniformly underutilized in surveyed practitioners. CAP guidelines were known to a minor subset within the surveyed participants. All this, combined with the variable understating of placental pathology reports, highlight the importance of raising awareness of CAP guidelines, formal placental pathology rotation for trainees and establishing a rapport between pathologists, and obstetricians to improve their understandings and use of the pathology reports.

PS-09-002

Accessory and cavitated uterine mass and the uterine rudimentary horn at an early reproductive age: differential diagnosis and management

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Background & objectives:
ACUM (Accessory and Cavitated Uterine Mass) is a form of the Müllerian duct malformation, more common in adolescents and is an isolated additional uterine cavity in the normal uterus and optimal diagnostics and management strategies are yet to be developed.
Methods: We recruited 14 patients (average age 14 ± 1.66) who were subdivided into two groups: with malformation of the genital organs, ACUM (n=4) and with a doubling of the uterus with rudimentary functioning uterine horn (n=10). The diagnosis was made on the basis of anamnestic data, clinical and laboratory examinations and instrumental methods (ultrasound, MRI, laparoscopy and histological examination).
Results: Patients with ACUM revealed a non-communicating accessory uterine cavity with haemorrhagic contents, lined with a functioning endometrium, surrounded by a concentrically organized myometrium, while the main uterine cavity was of the correct shape. At the same time the closed functioning uterine rudiment was a separate formation more often at the edge of the uterus (MRI data). Histologically, ACUM was a node represented myometrium with endometrioid heterotopies. All patients underwent laparoscopic removal of ACUM and a functioning uterine horn followed by metroplasty. Average size for ACUM: 3,0(±0,72) x 2,3(±1,04) x 2,7(±0,79) cm, average size for functioning rudiments: 4,5(±0,87) x 3,1(±1,04) x 3,8(±1,17) cm (USD data)
Conclusion: The presented clinical observations emphasize the importance of imaging methods in the differential diagnosis of ACUM and uterine rudiment, of particular importance is the use of MRI and histology, which determines the main features that distinguish ACUM from the rudimentary uterine horn. The increased awareness of the ACUM diagnosis facilitates the selection of the optimal treatment and management of these patients as early as possible.

Funding: state assignment 18-A21 'The role of energy metabolism and immune defense disorders in the development of various forms of endometriosis...' (2021-2023)

PS-09-003

Anti-Müllerian hormone levels in adolescent girls with benign ovarian tumours

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Background & objectives: Ovarian tumours in early reproductive cause the ovarian reserve reduction. Determination of the ovarian reserve with blood anti-Müllerian hormone (AMH) detection and its impact on benign ovarian neoplasm in adolescents requiring surgical treatment can help to reveal their prognostic value.
Methods: A retrospective study was conducted, 15 adolescent girls with benign ovarian tumours were included in the study. The average age of the patients was 14.9 (12-17) years. We analysed the data of anamnesis, clinical course, hormonal status, the level of tumour markers, the results of ultrasound examination of the ovaries, and pathomorphological analysis of the removed tumour.
Results: In mature teratomas (n = 11), the AMH level averaged 3.1 ± 1.45 ng / ml, in cystadenomas (n = 3) - 3.45 ± 3.18, and only with fibroma with a diameter of 4 cm was 10, 1 ng / ml. Regardless of the structure with a tumour size of 3-5 cm the AMH level was average 5.69 ± 1.40 ng/ml. Moreover, the AMH value was similar in girls with ovarian formations with a diameter of 6 to 19 cm (2.33-2.91 ng / ml). The thinned cortical layer in 6 out of 9 samples contained primordial and maturing follicles, even in cases of large ovarian tumours.
Conclusion: It is required to keep attention on the concentration of AMH when determining the further tactics of inpatient treatment of adolescents with benign ovarian tumours, even if the pathologist conclusion indicates the safety of the ovarian follicular apparatus in the damaged tissue.

Funding: State assignment 18-A21 'The role of energy metabolism and immune defense disorders in the pathogenesis of various forms of endometriosis...'

PS-09-004

Vulvar cancer: epidemiological, clinical and outcomes of 102 patients in the central region of Tunisia

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Background & objectives: Vulvar cancer is a rare gynaecologic malignancy. It is a pathology of women over 60y-o with a background of dystrophy and a mucous membrane oestrogen-deficient. Recently, it affects younger women due to the pathogenic-role of viral infectious agents such as the human-papilloma-virus, especially HPV16.

Methods: This is a retrospective cross-sectional descriptive study collected over a period of 20 years from January 1995 to December 2015. The study included all patients who were treated for primary malignant vulvar lesions in the obstetrics gynaecology department of Farhat Hached Hospital in Sousse, confirmed histologically on biopsy in the pathological anatomy department of the same hospital.

Results: A total of 102-patients were included with a mean-age of 66.45years (range 21 to 92 years). Only 12.7% of the patients were under 50y-o. The main reason for consultation was vulvar pruritus in 89.2% of cases, with an average delay of 15-months. The median tumour size was 3.75cm. A tumour biopsy was performed in all cases with the most frequent histological type was squamous cell carcinoma, representing 98%of cases. According to the FIGO classification, 65.68% (67) of patients were stage I-II, with more than50% stage I B (36/67). 34.3% (35) of patients were stage III or stage IV. Surgical treatment was performed in 94.68% of patients. The main objective of the surgery was to have free-surgical-margins over 8mm, objective achieved in 94.6%. 81.91% of the patients underwent inguinal lymph node dissection. The overall survival was 49.3% at 2 years and 28% at 5 years.

Conclusion: Vulvar cancer is a grave pathology, especially since it currently affects an increasingly young population since the incrimination of HPV in its genesis. Its treatment is heavy and burdened with a significant morbidity. However, its prognosis would be improved by an early diagnosis allowing a conservative surgical treatment. The prevention of this cancer passes by the exploration, the monitoring and the treatment of the chronic vulvar prurits, as well as the dystrophic and viral precursors.

PS-09-005

Role of hysteroscopy in the evaluation of tamoxifen induced endometrial abnormalities

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Background & objectives: Despite the large scientific evidence demonstrating that hysteroscopy examination is the gold standard of the management of abnormal uterine bleeding, data for accuracy of this procedure in symptomatic women under tamoxifen is less common.

Methods: the present study is a transversal retrospective descriptive study carried out in both gynaecological and pathological departments at Farhat Hached Hospital during a period of 10-years, from 1st-January-2006 to 31-December-2015. A total of 41-Tamoxifen-treated-patients with breast cancer who presented with abnormal -uterine-bleeding were enrolled. The mean age was 52,7-years at diagnosis. The mean period of taking tamoxifen was 31,8 +/– 14,6months.

Results: The mean cumulative dose of Tamoxifen was 19,1g. The Median endometrial thickness on transvaginal ultrasonography examination was 11mm. Hysteroscopy was indicated for abnormal-uterine-bleeding with thickened-endometrium in most of the cases (83,7%) and showed that atrophy was the most common finding (26%). Abnormal-hysteroscopy-findings were dominated by polyps and hyperplasia that were found in 27,9% and 25,6% of the cases respectively. Hysterescopic appearance suggestive of malignancy was found in one case (2,3%). Curettage of the uterine cavity was performed for the majority of the patients (95,3%), and targeted biopsies were required in two cases. Endometrial sampling yielded insufficient tissue in 18,6% of cases. Histological examination exhibited benign findings for the all patients except one for whom subsequent hysterectomy specimens that concluded to an atypical complex hyperplasia.

Conclusion: For distinguishing endometrial abnormalities from normal findings, hysteroscopy had an overall accuracy of 80%. For the diagnosis of polyps, leiomyoma and hyperplasia, hysteroscopy had an accuracy of 94.28%, 91.42% and 74.28% respectively.

Hysteroscopy represents an accurate and non-invasive method for the assessment of endometrium, and should be mandatory for patients under tamoxifen any time AUB occurs. The benefits and risks of prophylactic use of levonorgesterel intrauterine system are still to be determined.

PS-09-007

Exploring differentially methylated genes in vulvar squamous cell carcinoma

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Background & objectives: Aberrations in DNA-methylation are known to play a role in carcinogenesis, and methylation profiling has enabled the identification of biomarkers of potential clinical interest for several cancers. For vulvar squamous cell carcinoma (VSCC) however, methylation profiling remains an under-studied area.

Methods: We sought to identify differentially methylated genes (DMGs) in VSCC, by performing Infinium MethylationEPIC BeadChip (Illumina) array sequencing, on a set of primary VSCC (n = 18), and normal vulvar tissue from women with no history of vulvar (pre)malignancies (n = 6). Immunohistochemistry was performed with p16 and p53 to categorize the VSCCs as HPV-associated or HPV-independent.

Results: Using false-discovery rate of 0.05 and beta-difference ($\Delta\beta$) of ± 0.5 as cut-offs, we identified 387 probes located in the CpG islands that were differentially methylated in VSCC. These probes corresponds to 199 DMGs (195 hyper-methylated, 4 hypo-methylated). The majority of the hyper-methylated genes were found to be involved in transcription regulator activity, indicating that disruption of this process plays a role in VSCC development. The majority of VSCCs harboured amplifications of chromosomes 3, 9, and 10. By integrating methylation and copy number variation analyses, 5 DMGs were identified, namely, *APLP2*, *ARHGEF12*, *CSGALNACT1*, *GRM7*, and *PRICKLE2-AS1,* which harboured deletion in one allele and hypermethylation in another allele.

Conclusion: We identified a set of DMGs in VSCC in this study with a view to promote hypothesis-generation, and to provide a resource for future investigations to evaluate the diagnostic, prognostic, predictive, or therapeutic potential of these methylation-based bio-markers. Prognostic relevance of these DMGs deserves further exploration in larger cohorts of VSCC and its precursor lesion, vulvar intraepithelial neoplasia (VIN).

PS-09-008

Validation of MODEPLEX technology for the determination of POLE hotspot mutations in endometrial carcinoma samples

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Background & objectives: Molecular classification of endometrial cancer based on TCGA data recognizes 4 subtypes: 1)CNH, 2)Hypermutated, 3)CNL and 4)Ultramutated (POLE mutated). This study intends to explore the diagnostic performance of a novel technology (MODAPLEX) to study POLE mutations in endometrial carcinoma samples.
Methods: 96 endometrial cancers samples with available histological/molecular classification, were selected. For each case a tumoral block was chosen, obtaining eight sections of 10 μm thickness and subsequently isolating DNA with "Cobas DNA Sample Preparation Kit". DNA concentration was measured by Qubit, excluding those cases with a concentration under 10 ng/μl. Positive results were reconfirmed using Sanger sequencing.
Results: 94 samples were submitted to the test, discarding 20 of them for an invalid result. Among the final 74 samples, 15 were POLE mutated, 18 CNL, 25 CNH and 16 MSI. MODAPLEX identified 13 samples with mutations on POLE, which were: V411L,P286R,S297F,A456P and L424V. All these mutations were located in the exonuclease domain and had a functional impact on the protein. All the reported mutations by MODAPLEX, were afterwards confirmed by Sanger sequencing. Two cases previously classified as POLE were not identified by the test, but repeatedly confirmed by Sanger. These two cases harboured A456V and A465T mutations, described as uncommon and whose primers were not covered by the kit.
Conclusion: MODAPLEX is a promising technology still in development that allows the determination of the main "Hotspot" mutations in POLE gene in a fast, practical and efficient way. Following a Single-Gene approach and in this clinical context, this technology could compete with Sanger sequencing for the study of POLE mutations.
This test could emerge as a valid and fast alternative to Next – Generation Sequencing, especially in those centres where they do not have access to massive sequencing techniques.

PS-09-009
NFIB rearrangement and MYB-NFIB fusion are infrequent events in vulvar adenoid cystic carcinoma
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Background & objectives: MYB/MYBL1-NFIB fusions are driver events in adenoid cystic carcinomas (ACC). MYB rearrangement and MYB-NFIB fusion have been reported to occur in ~60 and 30% of vulvar ACCs, respectively. We aim to access the prevalence of NFIB rearrangement and MYB-NFIB fusion.
Methods: We retrieved four vulvar ACCs from our institution's archives diagnosed between 1994 and 2019 for which FFPE material was available. All histological slides and medical records were reviewed.
For detection of gene rearrangements by fluorescence in situ hybridization (FISH) two strategies were applied: 1) break-apart probes for MYB, MYBL1 and NFIB genes and 2) dual colour probes for MYB-NFIB fusion.
Results: Patients were 41-70 years old at the time of diagnosis. All cases were treated by surgery alone at presentation, 3 of which suffered local recurrence. The diagnosis of adenoid cystic carcinoma was confirmed in all cases, none with a high-grade component. All patients were alive and disease free at the time of the last follow-up appointment (median: 102,5 months). MYB rearrangement was detected in 3/4 cases, including one with concurrent MYB amplification. No MYBL1 nor NFIB rearrangements were found. MYB-NFIB fusion was absent in all four cases. One of our cases, despite having a classical ACC morphology, did not have NFIB, MYB or MYBL1 rearrangements, or MYB-NFIB fusion.
Conclusion: We report a lower rate of NFIB rearrangement and MYB-NFIB fusion than expected. In keeping with the other studies performed in this anatomical location, the prevalence of NFIB rearrangement and MYB-NFIB fusion seems to be lower in the vulva than elsewhere. Although MYB activation occurs in the majority of vulvar ACC, it is likely due to other mechanisms yet to be unravelled.

PS-09-010
HER2/neu expression in patients with primary uterine endometrial carcinomas in Batangas Medical Center, Philippines
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Background & objectives: Uterine cancer is the eighth leading cancer among women with an estimated age-standardized Philippine incidence rate of 5.6 per 100,000. To aid in the prognostication and management of endometrial cancers, expression of HER2/neu in Filipinos with endometrial cancer was determined.
Methods: Sixty-seven cases out of all 71 resection specimens with endometrial cancer, from 2017 to 2019, were included in the study. Exclusion of the 4 cases was due to unavailability of paraffin blocks. Histological section was taken for immunohistochemical staining with HER2/neu. Previously proposed HER2 testing algorithm for endometrial carcinoma (EC), based on the modified 2007 ASCO/CAP breast criteria, was used.
Results: Eighty-six percent of the patients were 45 years and older. Ninety-five percent were of endometrioid histologic type, 2 (2.98%) cases were serous, and 1 (1.49%) case was mixed Mullerian tumour. Lymph node metastasis was present in 6.0% of cases. Most of the cases (65.67%) belonged to FIGO Stage I. HER2/neu was positive (3+) in 27.3% (3/11) of endometrioid grade 3, 14.3% (3/21) of endometrioid grade 2, and 6.1% (2/33) of endometrioid grade 1. Among the two cases with serous EC, one was positive while the other was negative. The single case of mixed Mullerian tumour was positive for HER2/neu. HER2/neu was either negative or equivocal in cases with node metastasis.
Conclusion: Although most of the HER/neu positive cases in this study were seen in tumours with higher histologic grade, Fisher Freeman Halton test showed no sufficient evidence to say that age, lymph node involvement, FIGO grading and cancer staging were associated with HER2/neu expression. Since literatures show HER2/neu had significant association on prognosis, overall survival, and has potential for targeted therapy and/or as adjunct to chemotherapy, a larger, multicentre study is warranted.

PS-09-011
Nuclear beta-catenin expression - a prognostic marker for endometrial carcinomas
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Background & objectives: Numerous studies have shown that immunohistochemical nuclear beta-catenin expression in endometrial carcinoma (EC) is a successful substitute for CTNNB1 exon 3 mutation. Our purpose for this study was to evaluate the nuclear beta-catenin expression in 50 cases of endometrial carcinoma.
Methods: We tested immunohistochemical nuclear beta-catenin expression in 50 cases of endometrial carcinomas in Romanian female patients. We also performed statistical correlations between this marker and various parameters (histopathological, immunohistochemical etc.). Also, we analysed what molecular subgroup of endometrial carcinomas (MSS, MSI, p53wt, p53abn) showed the most frequent cases with beta-catenin expression.
Results: Our study revealed that ECs with nuclear beta-catenin positivity was observed in cases with higher FIGO grade (p=0.02), in endometrioid carcinomas (p=0.04) and in cases with lymphovascular invasion (p=0.05). ER and PR were frequently expressed in the positive beta-catenin subgroup (p=0.03, p=0.02). Our results show that ECs which express nuclear beta-catenin correlate with parameters that are already established as unfavourable.
Conclusion: Our struggle for affordable prognostic markers is a continuous battle. The immunohistochemical beta-catenin nuclear expression is an excellent replacement for CTNNBB1 exon 3 mutation in ECs and predicts

prognosis in certain cases of ECs. We believe that future research will include this marker as part of the routine immunohistochemical panel for ECs.

PS-09-012

Rhabdomyoblastic differentiation in uterine carcinosarcoma: impact on survival and recurrence

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Background & objectives: Uterine carcinosarcomas (UCS) are characterized by a carcinomatous and sarcomatous contingent. Heterologous mesenchymal components, most frequently show rhabdomyoblastic or chondroid differentiation. The aim of our study was to determine the impact of rhabdomyoblastic differentiation on survival and recurrence.
Methods: Study was retrospective, covering 52 patients operated by hysterectomy and whose diagnosis of UCS was confirmed on an operative specimen at the anatomy and pathological cytology department of the Salah Azaïez institute in Tunis from 2018 to 2000. Statistical analysis was done using the Kaplan-Meier method and the Log-Rank test in univariate analysis (The statistical significance level was ≤ 0.05).
Results: For the 52 patients with UCS, rhabdomyoblastic differentiation was present in 22 cases (42.3%) and absent in 30 cases (57.7%).
The overall survival rate at 1 year, 3 years and 5 years for patients who presented rhabdomyoblastic differentiation were 56%, 27% and 18% compared to 75%, 59% and 47% for those who did not present this differentiation. This difference was statistically significant ($p = 0.0193$).
The recurrence-free survival rate at 1 year, 3 years and 5 years for patients who presented rhabdomyoblastic differentiation were 45%, 31% and 30% compared to 71%, 53% and 43% for those who did not present this differentiation. This difference was statistically significant ($p = 0.05$).
Conclusion: UCS are high grade tumour, characterized by a poor 5-year overall survival rate (overall <35%). The role of heterologous sarcomatous elements as a prognostic factor has been widely discussed with discrepant results in different series. Whereas, like our study, the presence of rhabdomyoblastic differentiation is a factor of poor prognosis correlated, in univariate analysis, with a bad overall survival. It is also correlated with a bad recurrence-free survival.

PS-09-013

Comparison of endometrial biopsy and postoperative hysterectomy specimen findings in patients with uterine carcinosarcoma

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Background & objectives: Uterine carcinosarcomas (UCS) are biphasic tumours which diagnosis can be made on biopsy or surgical specimen.
The aim of study was to assess concordance between preoperative endometrial sampling and microscopic examination of hysterectomy specimens in patients finally diagnosed with UCS.
Methods: We analysed a group of 43 patients who had a biopsy and whose diagnosis of UCS was confirmed on operative specimen at the pathological anatomy and cytology department of the Salah Azaïez institute in Tunis, over a period of 19 years (from 2018 to 2000).
Results: Endometrial biopsy was performed in 43 patients. It made it possible to make the exact diagnosis of UCS in 20 cases (46.5%). In the 23 other cases (53.5%), the diagnosis was corrected postoperatively. The diagnoses mentioned were: endometrioid adenocarcinoma in 14 cases (32.6%), sarcoma in two cases (4.7%), undifferentiated tumour in one case (2.3%), undifferentiated carcinoma in one case (2.3%), serous carcinoma in one case (2.3%), adenosarcoma in one case (2.3%) and the result was non-contributory in three cases (7%).
Conclusion: In endometrial cancer, our findings demonstrate a low level of concordance between the histological diagnosis on endometrial curettage and at hysterectomy.
The sensitivity of this biopsy to detect sarcomatous elements is lower than that of carcinomatous elements. Many studies conclude that endometrial sampling is less precise in predicting the final histological diagnosis of the sarcomatous component than the carcinomatous component. Indeed, the diagnosis of UCS is often made on the surgical specimen.

PS-09-014

Complete hydatidiform mole with mosaic histology: a study of 10 cases with immunohistochemistry

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Background & objectives: Complete moles (CM) with mosaic histology may pose a diagnostic challenge. Differential diagnosis is very important for patient management. The objective is to clarify histologic and immunohistochemical features and its histogenesis.
Methods: Ten cases of CM with mosaic histology in the first trimester were retrieved, and their initial diagnoses included CM (3 cases), a twin placenta with CM (2), CM with mosaic histology (2), PM (2), and hydropic abortion with trophoblastic hyperplasia (1). They were analysed with immunostaining of p57 (Kip2) and TSSC3, which are products of paternally imprinted, maternally expressed genes.
Results: Histologically, 5 cases had both CM and placental mesenchymal dysplasia (PMD) components. The 5 remaining cases had CM and non-PMD components. Cytotrophoblasts and stromal cells of CM components were negative for p57. Cytotrophoblasts and stromal cells of non-PMD components expressed p57. In PMD components, cytotrophoblasts were positive for p57 and TSSC3, and stromal cells were negative for p57, indicating that the stromal cells were androgenetic, and the cytotrophoblasts were biparental.
Conclusion: The findings support the hypothesis that the misexpression of p57 and TSSC3 is involved in abnormal development of androgenic CM. CM with mosaic histology can be classified into two groups; CM with PMD components and CM with non-PMD components. None of the cases was CM with twin, but rather CM with androgenic/biparental chimera or mosaic molar gestation and PMD. Immunohistochemistry of p57 and TSSC3 can be a useful screening tool for cytogenetic analyses of CM with mosaic histology.

PS-09-015

Mast cell microenvironment in smooth muscle tumours of the gynaecologic tract

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Background & objectives: The scientific literature states that smooth muscle tumours of the gynaecological tract harbour a variable number of mast cells, similar to neural tumours. Several studies have reported a higher number of mast cells in atypical leiomyomas, compared to leiomyosarcomas.
Methods: A total of 98 smooth muscle tumours have been diagnosed in our laboratory during a period of 4 months, including 78 leiomyomas, 18 atypical leiomyomas and 2 leiomyosarcomas. The number of mast cells was evaluated per 10 HPF on both Hematoxylin Eosin and Toluidin Blue stains, and subsequently correlated with the presence of atypia, necrosis and mitotic index.
Results: The total number of mast cells varied from 0 to 156 per 10 HPF, with a mean of 28. Tumour size correlated best with a high number of mast cells. All leiomyomas larger than 10 cm had more

than 30 mast cells / 10 HPF. Apoplectic leiomyomas had a mean of 48 mast cells / 10 HPF, with more than 70% of cases featuring at least 40 mast cells / 10 HPF. High numbers of mast cells were also observed in cellular leiomyomas (45) and mitotically active leiomyomas (33). Less than 10 mast cells / 10 HPF were observed in epithelioid leiomyomas and in leiomyosarcoma.
Conclusion: The increased number of mast cells encountered in large leiomyomas, apoplectic and cellular leiomyomas can serve as a reassuring criterion, aiding in the differential diagnosis with leiomyosarcoma. Ordinary leiomyomas feature a low number of mast cells, 76% of them having less than 10 mast cells / 10 HPF.

PS-09-016
Choriocarcinoma in South African women: analysis of a series with genotyping
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Background & objectives: Choriocarcinomas can be either gestational, arising from a previous pregnancy, or non-gestational. The prognosis and treatment differ and correct categorisation is important. Genotyping can be used to make this distinction, but this technique has not yet been used in Africa.
Methods: In this study, we genotyped 20 choriocarcinomas and 6 control cases of complete hydatidiform mole (CHM) using a short tandem repeat multiplex polymerase chain reaction (PCR) assay for 15 loci and a sex marker, amelogenin.
Results: All the patients were of African descent. Amplification failed in two cases and these were excluded from the study. Of the remaining 18 choriocarcinoma cases, 17 were gestational and one was non-gestational. Sixteen of the gestational cases were purely androgenetic/homozygous XX compatible with a previous CHM, while one arose from a previous normal pregnancy. In addition, a rare variant allelic repeat, 22.2 at locus FGA, was identified in one case. This variant has a frequency of 0.0026 in the South African population.
Conclusion: In this study, 88.9% of the choriocarcinomas were gestational arising from a previous CHM, which is in keeping with previous international studies. Although molecular genotyping is not required in all cases of choriocarcinoma as the majority are gestational, molecular genotyping can be useful in cases that do not respond to first-line treatment and cases where the clinical history is suggestive of a non-gestational tumour so that the appropriate treatment can be implemented.

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PS-09-017
PTEN mutation enhances insulin-like growth factor 1 receptor expression in endometrial cancer
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Background & objectives: PTEN inhibits the Akt signalling pathway thus plays an important role in regulating cellular behaviors.
We investigated if PTEN (which seems to act as a negative regulator of IGF1R and IGFR2) enhances proliferation and the inhibition of apoptosis if mutated.
Methods: We analysed 102 cases of endometrial cancer treated between 2005- 2020. DNA extracted from 102 clinical specimens of endometrial cancer FFPE. Sixty-eight DNA samples were successfully processed with the AmpliSeq for Illumina Cancer Hotspot Panel Cancer according to manufacturer's manual. The analysis included hotspot regions of 50 genes with known associations to cancer. The data was analysed for sequencing coverage.
Results: Our initial data showed IGF-1R overexpression in 78% of samples. We observed PTEN mutation in 49% and PIK3CA in 35% of cases. The preliminary statistics suggests a strong correlation PTEN silencing with IGF1R overexpression ($p<0.05$). Interestingly, we have not noted the same with PIK3CA and KRAS mutation ($p>0.05$)
Conclusion: Our row data are still under biostatistics, but first the insight allows us to connect IGFR1R overexpression in endometrial cancer with the inhibition of PTEN activity.

PS-09-018
HOXA11 Receptors as an additional marker of implantation in assisted reproductive technology programs (ART)
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Background & objectives: HOXA genes and the proteins they encode are key regulators of endometrial reception. The aim of the study was to evaluate the effect of HOXA10 and HOXA11 expression levels in the stroma on the results of ART programs.
Methods: A prospective cohort study of IVF outcomes was performed in 68 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 HOXA10 and HOXA11 receptor antibodies were used. The percentage of HOXA10 and HOXA11-positive stromal cells was calculated.
Results: The threshold value of HOX11 expression in endometrial stromal cells at the cut-off point was 6.14%. When the threshold parameter is equal to or less than 6.14%, the endometrium is characterized as receptive, favourable for implantation, with a value of more than 6.14% of the threshold parameter unfavourable for implantation. The area under the ROC curve corresponding to the relationship between implantation prognosis and HOXA11 expression in endometrial stroma cells was 0.784=0.058; 95% CI: 0.672-0.897 (p=0.000). The sensitivity and specificity of the method were 80% and 73%. There were no significant differences in the expression of HOXA10 in endometrial stromal cells at different outcomes of ART programs.
Conclusion: The results of the study allow us to expand the range of markers of endometrial receptivity in infertility of tubal origin in women of older reproductive age. The revealed reference value of HOXA 11 expression in the endometrial stroma in the" implantation window " opens up prospects for the development of new approaches to the pathogenetic preparation of the uterine mucosa for blastocyst implantation.

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PS-09-019
Oxidative stress influence and ROS up-regulation on umbilical cord cytokines and their role in inflammatory complications after spontaneous preterm birth
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Background & objectives: The aim of this research was to examine the oxidative stress (OS) biomarkers, reactive oxygen species (ROS) up-regulation and inflammatory cytokines complications associated with changes in the endogenous antioxidant defense (EAD) in the umbilical cord, after spontaneous preterm birth (sPTB).

Methods: We assessed OS biomarkers- ascorbate, superoxide-anion, nitro radicals and ROS up-regulation in the umbilical cord in 101 women with sPTB. OS were measured by EPR spin-trapping spectroscopy in real time. The EAD levels- superoxide dismutase (SOD), catalase (CAT), glutation peroxidase (GSH), total antioxidant capacity (TAC) and interleukins (IL)-IL-6 and IL-17 inflammatory complications were measured by enzyme-linked immunosorbent assay (ELISA).
Results: The prospective case-control study was conducted at UMBAL, Stara Zagora, Bulgaria (2017-2020) and determined in two groups: n1=100 sPTB, cardiotocography confirmed for >32 g.a.; n2=100 healthy pregnant, with a registered singleton pregnancy, at 37-39+6 g.a. gave birth on the term (BT). The two-fold decrease ($p > 0.05$, t-test) expression of OS biomarkers (i.e. ascorbate radicals, superoxide radicals, nitric oxide, SOD, CAT, GSH, TAC); significant two-fold increase of ROS concentration ($R = 0.958$, $p<0.05$, t-test) and inflammatory factors levels, i.e. IL-6 ($p<0.003$, t-test) and IL-17 ($p<0.005$, t-test) were registered in umbilical cord homogenates in sPTB patients, compared to BT.
Conclusion: Generally, our findings suggest that OS involves many signalling molecules in the umbilical cord of sPTB, which are regulated in a dynamics manner. The additional sPTB mechanisms caused increased OS, ROS overproduction, and IL-6 and IL-17 inflammatory complications, which in turn leads to endogenous antioxidant system failure in the umbilical cord in preterm infants and elevated infant mortality.

Funding: The study was supported by Ph.D. program of Dr. Iliana Koleva- Kerkelia and scientific project 1/2020 of Medical Faculty, Trakia University, Bulgaria.

PS-09-020
Expression of PTEN in cervical lesions and its correlation with adhesion proteins
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Background & objectives: The role of PTEN and adhesion molecules in cervical neoplasia isn't well established.
The purpose of our study was the assessment of PTEN, B-catenin and E-cadhenin expression in cervical lesions and the evaluation of their potential role in cervical carcinogenesis.
Methods: 47 low and high grade cervical dysplasia specimens (CINI-II-III) and 10 specimens of invasive squamous cervical carcinomas were used and the proteins' expression was evaluated using immunohistochemistry. Statistical analysis was performed implementing SPSS16 for windows.
Results: PTEN and E-cadherin expression was found decreased in CIN III and invasive carcinomas ($p=0,022$) while a strong association was also found between PTEN and E-cadherin immunopositivity ($p=0,011$). The expression of B-catenin was strongly correlated with E-cadherin's immunostaining ($p=0,027$)
Conclusion: E-cadherin and β-catenin seem to correlate with each other, and their expression is probably involved in the development of cervical lesions. Furthermore, PTEN loss represents a crucial event in malignant transformation procedure; however, its correlation with the adhesion proteins deserves further investigation.

PS-09-021
Serous cell differentiation as a marker of neoplastic transformation in patients with ovarian endometrioid cysts
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Background & objectives: Endometriosis ranges up to 15% in women and is one of causes of the infertility. Many theories highlight pathogenesis of the endometriosis and endometriosis-associated tumours but none of them can explain its ability to neoplastic transformation and associated serum biomarkers.
Methods: This study was conducted on surgical specimens from ovarian endometrioid cysts (OEC) and the ovarian tumours obtained after surgical operation from 117 patients. Normal level of serum CA-125 was assumed to be up to 35 IU/ml. Immunohistochemical study of WT1, p53 antibodies was performed.
Results: The results revealed a direct correlation between the level of serum CA-125 and the appearing of serous IHC-phenotype in epithelial OEC cells with WT1 expression (Pearson $r= 0.84$, $p<0.0001$) and the p53 expression in the OEC epithelium (Pearson $r= 0.81$, $p<0.0001$) as well as direct correlation was found when studying the relationship between WT1 and p53 expression in OEC epithelium (Pearson $r= 0.79$, $p<0.0001$). A moderate direct relationship was found between the OEC size and the WT1 and p53 expression (Spearman r = 0,5 and 0,6 resp.), along with a moderate inverse relationship between BMI and the level of p53 expression (Spearman r = - 0,57 and - 0,6 resp.).
Conclusion: This research revealed the changes in OEC epithelium with serous epithelial type IHC-phenotype that were associated with an extensive rise in the serum biomarker CA-125 level, that could indicate the early neoplastic transformation of OEC.

PS-09-022
Parietal endometriosis on caesarean section scar: study of 8 cases
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Background & objectives: Parietal endometriosis is a rare pathology and represents 1 to 2 % of cases of extragenital endometriosis. It can occur on all scars, most often during surgery with hysterotomy, and is due to the implantation of endometrium in the scar.
Methods: The retrospective study concerns all the cases of parietal endometriosis taken in charge during one year in the Farhat Hached gynaeco-obstetrical service from January 1, 2018 to December 1, 2019.
Results: Six patients were operated during this period. The average age was 34 years. All patients had at least one history of caesarean section. The interval between the operation and the appearance of the first symptoms was on average four years. Only 50% of the patients presented a typical clinical picture with pain according to the menstrual cycle. The average size of the nodules was 2 cm. The diagnosis of parietal endometriosis was suspected before treatment in 100% of cases. The treatment was surgical, involving removal of the nodule. In 62.5% of cases the lesion was preaponeurotic. There were no complications except for a single case of homolateral recurrence.
Conclusion: Parietal cicatricial endometriosis is a rare pathology but its diagnosis must be evoked in particular in women who have undergone open gynaecological or obstetrical surgery and who present pain associated or not with menstrual disorders. The treatment is mainly surgical.

PS-09-023
Expression RIP3, a molecular switch for necroptosis and inflammation, in cases of placenta accreta
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Background & objectives: Recently, there has been an increase in the incidence (1:500) of the of placenta accreta spectrum (PAS). However, the pathogenic mechanisms of placenta accreta aren't clear. The receptor-interacting protein kinase 3 has emerged as a critical regulator of programmed necrosis.
Methods: The study included 63 patients of reproductive age (mean 34,64±3,69 y.y.), after caesarean section at 34-36 gestation weeks with

PAS. We performed histological (H&E, methylene blue) and immunohistochemical studies to primary antibody (1:500; Abcam) on paraffin- and epon-araldite-embedded preparations of 63 myometrium samples (accreta–36, 19–increta, 8–percreta), taken after caesarean section. Control group were 8 myometrium samples from women without PAS.
Results: As a results of the histologic examination reflected dystrophic damage and partial membrane bubbling, cytoplasm fragmentation and condensation of chromatin of some smooth muscle cells and fibroblasts in myometrium samples in cases of PAS group comparison to the control group ($p<0,05$). Immunohistochemical study showed significant increased RIP3 cytoplasmic expression in smooth muscle cells, fibroblasts, endothelium of blood vessels, and especially decidual cells than in the control group ($p<0,05$). In the sites of necrosis associated with placenta increta, the expression of RIP3 was absent.
Conclusion: Thus, disturbances of expression RIP3 the mechanisms of necroapoptosis in PAS are activated, which probably facilitates the placenta invasion into the myometrium.

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PS-09-024
PTEN mutation landscape in endometrial cancer
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Background & objectives: PTEN gene (tumour suppressor gene).PTEN protein maintains the balance of the PI3K/AKT pathway. The loss of PTEN gene function increases rate of occurrence of aggressive metastatic disease, it can be used as a biomarker for prognosis in distinguishing indolent tumours from aggressive.
Methods: we analysed 102 cases of endometrial cancer from 2005-2020 their complete clinical information, chemotherapy regiments and recurrence free survival was tabulated. 68 DNA samples (67%) were successfully processed with AmpliSeq for Illumina Cancer Hotspot Panel Cancer (Illumina Inc, San Diego, California). The analysis included hotspot regions of 50 genes with known cancer associations. Analysis for sequencing coverage and variant frequency cut-off occurred
Results: In the group that was studied we observed a 49% frequency of PTEN mutations. There was a large mutational heterogeneity noted. In comparison to the Cosmic Database the frequency of nonsense, missense and frameshift insertion were on a similar level, however the frequency of frameshift deletion was much higher reaching 30% compared to 15%. On the other hand, PIK3CA, KRAS, FGFR2, CTNNB1, FBXW7 genes have shown great homogeneity with almost only missense type mutations. The TP53 gene mutation was mostly missense type in 80% of cases.
Conclusion: Our study confirms a leading role of PTEN gene in endometrial cancer. Our results differ from Cosmic Database only in the aspect of frame shift deletion mutations, where we observed frequency that was two times higher. Interestingly we noted mutational homogeneity concerning other important genes.

PS-09-025
Somatic neoplasms ranging from benign to malignant arising in the setting of ovarian mature teratomas: a series of cases examined in our laboratory during the course of the last year
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Background & objectives: This study is a review of all pure mature ovarian teratomas that were examined in our institution from March-2020 to March-2021, in order to depict somatic neoplasms arising in this setting. In 4/36 cases we identified neoplasms with benign, borderline or malignant features.
Methods: All tumours had macroscopic features of mature cystic teratomas, filled with hair & sebum.
Case-1: a 45-year-old pregnant woman with an 8cm-ovarian-tumour excised during delivery/caesarean section. On dissection, a 1.8cm solid soft nodule was identified embedded in mature fatty tissue.
Case-2: a 33-year-old woman with a 4cm-unilocular-ovarian-tumour with a 1.2cm Rokitansky-tubercle.
Case-3: a 59-year-old woman with a 12cm-multilocular-ovarian-tumour.
Case-4: a 71-year-old woman with a 10.5cm-unilocular-ovarian-tumour with a 2cm Rokitansky-tubercle.
Results: Case-1: Microscopically, the 1.8cm nodule was situated in the reticular dermis & adipose tissue, underneath the dermal epithelial lining of the cyst. It consisted of hyperplastic apocrine glands with eosinophilic/foamy cytoplasm, apical snouts & luminal secretions, surrounded by a layer of myoepithelial cells. Immunohistochemically, the epithelial cells stained positive for CkAE1/AE3&GCDFP-15. p63&S-100 highlighted the myoepithelial cell-layer. Chromogranin, synaptophysin, TTF-1, PAX-8, CDX-2 & Thyreoglobulin were negative. The glands were reminiscent of lactational-breast-tissue but since ER&PR-receptors were negative, a final diagnosis of tubular apocrine adenoma was reached.
Case-2: Microscopically, inside the Rokitansky-tubercle, we identified a 0.6cm carcinoid tumour (chromogranin & synaptophysin positive) with insular-growth-pattern. The Ki-67 proliferation-index was 4% and mitotic activity was low (1 mitoses/10 HPF).
Case-3: Microscopically, the dermal epithelial lining of the cyst transitioned smoothly to dysplastic mucinous epithelium & a gastrointestinal-type-mucinous tumour with borderline features.
Case-4: Inside the Rokitansky-tubercle, a 1.6cm squamous-cell-carcinoma was identified.
Conclusion: Skin adnexal neoplasms in ovarian teratomas are rare. To the best of our knowledge, this is the first case of a tubular apocrine adenoma reported in the literature.
Our findings in Case-3 are in keeping with the well-established theory that a subset of ovarian mucinous tumours arise in the setting of teratomas.
The percentage of somatic neoplasms arising in otherwise mature teratomas was 11% in our series, surprisingly higher than originally expected and therefore we underline the importance of adequate sampling.

PS-09-026
"The Blinded Guardian": clinical relevance of p53-null phenotype in high-grade serous ovarian cancers
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Background & objectives: TP53 is known as the "guardian of the genome" and it is crucial for high grade serous ovarian carcinoma (HGSOC) cancerogenesis, usually manifesting with p53-null or p53-overexpressed immunophenotypes. Clinical significance of the two presentations is investigated.
Methods: TP53 status was investigated on FFPE specimens with IHC (Clone DO7, Roche Benchmark®) and Sanger Sequencing (exons 2-11) in 34 HGSOCs: 16 consecutive cases of p53-null were compared with 18 cases of p53-overexpressed. The impact on overall survival (OS) between the two groups was evaluated with Kaplan-Meier curves.
Results: Cases with p53-null phenotype showed: 9 nonsense mutations, 4 in-frame deletions, 2 splice variants, and 1 in frame variants while p53-overexperessed showed 16 missense mutations and in 2 cases no mutation was detected; p53-null patients resulted slightly older, no significant differences was observed for Stage at presentation and follow-up duration, 7 p53-null and 3 p53-overexpressed patients died of the disease.

P53-null patients demonstrated a significantly worse OS in the first 24 months of follow-up (HRp53-null=6.09; 95%CI: 1.52–24.51).
Conclusion: Aberrant p53 IHC expression was confirmed as a reliable characteristic of HGSOC. P53-null phenotypes harboured a peculiar set of mutations leading to an unfavourable prognosis if compared with patients with p53-overexpression. The functional reason of why p53-null HGSOC showed an unfavourable prognosis with respect to p53-overexpressed ones, need further investigation however TP53 status could be systematically investigated even in light of new target therapies in future.

PS-09-027
Multivariate analysis of histomorphological and immunohistochemical prognostic factor in endometrial carcinoma
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Background & objectives: To investigate the prognostic value of some of the most widely studied histomorphological and immunohistochemical factors, easily accessible in every routinely pathology lab set, in endometrial carcinoma.
Methods: We enlisted patients who underwent radical hysterectomy for endometrial carcinoma. The following histomorphological and immunohistochemical factors were analysed: histotype, stage, type of infiltration, desmoplasia, intratumoral necrosis, tumour infiltrating lymphocytes, lymphovascular space invasion, oestrogen receptor α, progesterone receptor, Ki67, p53, β-catenin, e-cadherin, bcl-2 and cyclin D1. Primary endpoints were disease free survival and overall survival.
Results: Out of 206 cases eligible for our purpose, we found 151 low-grade endometrioid, 20 high-grade endometrioid and 35 non-endometrioid carcinomas. At univariate analysis, all prognostic factors excluding tumour infiltrating lymphocytes, e-cadherin, bcl-2 and cyclin-D1 were significantly associated with disease-related relapse and death. Multivariate analyses were conducted separately for the histomorphological and immunohistochemical factors and showed a significant correlation between disease recurrence and non-endometrioid histotype and low β-catenin expression. Moreover, a significant association was observed between disease-related death and non-endometrioid histotype and low β-catenin expression.
Conclusion: Our study confirms the key prognostic role of histotype in endometrial carcinoma. While the other histomorphological factors did not achieve statistical significance, at least tumour grade, stage and lymphovascular space invasion should be included in the pathologist's report as recommended by the Royal College of Pathologists. Furthermore, in order to improve patient risk stratification, we propose to include β-catenin evaluation in the report.

PS-09-028
Adenomatoid tumours – a ten-year retrospective clinicopathological study on a rare neoplasm
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Background & objectives: Adenomatoid tumours are rare benign mesothelial neoplasms that usually arise both in the female and male genital tract. The purpose of this study was to give insight into an infrequent neoplasm.
Methods: This study includes 16 cases of adenomatoid tumours from both female and male genital tract which were diagnosed in our centre between 2011 and 2020. Most cases were identified morphologically, but some specific cases required to be further confirmed immunohistochemically either by calretinin, D2-40, WT1, CK7 and vimentin or a combination between these markers.
Results: Of 16 tumours, 9 occurred in the female genital tract and the rest in males. 5 tumours from the male genital tract presented as mass lesions, one being diagnosed in an ectopic testicle, whereas 7 tumours from female genital tract were diagnosed incidentally. The most common location for female patients was the uterus body and for male patients the epididymis. One case was a synchronous tumour with uterine leiomyosarcoma and a mature ovarian teratoma. Histologically, half cases had tubular pattern, while the rest were trabecular or cystic. 6 tumours showed mild to moderate atypia and Ki-67 expression was evaluated in these cases, but all tumours had values below 1%.
Conclusion: Adenomatoid tumours are uncommon benign tumours that can be symptomatic most commonly in male patients because of their localization. Even though they usually present as small incidental masses, a thorough gross and microscopic examination could reveal even more cases. This neoplasm is often easily diagnosed, but in cases with unusual morphological features and nuclear atypia, immunohistochemical markers like calretinin, CK7, D2-40 and WT1 should be used in order to exclude other differential diagnoses.

PS-09-029
Importance of DNA ploidy in endometrial carcinoma
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Background & objectives: The estimated incidence and mortality in Europe of corpus uteri cancer in the year 2020 was 6.9% and 31.3% respectively. The aim of our survey was the evaluation of DNA ploidy as predictive and prognostic factor in patients with EC.
Methods: Endometrial samples freshly resected from 168 women who underwent total abdominal hysterectomy were studied. The cytological diagnosis was confirmed by pathologists. Cytological imprint smears were obtained by touching the cut surface of fresh cancer tissues and stained with Feulgen stain.
Results: According to our results, in terms of quantitative estimation of cellular DNA, all case-control samples from proliferative, secretory and atrophic endometrium (total number 15) were exclusively diploid (DNAindex 0.9-1.1), while at least 82% of Grade 3 (total 39/168) tumours present an euploidy of DNA (DNA index <0.9 or >1.1) as opposed to about of 44% of Grade 1 (total 52/168) and Grade 2 (total 77/168) endometrial carcinomas. Furthermore, regarding the DNA intex, the ploidy balance, the degree of hyperploidy and its proliferation index, observed a statistically significant difference between all malignant lesions as well as between benign and malignant lesions ($P<0.05$).
Conclusion: We believe that the use of the quantitative assessment of cellular DNA may help identify tumours with high malignant potential and possible aggressive behaviour or ability relapse offering valuable information, both in prognosis and in the treatment of patients with EC. According to international literature, aneuploidy is an independent prognostic marker of relapses, a sign of malignant transformation and can therefore predict a poor prognosis.

PS-09-030
Placental infection with SARS-CoV-2 in an asymptomatic pregnant woman
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Background & objectives: The COVID-19 pandemic raised attention to the possible complications of the disease during pregnancy. Meanwhile, no consensus has yet emerged as to the placental morphological features

of this viral infection. We propose to describe a case of SARS-CoV-2 positive pregnancy.
Methods: A 28yo primigravida with asymptomatic COVID-19, presented with reduced foetal movements at 35W,5D of gestation. A pathological cardiotocography prompted a C-section. The female live birth had low weight for gestational age, respiratory distress and bradycardia, Apgar 2/7/9, and was negative for SARS-CoV-2. A week after neonatal unit admission, she fully recovered. The placenta was sent to pathologic examination.
Results: It was received a monochorionic and monoamniotic, discoid placenta, with 18x17x2cm and 338g (weight below the 25th percentile for gestational age), mild opaque, yellowish foetal membranes, a normocoiled umbilical cord with 31x1.2cm, paracentral insertion and three vessels. Examination of the cut surface showed a central area of infarction, with 4cm in the greatest dimension. Microscopically, the placental parenchyma showed accelerated villous maturation, diffuse and severe chronic histiocytic intervillitis, areas of organized infarction, fibrin deposition and chorangiosis. Immunohistochemistry for SARS-CoV-2 antibody was performed, showing diffuse villous trophoblastic staining.
Conclusion: The study of the placental pathology could allow us to understand the complications or eventual defensive mechanisms of the SARS-CoV-2 infection. Chronic intervillitis is an inflammatory response for this viral infection, as referred in other related studies, and is associated with worse foetal outcome. Furthermore, the strong immunostaining in the villous trophoblast cells, a rare feature in asymptomatic COVID-19 cases, raises questions about the possible protective function of this cells in containing the infection.

PS-09-031
Heavy metals exposure decrease the progesterone expression in the rat myometrium
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Background & objectives: The progesterone receptors (PR) activity in the uterus helps to regulate critically important reproductive functions in mammals. However, impaired progesterone production and sensitivity caused by the exogenous pollutants may lead to unpredictable sexual health disorders.
Methods: Uterine tissue samples were obtained from adult female rats in the estrus phase. Before uteruses removal, rodents were randomly divided into two groups: rats of Group I received HM salts mix (Zn/Cu/Fe/Mn//Pb/Cr) for 30 days, whereas rats of Group II served as control. The immunohistochemical investigation was performed utilizing primary antibodies to PR (rabbit anti-PR Monoclonal Antibody – SP2 clone).
Results: The strong positive nuclear PR immunolocalization was found in almost all myocytes of rat uterine circular and longitudinal muscle layers of Group II. Compared to the control PR expression, an immunohistochemical investigation of rats myometrium of Group I allowed to detect the decrease of PR-positive muscle cell number ($p<0.01$). Besides, the nuclear PR signal intensity in the myometrium was simultaneously reduced.
Conclusion: Rat myometrium undergoes changes of progesterone receptors level physiological activity due to the prolonged influence of heavy metals. The pollutants-induced changes contribute to the significant decrease of progesterone receptors positive cells and their expression intensity by uterine myocytes, although not reaching the critically low level.

PS-09-032
Mismatch repair protein expression in endometrial cancer: are clinicians using it?
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Background & objectives: Mismatch repair protein expression (MMR) universal testing is recommended for endometrial cancer allowing Lynch syndrome (LS) identification, assists diagnosis, prognosis and guides treatment but is still mostly unused[1]. We reviewed our recent testing experience in MMR-immunoexpression (MMR-IHC).
[1] (ESMO guidelines)
Methods: Between 2018 to 2020, we found 478 endometrial carcinoma (EC) cases and checked the report for MMR-IHC for the 4 MLH1, PMS2, MSH2, MSH6 proteins and for further molecular studies (methylation and Next Generation Sequencing/MLPA) of cases with abnormal IHC testing.
Results: Mean age was 69yrs. (range: 31-92); distributed as endometrioid(71.8%); serous(9.8%); clear cell(4%); carcinosarcoma(6.7%); undifferentiated(4.2%); mixed(3.1%); others(0.4%). Although universal study is recommended in our hospital since September 2019, only 146 cases(30.5%) had MMR-IHC performed distributed by year as follows: 20/165(2018); 54/181(2019) and 72/132(2020). 50 cases had abnormal MMR-IHC(34.2%). The loss of MLH1 occur in 74%; PMS2 in 78%; MSH2 in 22% and MSH6 in 14%. Loss by histological-type: endometrioid(74%), clear cell(2%), mixed(8%), undifferentiated carcinomas(14%), others(2%). Carcinosarcomas(0/32) and serous carcinomas(0/47) had normal MMR-IHC. Molecular testing identified 2 cases of Lynch Syndrome, 2 with MLH1 methylation, 5 without MMR gene mutations and 20 still in evaluation.
Conclusion: The rate of the immunohistochemistry testing in EC was around 35 % in our hospital, in the last 3 years. The immunohistochemical results of MMR evaluation are similar to what is described in the literature. The rate of confirmation of MMR-IHC is very low (patients refusal, death) and lengthy. The large absence of MMR-IHC in the pathological reports may indicate that clinicians are not using the MMR data.

PS-09-033
High-grade ovarian carcinoma molecular subtypes: manual and neural networks ensemble-based reproducibility
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Background & objectives: Primary ovarian high-grade serous carcinoma (HGSC) has been classified into 4 molecular subtypes: Mesenchymal, Immunoreactive, Proliferative and Differentiated. In 2016 R. Murakami et al. proposed the algorithm based on morphological and immunohistochemical findings to determine them in histological slides.
Methods: In our study we tested the morphology-based classification system presented by R. Murakami et al. and compared the results of manual and neural network-based analysis. The latter identifies the molecular subtype using both whole slide images and patient sequencing data from the TCGA database. The agreement between pathologists pairs were analysed with Cohen's kappa.
Results: The study revealed that convolutional neural network showed high level of reliability (resulting multi-class accuracy on separate test set after 40 epochs equals 0.816), whereas the accuracy of morphological diagnoses was low to moderate (Cohen's kappa for all pathologists was 0,305 – 0,605). Mesenchymal subtype was diagnosed by pathologists correctly in 56,1% cases, immunoreactive - in 17,9 %, proliferative - in 21,1% and differentiated subtype - in 25,7%.
Conclusion: Obtained dataset indicates that using only morphological criteria to distinguish molecular subtypes of HGSC does not seem to perform in routine practice. It may be feasible to use artificial intelligence as a powerful diagnostic tool for molecular subtyping of HGSC, but the neural network needs a larger sampling for high precision results.

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PS-10-001

Solitary plasmocytoma of chest wall: clinicopathological study of 15 cases

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Background & objectives: Solitary plasmocytoma of the bone is a rare disease that account for only about 5% of malignant plasma cell tumours. Infrequently, it is seen in ribs and sternum. The aim is to present clinicopathological features of this disease.
Methods: We report a retrospective study of 15 cases of solitary plasmocytoma diagnosed at our department of pathology between 2004 and 2020. Radiological findings and bone narrow examination does not show any other localisation. The immunohistochemical study includes CD20, CD79, CD138, Kappa and Lambda light chain antibodies.
Results: There were 12 male and 3 female patients, aged between 50 and 81 years with a mean of 67. Ten plasmocytoma were localized in ribs, four in the sternum and one in the scapula. The diagnosis was made on transparietal biopsy in 13 cases and on surgical resection in 2 cases. Microscopic examination showed diffuse sheet of monotonous population of dark blue round cells, few with eccentrically placed nucleus and eosinophilic cytoplasm. Bi–nucleated forms were seen. On immunohistochemistry, tumour cells express CD138 in 15 cases, CD79a in 15 cases, Kappa light chain in 6 cases and lambda light chain in 9 cases. They were negative for CD20 and CD3.
Conclusion: Solitary plasmocytoma of chest wall is a rare entity with low specific clinical and radiological expression. The diagnosis is based on histology with identification of localized tumour composed of monoclonal plasma cells.

PS-10-002

Low indoleamine 2,3-dioxygenase 1 (IDO1) and high CD204 expression in the tumour microenvironment are independent adverse prognostic factors in mantle cell lymphoma patients

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Background & objectives: Indoleamine 2,3-dioxygenase (IDO)1(+) dendritic cells and CD204(+) macrophages contribute to immune regulation in tumour microenvironment, but their clinical significance in mantle cell lymphoma (MCL) is largely unknown. We studied the prognostic value of IDO1(+) cells and CD204(+) cells in MCL.
Methods: A total of 127 cases of MCL from Taiwan were included. The mantle cell lymphoma international prognostic index (MIPI) was calculated, and a MIPI of 5.7 or higher was considered high. Immunohistochemical study for Ki-67, MYC, p53, IDO1 and CD204 was performed, and the cut-off for high expression was at least 30%, 20%, 30%, 5% and 5%, respectively.
Results: Ki-67, MYC and p53 were expressed by tumour cells, whereas IDO1 and CD204 were mainly expressed by dendritic cells and macrophages, respectively. Using univariate analysis, high MIPI score, high Ki-67 expression, high MYC expression, high p53 expression, low IDO1(+) dendritic cells and high CD204(+) macrophages were significant adverse prognostic factors (P = 0.00059, 0.026, 0.00080, 0.026, 0.010 and 0.0032, respectively). Using multivariate analysis, only high MIPI score (hazard ratio (HR) 2.98; 95% confidence interval (CI) 1.66-5.35; P = 0.00026), low IDO1(+) dendritic cells (HR 2.95; 95% CI 1.57-5.54; P = 0.00076) and high CD204(+) macrophages (HR 2.35; 95% CI 1.29-4.27; P = 0.0050) were independent adverse prognostic factors.
Conclusion: Here we report for the first time that low IDO1(+) dendritic cells and high CD204(+) macrophages in the tumour microenvironment are independent adverse prognostic factors for MCL patients. Modification of the tumour microenvironment might be of therapeutic valve for MCL patients. Future functional studies would be helpful to clarify the roles of these cells in MCL.

PS-10-003

Neoplasm of large B lymphoid cells - a rare central nervous system lymphoma: analysis of 2 cases

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Background & objectives: Central nervous system (CNS) involvement by lymphoma is distinctly rare and clinically aggressive. The aim of this study is to present the clinicopathological features of histopathologically-proven cases of CNS lymphoma to further characterise this rare entity.
Methods: We performed a retrospective study on Non-Hodgkin Lymphoma cases from 2015 to 2021 in South-Eastern Romania. To date, 105 cases suitable for our study have been reported and we describe the only 2 cases of CNS Lymphoma. Further to the histopathological examination, an immunohistochemical evaluation was mandatory by using monoclonal antibodies (CD3, CD10, CD15, CD20, CD45, CD79a, Bcl-2, Bcl-6, Ki67).
Results: Two patients, a 57-year-old female and a 65-year-old male, who presented clinical and imagistic features of a CNS malignancy, both localized in the frontal and fronto-parietal lobe. Clinical and imagistic correlations raised the possibility of glioblastoma but histopathological examination established the diagnosis of CNS lymphoma. Histopathologically, both cases were characterized by a diffuse proliferation of medium/high-sized lymphocytes, with a high mitotic rate. Immunohistochemistry study showed positivity for CD20, CD45, Bcl-2, CD79a with a high nuclear proliferation marker (Ki67 80-90%), while the other biomarkers (CD3, CD10, CD15, CD30, EMA) were negative. These findings established the certainty diagnostic of diffuse large B-cell central nervous system lymphoma.
Conclusion: Clinical and imaging features of primary CNS lymphoma and glioblastoma are highly variable and sometimes similar, difficult to differentiate, and this is why it is important to recognize this entity in order to avoid misdiagnosis. The morphological evaluation of the presented cases has confirmed the diagnosis and has ensured adequate treatment and follow-up. The histopathological and immunohistochemical evaluation played an essential role in establishing the final diagnosis, in order to determinate the neoplastic proliferation line and the subtype of lymphoma.

PS-10-004

Matrix metalloproteinases and their inhibitors in JAK2-mutated myeloproliferative neoplasms

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Background & objectives: The aim of study was to assess the specificity of expression of matrix metalloproteinases 2 and 9 (MMP2, MMP9) and their inhibitors (TIMP1, TIMP2) in JAK2-mutated myeloproliferative neoplasms (MPN) and their possible correlation with the grade of bone marrow fibrosis.
Methods: We investigated 55 bone marrow biopsies of patients with JAK2-mutated MPN. Whole-slide sections were immunostained using antibodies against MMP-2, MMP-9, TIMP-1, TIMP-2 and scored by ImageJ plugin software. The same biopsies were silver-stained and assessed using the semiquantitative bone marrow fibrosis (MF) grading system proposed by Thiele Jet al.

Spearman's rank-order correlation was calculated. Statistical significance was set at $p<0.05$.

Results: MMP2 and TIMP2 expression was observed mostly in megakaryocytes. MMP9 expression was observed in neutrophils, macrophages, and stromal fibroblastic components. TIMP1 expression was observed exclusively in stromal fibroblastic components.

Grade of fibrosis was assessed as MF0 in 19/55 (34,5%), MF1 in 15/55 (27,3%), MF2 in 14/55 (25,5%), MF3 in 7/55 (12,7%). The overall number of cases with fibrosis of any grade was 36/55 (65,5%).

There was weak negative correlation between TIMP2 and the grade of fibrosis (rho= -0.293, p=0.030, n=55), weak negative correlation between MMP2 and fibrosis of any grade (rho= -0.299, p=0.027, n=55) and moderate negative correlation between TIMP2 and fibrosis of any grade (rho= -0.367, p=0.006, n=55).

Conclusion: In a bone marrow MMP and TIMP expression was observed in megakaryocytes in addition to the typical expression in inflammatory cells and stroma.

The existence of correlation between MMP regulation and bone marrow fibrosis is likely to improve understanding of JAK2-mutated MPN pathogenesis. It may be useful for supporting the diagnosis, evaluation of prognosis and the development of possible matrix-targeted treatment.

PS-10-005

Precision medicine development and validation of a multi-fluorescent automated assay to quantify BCL2 and CCND1 expression in CD138 positive bone marrow multiple myeloma (MM) cells

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Background & objectives: MM remains incurable despite adoption of novel therapeutics. We describe the development and validation of an automated platform from bone marrow trephines to identify t(11;14) patients with overexpression of CCND1 or BCL2 who may benefit from venetoclax, a BCL2 inhibitor.

Methods: Antigen retrieval (Dako PT Link) were performed on bone marrow trephines followed by primary antibodies staining (anti-CD138, anti-BCL2 and anti-CCND1) then specific fluorophores (CD138–AF647, BCL2–AF594 and CCND1–AF488) on an Auto-Stainer Link 48 and scanned using Olympus VS120 slide scanner. Scanned images were assessed by 2 haematologists using the OlyVIA software (Olympus) and with an automated assay (in-house ImageJ script).

Results: 41 trephines comprised of 4 cohorts; t(11;14), t(4;14), chr14-translocation-other-than t(4;14), and MM with normal karyotype/FISH (normals) were analysed. Comparisons between two haematologists and the automated script had Spearman correlation of r=0.974 (CD138), r=0.778 (BCL2) and r=0.6744 (CCND1). With the automated assay, CCND1 was over-expressed in the CD138+ cells in the t(11;14) cohort compared to normals (p=0.02). 50% of the chr14-other cohort over-expressed CCND1 in CD138+ cells, possibly from patients harbouring t(11;14). No CD138+/CCND1+ cells were observed in the t(4;14) cohort. Utilising automated quantification and defining low BCL2 expression as < 28.17% (median-1STDEV); intermediate/high BCL2 expression on CD138+ cells was identified in 73% of cases and not restricted to t(11;14) subgroup.

Conclusion: We identified MM patients with CD138+ cells expressing high CCND1 and/or high BCL2 expression utilising automated triple immunofluorescent staining of bone marrow trephines. CCND1 and BCL2 expressions, in accordance with the literature, surpasses the t(11;14) subgroups defined traditionally by FISH, identifying a larger cohort of patients that could potentially benefit from the addition of venetoclax in their therapeutic algorithm.

PS-10-006

Next Generation Sequencing (NGS) in acute myeloid leukaemia: a centre experience

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Background & objectives: Acute myeloid leukaemia (AML) is an aggressive malignancy of hematopoietic precursor cells. Incidence increases with age. Although the aetiology is unclear, evolution from a clonal haematopoiesis or any other stem cell disorder is most likely in older patients.

Methods: Mutational profile, clinical data and histopathological findings of 30 patients, diagnosed with AML based on the 2017 update of World Health Organization (WHO) classification of myeloid neoplasms were evaluated. Bone marrow biopsy was done for histopathological examination. CD34 and CD117 immunoexpression were evaluated on the blasts. Bone marrow aspiration was used for flow-cytometric analysis and molecular studies.

Results: Mean age was 64,40 years. 13 were female (43,3%),17 were male (56,7%). Based on initial clinical evaluation, 18 patients were considered as de-novo AML (60%), 12 patients as transformed/relapsed AML. Mean survival was 9,13 months. 12 patients died (40%). QIAact Myeloid DNA NGS Panel revealed following results: Mutations of TP53 and RAS gene in 7 (23,3%), ASXL1 in 9 (30%), TET2 in 9 (30%), DNMT3A in 9 (30%), IDH mutations in 7 (23,3%), FLT3 in 6 (20%), SF3B1 in 7 (23,3%) patients. Among de-novo AML patients (5 cases) with TP53 or RAS mutation, mean survival was 2,2 months, while in patients without these mutations, mean survival was 21,57 months (p=0,045).

Conclusion: As a novel and sophisticated method, NGS supports the clinical assessment of AML patients and contribute to the concept of individualized prognostic expectation as well as treatment. Particularly in patients who are otherwise considered as de-novo AML, determination of clonal haematopoiesis may effect on both treatment, stem cell transplantation as well as follow up decisions.

PS-10-007

Langerhans cell histiocytosis: an institutional experience

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Background & objectives: Langerhans Cell Histiocytosis' pathogenesis (LCH) is still debated nowadays between a reactive or neoplastic aetiology, the latter supported mainly by BRAF p.V600E mutation.

We describe the association between cases diagnosed with LCH in our entity and their association with BRAF.

Methods: Retrospective observational study of cases diagnosed with LCH in our institution from 2010 to 2020. Epidemiological data, clinical course and evolution are collected. Histological preparations are reviewed, including BRAF antibody (VE1, Roche) by immunohistochemistry (IHQ). Quantitative PCR (qPCR, IdyllaTM) for BRAF is performed in 8 of the 11 cases at the time of writing.

Results: Eleven diagnosed cases of LCH have been collected, 9 in adults (8 female, mean age: 56 years). Five cases (66%) were associated with some neoplasm, most of them being solid (75%). In 2 of these 5 cases, the neoplasm was diagnosed concomitantly with LCH. In another 2 cases the neoplasm preceded the LCH and in the other one the diagnosis of LCH was concomitant with the recurrence of the neoplasm.

Of the 11 cases, 6 (54%) were positive for BRAF by IHQ. Of the 8 cases evaluated by qPCR, 3 (37.5%) showed BRAF mutation (all 3 with

immunohistochemical staining), of which 2 were associated with second neoplasms and poorer prognosis.
Conclusion: Langerhans Cell Histiocytosis is a rare entity of controversial aetiology. It is more frequent in women, and its presentation should raise the suspicion of a second neoplasm. Its association with BRAF mutation has been observed by IHQ and by qPCR, which would support its clonal origin. BRAF-mutated LCH could be more frequently associated with second malignancies and, thus, worse prognosis.

PS-10-008
Association of STAT3 expression and enhanced angiogenesis in primary extranodal diffuse large B cell lymphoma
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Background & objectives: Signal transducer and activator of transcription 3 (STAT3) is critically involved in fundamental cellular processes, including cell survival, proliferation, and angiogenesis. We investigated the correlation between STAT3 and intratumoral microvascular density in primary extranodal diffuse large B cell lymphoma (DLBCL).
Methods: Immunohistochemical analysis of STAT3 expression was performed on tissue samples of 59 patients with primary extranodal DLBCL, treated with R-CHOP. Microvessel density (MVD) was assessed as a number of blood vessels per 1 mm2 of tumour tissue, via identification of endothelial cells by immunostaining to CD31. Based on the average value, tumours were divided into low- and high-MVD groups.
Results: Strong expression of STAT3 was found in 37.3% of cases, while high MVD was observed in 52.5% of the tumours. STAT3 overexpression was significantly associated with high MVD in the tumour microenvironment ($p=0.001$). Moreover, STAT3 was strongly linked to non-GCB immunophenotype of DLBCL, determined by Hans' immunohistochemical algorithm ($p=0.002$) and poor overall survival of the patients ($p<0.001$).
Conclusion: Our study indicates that strong STAT3 immunoexpression in primary extranodal DLBCL is firmly associated with increased intratumoral angiogenesis determined by MVD. This suggests that STAT3 positive cases of this aggressive disease may benefit from antiangiogenic therapeutic strategies.

PS-10-009
Anaplastic large cell lymphoma (ALCL) – the expression profile of CD30-IRF4-MYC axis
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Background & objectives: Anaplastic large cell lymphoma (ALCL) is a T cell neoplasm with uniform CD30 expression, loss of T cell antigens, and the presence[ALCL-ALK(+)]/lack[ALCL-ALK(-)] of *ALK* fusion gene. Recently, MYC expression was identified as an adverse prognostic factor that IRF4/MUM1 could modulate.
Methods: We included in the study 39 cases of ALCL: 25 (64%) ALCL-ALK(-).and 14 (36%) ALCL-ALK(+). All cases were revised according to the WHO diagnostic criteria. The immunohistochemical assessment included expression profile of CD30 (Ber-H2,RTU,Agilent/Dako), IRF4/MUM1 (MUM1p,RTU,Agilent/Dako), and MYC (Y69,1:100,pH 9.0,Abcam) on ALCL cells. The CD30 and IRF4/MUM1 were evaluated as positive/weak/negative cases and MYC as low/high "expressors".
Results: The CD30-IRF/MUM1-MYC expression profile in the ALCL-ALK(-) vs. ALCL-ALK(+) groups showed minor differences. All cases were CD30 positive, but ALCL-ALK(+) demonstrated a higher percentage of weak expression (14.3% vs. 8.7%). Strong IRF4/MUM1 was exhibited in 87% of ALCL-ALK(-) and 76.9% of ALCL-ALK(+) cases. Low vs. high expression of MYC was seen in ALCL-ALK(-) and ALCL-ALK(+), respectively: 47.8% vs. 52.2% and 61.5% vs. 38.5%. High MYC "expressors" were accompanied by stronger CD30 (94.1% vs. 81.3%) and IRF4/MUM1 (94.1% vs. 73.7%) reactions.
Conclusion: ALCLs, both ALK(-) and ALK(+) show a high level of IRF4/MUM1 and MYC expression profile. It is essential since IRF4/MUM1 targets immunomodulatory drugs such as lenalidomide which has a clinical impact on patients with peripheral T-cell lymphomas. Also, single studies reported the importance of MYC in stratifying or predicting the prognosis. We believe that further analysis, including clinical data, will be the crucial point of evaluating IRF4/MUM1 and MYC expression as prognostic biomarkers.

PS-10-010
Bone marrow immune microenviroment in patients with myelodysplastic syndromes
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Background & objectives: Myelodysplastic syndromes (MDS) constitute a group of clonal expansions of hematopoietic stem cells. Our objective is to investigate the immune landscape in bone marrow biopsies from patients with intermediate/high risk MDS, and its role in the outcome of 5-Azacytidine treatment.
Methods: The study population consists of 82 patients treated with 5-AZA. BM specimens before (n=82) and during treatment (n=31) were immunostained for CD3, CD8, CD20 and CD138 for T, cytotoxic T, B and plasma cells respectively. Positive cells were counted in 5 areas with the highest density of CD8 cells and all cell counts were normalised to 100.000μm2 of tissue area.
Results: In biopsies before treatment, the presence of lymphoid aggregates significantly correlated with high densities of CD8+ T and B cells ($p=0.013$ and $p=0.035$ respectively). In addition, higher CD3+ T cell densities also significantly correlated with increased overall survival (OS) ($p=0.016$), overall response ($p=0.035$) and complete remission (CR) ($p=0.035$). Moreover, higher plasma cell density was found in patients that eventually transformed to AML ($p=0.022$). In biopsies after treatment, higher BM cellularity was negatively correlated to OS ($p=0.009$), whereas responders showed decreased cellularity ($p<0.001$). Moreover, responders in general, as well as complete responders in particular showed decreased CD8+ T cell densities ($p=0.010$ and $p=0.026$, respectively) in follow-up biopsies.
Conclusion: Our preliminary results indicate that the density of cells of adaptive immunity in the bone marrow specimens may significantly contribute to both response and survival of high risk MDS patients treated with 5-AZA.

PS-10-011
Comparative immunohistochemical study of T4, T8 and FOXP3+ cells in tumour microenvironment of primary mediastinal B-cell lymphoma and mediastinal nodular sclerosis classical Hodgkin lymphoma
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Background & objectives: Primary mediastinal B-cell lymphoma (PMBL) and nodular sclerosis classical Hodgkin lymphoma (NSCHL) are the most common primary mediastinal B- cell lymphomas, which share similar clinical and histopathological features. We compare the T-cell populations in their microenvironment (TME) using immunohistochemistry.
Methods: Twenty-five cases were retrieved from the archives of our Department, 13 histologically diagnosed as PMBLs and 12 as mediastinal NSCHLs. Tissue microarrays (TMAs) with two cores per case were constructed and immunohistochemistry with CD4, CD8 and FOXP3 antibodies was performed. CD4+/CD8+ ratio, FOXP3+ cell percentage, eosinophil and mast cell densities were evaluated. A statistical analysis using IBM SPSS Statistics v25 followed.
Results: CD4+/CD8+ lymphocytic ratio, FOXP3+ cells, eosinophil and mast cell densities were significantly higher in NSCHL ($p<0.05$). FOXP3+ cells were negatively associated with eosinophil density in NSCHL ($r=-0.676$, $p<0.05$). In PMBL, CD4+ cell percentage of total TME cells was positively associated with FOXP3+ cell percentage ($r=0.889$, $p<0.01$). Interestingly, in three (3/13, 23.1%) PMBL cases, FOXP3 positivity was observed in neoplastic B-cells, as well. In these cases, staining intensity was variable, often weak to moderate, in a proportion of positive cells ranging from almost 50 to 90% of the total neoplastic population. In addition, a positive association was found between mast cell density and CD8+ cells ($r=0.585$, $p<0.05$) in PMBL.
Conclusion: Our findings exhibit a clear difference between the TME of the two entities. Globally, T4 cells are predominant in NSCHL and T8 cells in PMBL. FOXP3+ T-cells are more abundant in NSCHL than in PMBL. There seems to be an interaction between T8 cells and mast cells in PMBL, which needs further investigation. The observation of FOXP3+ neoplastic B-cells in a subset of PMBLs should be established in larger series, as well as its possible clinical and biological significance.

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PS-11-001
Visual versus computer-assisted evaluation of PD-L1 expression in head and neck squamous cell carcinoma

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Background & objectives: Guidelines to assess PD-L1 expression in head and neck squamous cell carcinoma (HNSCC) have been published. However, interpretation is challenging and time consuming. The aim was to develop a computer-assisted evaluation of PD-L1 expression and compare to the visual assessment.
Methods: 37 samples from HNSCC patients from the Colombian cohort of the InterCHANGE study (IARC) were included. TMAs were constructed and Immunohistochemistry with PD-L1 (22C3-PharmDx-Agilent/Dako) was performed. The Combine Positive Score (CPS) was assessed independently by five pathologists. Their scores were compared to digital scores obtained by a machine learning-assisted methodology using QuPath (v0.2.3).
Results: PD-L1 expression (CPS ≥1) was 89% (33) and 97% (36) in the visual and digital assessment, respectively. CPS ≥20 was more frequently seen in the digital methodology (78%) than in the visual scoring (40%). Visual and digital CPS scores showed a spearman correlation coefficient of 0.7146 ($p=0.0001$), and there was a moderate agreement between the pathologist scores and the digital ones when grouped into ranges (<1, ≥1-19, ≥20) (weighted-kappa of 0.4127, $p=0.0003$).
Conclusion: We show a high prevalence of PD-L1 expression in HNSCC as previously reported. There was a substantial correlation between the visual and digital scores. However, some cases (3) reported as negative (CPS <1) by the pathologists were detected as positive by the digital methodology. We consider that digital assessment of PD-L1 expression is feasible and especially helpful when evaluating cases that are close to a cut-off score. However, this requires an excellent digital slide resolution and exclusion of artifacts.

PS-11-002
Adamantinoma-like Ewing sarcoma of the head and neck: a case series of a rare and challenging diagnosis

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Background & objectives: Adamantinoma-like Ewing sarcoma (ALES) is a rare malignancy characterized by EWSR1-ETS related fusions and epithelial differentiation. ALES is being increasingly recognised in the head and neck. We aimed to study the clinicopathologic spectrum of ALES diagnosed at our institute.
Methods: A retrospective review of the clinical and pathologic features of all ALES cases was performed after confirming the diagnosis.
Results: Seven patients were analysed. The age range was 7-44 years (4 males; 3 females). Tumours were distributed in the maxilla (n=2), parotid (n=2), nasal cavity (n=1), alveolus (n=1), and thyroid (n=1). Tumour size was 1.6-5.5 cm. Tumours had infiltrative edges, monomorphic cells, nested-lobular architecture, and interlobular fibrotic stroma. Cells were round (n=4) /basaloid (n=3). Palisading (n=3), squamous differentiation (n=2), keratinization (n=1), follicle-like cysts (n=3), calcification (n=4), necrosis (n=5) was observed. On immunohistochemistry, cytokeratins (100%), p40 (100%), CD99 (100%), and synaptophysin (57%) were positive; markers for NUT/SMARCB-1 deficient/myoepithelial/ lymphoid/myoid/melanoma were negative. EWSR1 rearrangements were identified in 5/5 patients who were tested. One patient developed recurrence; 3 developed metastases.
Conclusion: ALES is a rare and aggressive malignancy that mimics diverse neoplasms common in the head and neck region. Awareness of the morphologic and immunohistochemical spectrum of this tumour is essential to avoid diagnostic errors.

PS-11-003
Subepithelial fibrinous accumulation and associated epithelial downward proliferation in laryngeal nodules

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Background & objectives: Fibrinoid accumulation in larynx and in time results with overgrowths. Mucosal epithelium may proliferate downward to organize and remove the fibrinoid accumulation. This study focused on the fibrinoid substance accumulation and the mechanisms of the associated squamous epithelial proliferation.
Methods: Five hundred and seventy-five laryngeal nodules re-examined and 111 of them with varying degrees of irregular downward squamous epithelial proliferation included to study. Immunohistochemically for CK5/6, CK17, CK14, collagen type I, collagen type III, collagen type IV, and fibrinogen was performed. The modified Masson's trichrome method was used for histochemical staining of collagen.
Results: Some of the nodules showed acute lesions having mostly subepithelial fibrin accumulation and oedema. The relatively mature lesions mostly contain dense collagen fibres. The intensity of collagen type III was inversely proportional to the amount of fibrin accumulation. Collagen type IV was found only in the epithelial and vascular basement membranes. The decrease in fibrin staining intensity and presence of collagen type I and type III indicates the replacement of fibrin with collagen. Basal-type keratins show more pronounced staining in the

regenerated areas of the epithelium. As the laryngeal subepithelial fibrinoid accumulation was replaced with collagen, the regression of the lesion became difficult.
Conclusion: Irregular squamous epithelial proliferation exists independent of the stage of the lesion. Although the aetiology is different, the resulting lesions are histologically similar to those seen in the ligneous mucosal disease.

PS-11-004
Sarcoidosis in metastatic lymph nodes of solid cancer: a fortuitous discovery and complex association
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Background & objectives: Sarcoidosis is a benign multisystem granulomatous disease. It is being reported to be associated with malignancies, however, the exact frequency is not yet established.
We tried to evaluate a possible causative association with literature review.
Methods: We report four cases of fortuitous discovery of sarcoidosis in metastatic lymph nodes of thyroid and breast carcinoma collected over a period of 4 years in the department of pathology of the university hospital of Monastir.
Results: All patients were female. Patients ages ranged from 40 to 65 years with an average age of 54 years.
In 3 cases, the diagnosis of sarcoidosis was made in metastatic lymph nodes from lymph node dissection in papillary thyroid carcinoma. In the last case, the diagnosis was made in metastatic lymph nodes from axillary lymph node dissection for breast carcinoma. No patient has a history of systemic disease. Histologically, metastatic lymph nodes show a granulomatous inflammation without caseous necrosis. Slight fibrinoid necrosis in the centre of some sarcoidotic granulomas has been observed. Schumann bodies were seen in 2 cases without any astroid body.
Conclusion: Relationships between granulomatosis and cancer have been described for a long time herefore, it is important for clinicians to be aware of the simultaneous occurrence of sarcoidosis and metastatic malignancy, especially when the biopsy shows a granulomatous reaction. All cancer types can be observed. Hypothesis of a possible association and a possible increased risk of cancer include the chronic inflammation, the immune system dysregulation and of sarcoidosis. However, this association could be considered as a protective factor against cancer relapse.

PS-11-005
Ameloblastoma of the jaw: clinico-pathological study
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Background & objectives: Ameloblastoma is rare benign tumour of the odontogenic epithelium. It accounts for only 1% of all jaw tumours and about 11% of all odontogenic tumours. Our objective is to report the characteristics of the different types of ameloblastoma and their evolutionary aspect.
Methods: In this work, we included 6 cases of ameloblastoma, collected in the pathology department at the Sahloul University Hospital in Sousse (Tunisia), over a period of two years: (January 2019-December 2020).
Results: The sex ratio was 1:5. The average age of this population is 52 years. The mandibular localization represented in 5 cases, including 3 cases at the level of the mandibular angle,1 case at the level of the ascending branch and 1 case at the level of the horizontal branch. One patient had a double mandibular localisation. Macroscopically 3 tumours were cystic,2 cases were firm and brownish. Histologically,5 cases had a conventional ameloblastoma including 4 cases in its follicular form and 1 case in its acanthomatous form. The 6th case had unicystic ameloblastoma. The patient, who presented with dual tumour localization, had both a macrocystic ameloblastoma and a conventional follicular ameloblastoma infiltrating the mandibular bone.
Conclusion: Ameloblastoma expands from the odontogenic epithelium. The most frequently reported aspect is cystic (90% of cases for 75% of cases in our work). The architectural variants are in order of frequency - both in the literature and in our results -: follicular, plexiform, acanthomatous type and granular cell type. It is a benign tumour with local development which only very exceptionally degenerates. The treatment is exclusively surgical, justifying a large excision to avoid recurrences which require uncertain and mutilating salvage interventions.

PS-11-006
The importance of EGFR gene amplification in the malign salivary gland tumours
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Background & objectives: Epidermal growth factor (EGFR) is an important treatment target in several cancers. We aimed to investigate the contribution of this marker to the prognosis of salivary gland tumours by analysing the EGFR amplification status of the salivary gland tumour.
Methods: Forty-four cases of salivary gland carcinoma reported at Pamukkale University between 2001-2021 were included in the study. These tumours were re-evaluated according to the 2017 WHO classification. EGFR amplification was examined in these cases with the FISH method. Amplification rate ≥ 15% in tumour cells was considered positive.
Results: Of the 44 salivary gland carcinomas, 21 were adenoid cystic carcinomas, 20 were mucoepidermoid carcinomas, 2 were acinic cell carcinomas, and 1 was salivary gland ductus carcinoma. EGFR amplification was observed in a total of 6(13.6%); 3(6.8%) of them were mucoepidermoid carcinoma, 2(4.5%) were adenoid cystic carcinoma, 1(2.3%) was salivary. gland ductus carcinoma(p=0.072). EGFR amplification positivity was seen in 67%(4/6) of stage 1 cases, 83%(5/6) in cases <65 years old, and 67%(4/6) in women. The disease-free survival time was shorter in male patients(p=0.001), patients with neck dissection(p=0.007), patients with metastatic lymph nodes(p=0.011) and angiolymphatic invasion(p=0.013). Mortality rate was higher in patients with EGFR amplification(p=0.032).
Conclusion: EGFR mutations in salivary gland tumours are rare, however, EGFR amplification has been reported in the literature at a rate of 5-14%. We found the EGFR amplification as 13,6% in this study. EGFR amplification is common in early-stage and female patients under 65 years of age and the mortality rate is higher in these cases. Our findings should be supported by more studies.

PS-11-007
Synchronous adenolipoma and follicular variant papillary carcinoma of thyroid: a case report of a rare condition
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Background & objectives: Adenolipomas are rare benign neoplasms composed of mature adipose tissue and glandular elements. We report a case of a adenolipoma coexisting with follicular variant papillary thyroid carcinoma.
Methods: A 55-year-old woman presented with multinodular and enlarged thyroid in neck ultrasound. Computed tomography revealed a thyroid with heterogeneous parenchyma by nodules, the largest in the right lobe, with apparent fat content, measuring 2.0 cm. Fine needle aspiration (FNA) of one of the nodules was suspicious for papillary thyroid carcinoma (Bethesda category V). The patient underwent total thyroidectomy.

Results: Gross examination revealed a nodular and bumpy thyroid gland. Cut surface featuring a dull and whitish nodule with 1,2 x 1,0 x 0,9 cm, in right lobe. There were brown gelatinous colloid nodules exhibiting variegated size, the largest measuring 2,0 cm in greatest dimension, situated in the same lobe and showing soft and yellowish areas. Histologically, the features were consistent with follicular variant papillary carcinoma and adenolipoma in addition to multinodular hyperplasia.
Conclusion: Only few cases of lipoadenomas of the thyroid have been reported in the literature. Its origin is unknown; a number of authors explain it as an abnormality arising during thyroid encapsulating or from fibroblast metaplasia following hypoxia. The coexistence of adenolipoma and follicular variant papillary thyroid carcinoma as different lesions is a rare occurrence. However, it doesn't complicates the evolution and treatment. Surgical resection of thyroid adenolipoma is curative with no recurrence or malignant potential.

PS-11-008
Relationship of E-cadherin, Beta-catenin, N-cadherin, ZEB1 and αSMA as epithelial mesenchymal transition markers with prognostic factors in early and advanced stage laryngeal squamous cell carcinomas
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Background & objectives: To investigate the relationship between E-cadherin, Beta-catenin, N-cadherin, ZEB1 and αSMA as epithelial mesenchymal transformation markers with tumour stage, lymph node metastasis and overall survival in laryngeal squamous cell carcinomas.
Methods: A total of 100 cases diagnosed with laryngeal squamous cell carcinomas in our hospital between 2013-2020 were included in the study. Data about lymphovascular invasion, perineural invasion, necrosis and lymph node metastasis were recorded by evaluating hematoxylin-eosin stained slides. Markers of E-cadherin, beta-catenin, N-cadherin, ZEB1 and αSMA were applied to the sections prepared from paraffin blocks of tumour samples.
Results: Ninety-five male and five female patients were included in the study, and 38 of them exited. The average overall survival time of the cases was 35.8 months. A significant relationship was observed between overall survival with advanced tumour stage, presence of lymph node metastasis and perineural invasion. A significant relationship was found between increased tumour Zeb1 expression and advanced tumour stage. In univariate and multivariate analyses, a significant negative relationship with overall survival, and increased Zeb1 expression in tumour and tumour stroma was seen. Any relationship was not observed between E-cadherin, beta-catenin, N-cadherin and αSMA and overall survival.
Conclusion: Among the epithelial mesenchymal transformation markers we evaluated in our study, it was seen that Zeb1, which is an epithelial mesenchymal transformation transcription factor, is associated with tumour stage, lymph node metastasis, and overall survival. Remarkably, Zeb1 expression observed in tumour stroma was also significant for overall survival. Any similar data reported for laryngeal squamous cell carcinomas have not been encountered in the literature, and it was thought that it would be appropriate to support our findings with further studies to be performed on this subject.

PS-11-009
Primary laryngeal angiosarcoma with neuroendocrine marker expression, metastatic to lymph node: a case report
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Background & objectives: Primary laryngeal angiosarcoma (AS) is among the rarest laryngeal sarcomas. AS is an aggressive vascular tumour that usually metastasizes via the hematogenous route, while lymphatic spread is uncommon. A few recently reported AS cases showed an aberrant neuroendocrine marker expression.
Methods: A 37-year-old male patient complained of left side neck swelling. Computed Tomography revealed small soft tissue mass at the left pyriform fossa and ipsilateral cervical lymphadenopathy. The patient underwent biopsy of the mass and lymph node and diagnosed elsewhere as neuroendocrine carcinoma with lymph node metastasis. The patient admitted to the oncology-clinic and the paraffin blocks were requested for review.
Results: Microscopically, the pyriform fossa mass biopsy showed fragments lined focally by stratified squamous epithelium infiltrated by malignant neoplasm, formed of anastomosing vascular channels lined by high-grade multi-layered endothelial cells. The lymph node biopsy revealed a metastatic neoplasm, exhibiting a biphasic morphology. The predominant pattern was solid sheets of highly pleomorphic epithelioid cells, and the other pattern was similar to the mass biopsy. Immunohistochemically, the tumour cells of both biopsies were diffusely positive for CD31 and ERG, while negative for CD34. However, the epithelioid cells in the lymph node were positive for CK, Synaptophysin and CD56. The final diagnosis was laryngeal epithelioid angiosarcoma with neuroendocrine differentiation and ipsilateral cervical nodal metastasis.
Conclusion: To the best of our knowledge, this is the first reported case of angiosarcoma combining three rare conditions; the unusual laryngeal location, the initial presentation by nodal metastases and the aberrant NE marker expression. This unusual immunoexpression represents a challenging diagnostic pitfall that pathologists should be aware of to avoid misdiagnosing AS, especially the epithelioid variant, as poorly differentiated neuroendocrine carcinoma.

PS-11-010
Carcinoma ex pleomorphic adenoma. A clinicopathological study in a 10-year period
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Background & objectives: Carcinoma ex pleomorphic adenoma (CXPA) reported in the literature ranges from 1.5% to 14% of all salivary gland tumours. We study the frequency of CXPA recorded in the Department of Pathology of Metaxas Cancer Hospital in a 10-year period.
Methods: Over the last decade, 22 cases of malignant tumours were identified among 276 salivary gland specimens examined. The age range was between 34 to 78 years.
Results: Out of these 22 cases, 4 of them consisted of CXPA and the rest were distributed as mucoepidermoid (6), adenoid cystic (5), acinic cell (1), squamous cell carcinoma (2), adenocarcinoma NOS (3), and cystadenocarcinoma (1). Regarding the CXPA cases, two of them showed histopathological features of adenoid cystic carcinoma and the rest were myoepithelial carcinomas. In all cases residual element of pleomorphic adenoma (PA) was demonstrated at least in small part of the tumours.
Conclusion: PA is the most common salivary gland tumour, representing about 50% of all primary salivary gland neoplasms, followed by Warthin tumour. Although local recurrence is usual, a malignant transformation is rare. The incidence of malignant salivary gland tumours in our material is 8% with CXPA accounting for only 1.5%. The mean patient age was 67 years. Since various carcinoma subtypes can be encountered, misdiagnosis is common.

PS-11-011

The diagnostic value of the extemporaneous examination in thyroid surgery

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Background & objectives: The extemporaneous-examination (EE) allows to obtain a rapid diagnosis of benignity or malignancy of Thyroid nodules and to avoid abusive initial surgery. However, its efficiency and limits remain controversial. Our study aimed to evaluate the diagnostic value of the EE.
Methods: We conducted a retrospective study, carried out from January 2016 to June 2017, of EE performed on thyroid resection specimens at Habib Thameur hospital. We compared the results of the EE to final histological examination (FHE). The diagnostic value of EE was evaluated by calculating sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV).
Results: 319 EE have been included, 190 (59.5%) were benign, 41 (13%) were malignant and in 88 of the cases (27.5%) the response was delayed. Among the 190 nodules considered benign on EE, 168 were truly benign on EHD while 22 results were malignant. Among the 41 EE malignant lesions, 39 were carcinomas: papillary (91%), vesicular (6.5%), medullary (1%) and undifferentiated (1%). The specificity was 98.8% with a PPV of 95.12% and the sensitivity was 64% with a NPV of 88.4%. The delayed results were benign in 64%, malignant in 34% and lesions of uncertain malignancy in 2%. The diagnostic efficiency of EE was 65%.
Conclusion: Our study confirmed the perfect sensitivity of the EE with excellent VPN. However, its low specificity is mainly linked to the diagnostic difficulties of encapsulated tumours with vesicular architecture and to technical problems such as difficulty in handling fresh tissue.

PS-11-012

Single institutional morphological study of HNSCC focused on perinerual invasion

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Background & objectives: Head and neck squamous cell carcinoma (HNSCC) is a cancer with squamous differentiation arising from mucosal epithelium in the oral cavity, tongue and oropharynx. It is the 6th most common cancer in the world with mortality 4-6/100000 people.
Methods: We have retrospectively analysed cases of 487 patients in age 29-85 years with HNSCC who underwent curative surgery with bilateral cervical block dissection in period 2006-2016. We focused on the evaluation of stage (AJCC2017), nodal status, PNI, BVI and LVI. Moreover, we added new parameters such as the mode of invasion, the worst pattern of invasion, tumour budding a lymphocyte infiltration.
Results: Most of our cases exhibited 3rd degree of MOI (288cases) or 4th degree of WPOI (212cases). PNI was present with an increasing frequency in both of these classifications of tumour growth - MOI3: 17%, MOI4: 32,6%, MOI5: 50% and WPOI3: 12,9%, WPOI4: 26,9% WPOI5: 55,6%. Tumour budding (LG: less than 5 buds, IMG: 5-10 buds, HG: more than 10 buds) correlated with the incidence of PNI, 85% HNSCC with PNI developed HG budding. Brisk (49,5%) and non-brisk (42,9%) immune response presented by TIL correlated with these morphological signs. Moreover, we evaluated the morphology of PNI with following incidence: type A(1%), type B(58,6%), type C(31%), type D(6%), type E(6%), type F(0%).
Conclusion: Here, we focused mostly on PNI occurrence, morphology of PNI and other negative morphological prognostic factors in HNSCC patients. Our study revealed an association between PNI and other analysed common diagnostic factors as well as newly selected morphological features. Next, we plan to focus on cellular and molecular processes accompanying the initiation of PNI with aim to uncover main cancer characteristics and possible involvement of neural chemoattractant.

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PS-11-013

Cribriform adenocarcinoma of the minor salivary glands: an entity on the rise

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Background & objectives: Cribriform adenocarcinoma of the minor salivary glands, or cribriform variant of polymorphous adenocarcinoma according to the current WHO classification, is a rare tumour of the head and neck, with increasing evidence of histopathological and prognostic features distinct from conventional polymorphous adenocarcinoma.
Methods: We present the case of a 91-year-old male without relevant medical history. He was referred to our institution due to a painless tumefaction in the mouth floor, detected by the caretakers two days before. Physical examination revealed a well-defined, mobile and elastic tumour, measuring up to 4cm and covered by intact but erythematous and papillomatous mucosa, which was biopsied.
Results: On histopathological examination, a malignant epithelial neoplasm was found within the submucosa, lined by preserved epithelium. The tumour was comprised of solid or microcystic nests of neoplastic cells, displaying peripheral retraction artifact and a fibrous surrounding stroma. Nuclei were round, clarified and with vesicular chromatin, sometimes with nuclear crowding. Immunostaining showed heterogeneous positivity for CK5/6 and CK7 and diffuse and strong positivity for S100 and SOX10, in the absence of expression of SMA, D2-40, p40 and TTF-1. From these findings, the patient was diagnosed with cribriform variant of polymorphous adenocarcinoma. This is a rare and still mysterious entity and we reviewed the most recent findings in medical literature.
Conclusion: There is still much debate if the cribriform adenocarcinoma of the minor salivary glands is a separate entity from polymorphous adenocarcinoma, a variant or if they are both part of a same morphologic spectrum. Both harbour genetic changes in the PRKD1, PRKD2 and PRKD3 genes, although these are essentially translocations in the former and somatic point mutations in the latter. Most importantly, cribriform adenocarcinoma metastasizes more frequently to the cervical lymph nodes (50% at presentation), requiring lymph node dissection.

PS-11-014

HPV-related multiphenotypic sinonasal carcinoma: a case report and literature review

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Background & objectives: Human papillomavirus (HPV)-related multiphenotypic sinonasal carcinoma is a recently described tumour of the sinonasal tract which displays both characteristics of salivary gland and surface-derived carcinoma and is linked to high-risk HPV.
Methods: We report the case of an 86-year-old male with a destructive lesion involving the hard palate, maxillary sinus, nasal fossa and left frontal sinus. Histological, immunohistochemical and molecular testing were performed on the biopsy specimen. This case report includes a review of the most recent medical literature.

Results: Morphological evaluation revealed a basaloid neoplasm infiltrating the mucosa, with a nested and cribriform architecture. It was comprised of cells with round, hyperchromatic and vesicular nuclei and scarce eosinophilic cytoplasm. There were abundant mitoses and apoptotic bodies. Immunostaining was positive for p16, CK5/6, CK7, BerEP4, Bcl2 and SOX10 and negative for S100, GFAP, calponin, synaptophysin, calretinin and TTF1. Molecular testing detected the presence of high-risk HPV. Based on these findings, the patient was diagnosed with HPV-related multiphenotypic sinonasal carcinoma.
Conclusion: Previously known as HPV-related carcinoma with adenoid cystic carcinoma-like features, this entity is a potential diagnostic pitfall with high grade adenoid cystic carcinoma. Morphologic range is wider than initially thought and not all cases display basaloid features. Although p16 is a useful screening tool, definitive diagnosis requires HPV-specific testing. Correct diagnosis is crucial, since despite frequent presentation at high stages and exhibition of high-grade cytological features, its behaviour is remarkably indolent, with rare metastasization and no reported tumour-related deaths.

PS-11-015
Effect of blood corticosterone concentration on mast cell degranulation in the mesentery in rats after maxillofacial surgical trauma
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Background & objectives: The release of glucocorticoids by the adrenal cortex reduces the immune response, but degranulation of mast cells (MC) can increase, provoking the release of inflammatory mediators. Objective. To study the relationship between MC degranulation and blood corticosterone concentration after trauma to rats nasal septum (NS).
Methods: Wistar rats were simulated with septoplasty using zoletil 100 (5 rats). 5rats were a control group (CG). After surgery, the rats were determined the concentration of corticosterone on the 2nd, 4th, 6th days and then sacrificed, stained the mesentery on a slide with toluidine blue. mast cells with varying degrees of degranulation (0-3) were counted in 20 visual fields.
Results: On the 2nd, 4th, 6th days after surgery, the number of mast cells of type 0 significantly decreased (24.12±2.88; 13.22±1.87;14.88±2.84), compared with the control group (CG) (40.45 ± 2.21) ($p<0.001$). The number of MC type II on the 4th (2.87±0.31) and 6th (2.27±0.47) days decreased, but the number of MC type III increased (1.87±0.11 and 1.61 ±0.1, respectively), compared with the control (type II - 1.3±0.17; type III - 0.8±0.13). After septoplasty, compared with CG (38.56±2.12 ng/ml), corticosterone increased on day 2, and on day 4 (122.55±5.38 ng/ml) and 6 (118.35±5,69ng/ml) decreased and maintained its stable blood concentration ($p<0.001$).
Conclusion: An increase in the degree of mast cell degranulation coincides with an increase in the concentration of corticosterone in the blood plasma in rats 4-6 days after surgery. When simulating a surgical trauma in the maxillofacial region, the release of glucocorticoids can provoke the development of general inflammation, including in the mesentery, which is confirmed by an increase in the number of mast cells of grade III degranulation.

PS-11-016
Immunohistochemical criteria for pathological transformation of cells of nasal cavity mucous membrane in case of recurrent inverted papillomas
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Background & objectives: In 8-10% of cases inverted papillomas (IP) in situ, papillomavirus DNA(HPV) is detected. Aim. Identification of immunohistochemical criteria for pathological cells transformation of nasal cavity (NC) mucous membrane (MM) in case of recurrent IP using expression of the Ki-67 marker.
Methods: Materials and methods. Ki-67 & HPV-positive cells were determined in NC mucosa. 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: Dysplastic processes of MM surrounding the IP at an average distance of up to 0.5 cm and identified in all our observations were characterized by a general proliferative activity of epithelial cells of 17.25±4.11%, which was higher ($p<0.01$) than proliferation cells in unchanged epithelium, with hyperplasia of MM and with IP. Most immunopositive cells were localized in 2nd 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.

PS-11-017
Comparison of morphological changes during modeling of bone tissue damage and after implantation of a titanium implant in the upper jaw in rats.
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Background & objectives: Morphological changes against the background of inflammation during manipulations in dental surgery can lead to various complications-pain, implant rejection, etc. Aims. To compare morphological changes during modelling of bone tissue damage and during implantation of a titanium implant in the rats maxilla.
Methods: Under anaesthesia with zoletil 100 to 30rats, a bone socket was formed between the incisors and molars on one side. In 1group(15 rats),implantation was not performed, and in 2group(15rats), titanium implants were screwed in. Five animals from both groups were sacrificed on days 2,4,6 after surgery, the damaged parts were placed in a decalcifying solution, and then were stained with H&E.
Results: Around the dead tissues in both groups, there is a reactive inflammation limiting them. In the demarcation zone, full-blooded vessels, oedema, leukocyte shaft, multiplying cells of connective tissue, which is involved in the formation of the demarcation shaft, were found. The collagen fibres were swollen and impregnated with fibrin, forming dense homogeneous masses.
Conclusion: Damage to bone tissue, both with and without implantation, leads to the development of typical reactions of necrosis and inflammation. The simple application of damage to the upper jaw with a boron in rats can be considered as an analogue of the implantation model.

PS-11-018
Case report: potential drivers of metastatic progression in CPGL
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Background & objectives: A 38-year-old female was diagnosed with a left carotid paraganglioma (CPGL). The patient had undergone surgery for tumour resection. Histopathology of the resected specimen was consistent with paraganglioma of carotid origin with lymph node metastasis.
Methods: We performed exome sequencing of tumour, lymph node metastasis, and normal tissue from the patient. Exome libraries were prepared using the TruSeq DNA Exome Kit (Illumina, USA). Paired-end

sequencing of libraries (76x2) was performed on an Illumina NextSeq 500 System. The search for pathogenic/likely pathogenic variants was carried out using GATK HaplotypeCaller.
Results: Exome analysis revealed no pathogenic/likely pathogenic variants in known susceptibility genes for paragangliomas/pheochromocytomas (RET, FH, VHL, NF1, SDHx, SDHAF2, TMEM127, MAX, EGLN1, HIF2A, MET, and KIF1B). Somatic likely pathogenic frameshift mutations in the OR2T7, CTU2, LMTK3, HLA-DRB1, CBS, and FAM83H genes, as well as missense mutation in the EIF2AK3 gene, were found in both tumour and metastasis samples. Notably, in the metastasis sample, we detected variants in many genes that were not mutated in the primary tumour.
Conclusion: According to the literature, one of the main factors, indicating risk for metastatic paragangliomas/pheochromocytomas, is the SDHB mutation. However, in the study case, we have not identified variants in any known susceptibility genes. In primary tumour and metastasis, we detected common somatic likely pathogenic variants in six genes, when much more novel genes were mutated only in metastasis. Identified genes affected by metastasis-specific mutations and mutations shared between primary tumours and metastases can be potential drivers of metastatic progression.

This work was performed using the equipment of EIMB RAS "Genome" centre (http://www.eimb.ru/ru1/ckp/ccu_genome_c.php).
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PS-11-019
Somatic SDHx variants in patients with vagal paragangliomas
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Background & objectives: Vagal paragangliomas (VPGLs) are rare tumours of the head and neck that arise from paraganglionic tissue surrounding the vagus nerve. More than twenty susceptibility genes associated with the PGLs are currently known. However, oncogenic somatic events have been poorly investigated.
Methods: The exome sequencing and analysis of 16 tumour and normal tissues derived from the patients with VPGLs were performed. Exome libraries were prepared using the TruSeq DNA Exome Kit (Illumina, USA) and were sequenced on an Illumina NextSeq 500 System with the paired-end mode, 76x2 reads. Somatic pathogenic/likely pathogenic variants were identified using GATK HaplotypeCaller.
Results: We analysed 16 exomes from patients with VPGLs on the presence of somatic mutations in the *SDHx* genes. Three somatic likely pathogenic variants were revealed in the *SDHB* gene in a patient: frameshift variant NM_003000: c.308_309insTAAG, p.M103fs (chr1: 17355209), missense variant NM_003000: c.A307G, p.M103V (chr1: 17355211), and frameshift variant NM_003000: c.304_305insATGAT, p.A102fs (chr1: 17355213). Pathogenicity of the missense variant was predicted by all *in silico* prediction tools (PolyPhen2, LRT, SIFT, and others); the variant was also characterized by a high conservation score according to PhastCons.
Conclusion: Mutations in the *SDHx* genes, encoding for subunits of succinate dehydrogenase, are typically associated with the hereditary PGLs when somatic variants in these genes are very rare events. In the study cohort, we found one patient with somatic likely pathogenic variants in the *SDHB* gene. The patient did not carry any germline variants in the known susceptibility genes. Thus, these somatic variants appear to be a driver event in the development of the tumour.

This work was performed using the equipment of EIMB RAS "Genome"center (http://www.eimb.ru/ru1/ckp/ccu_genome_c.php).
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PS-11-020
Expression of CK 17 in squamous laryngeal carcinomas
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Background & objectives: Cytokeratins are proteins of the cytoskeleton with diverse expression in several epithelial neoplasms.
The purpose of the present study is the detection of CK17 expression in squamous laryngeal carcinomas and its correlation with several clinicopathological parameters.
Methods: CK17 expression was studied in 58 cases of squamous laryngeal carcinomas (24,1% Grade I, 50% Grade II, and 25,9% Grade III) For every patient included in the study there was a mean follow up time of 30 months during which 27 (46,6%) patients died from their disease. Statistical analysis was interpreted using SPSS16 for windows.
Results: CK17 expression was strongly correlated with tumour Grade (p=0,028) with loss of its expression in high-Grade tumours. In multivariate (Cox regression) analysis the correlation between absence of CK17 and adverse patients' outcome approached borderline (p=0,056).
There was no significant association between the presence of CK17 with either tumour size or positive cervical lymph nodes. The adjacent normal epithelium was CK17 negative while low expression of the protein was detected in dysplastic areas.
Conclusion: Our results agree with the existent literature which suggests that high expression of CK17 predicts poor patients' prognosis. Our findings indicate that CK17 is associated with early malignant transformation and might be a suitable marker for detecting the presence of dysplasia. Furthermore, the protein may be a prognostic factor in squamous carcinomas since its expression is lost during tumour progression and may have a key role in predicting worse patients' outcome.

PS-11-021
Dysgenetic polycystic disease of the parotid gland: a rare case report
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Background & objectives: Dysgenetic polycystic disease (DPD) is a benign rare cystic lesion arising from distal ductal system salivary glands, primarily affecting the parotid glands, mainly the superficial lobe. It is more prevalent seen in young females, usually with bilateral involvement.
Methods: We report a case of a 48-year-old woman with complains of a slowly progressive and non-painful bilateral parotid gland swelling, posteriorly to the angle of the mandible, since childhood. Recently she complained of a sudden increase in size and associated dull, aching and continuous pain.
Results: Control magnetic resonance imaging (MRI) scan revealed bilateral enlarged parotid glands, almost completely occupied by multiple cysts, some with septa and others confluent, of "pure content", the largest on the left side with 4.4 cm. Multiple fine needle aspiration (FNA) were performed always with the diagnosis of simple cyst (The Milan System - category II). She was submitted to partial parotidectomy and histopathological evaluation revealed multiple cysts of varying sizes some interconnected, replacing the parotid parenchyma with lobular architecture preserved. The cysts were lined by a flattened cuboidal epithelium with no atypia. Short, finger-like epithelial septations extended into lumen were found, as well as proteinaceous, eosinophilic and calcified material.
Conclusion: The diagnosis of DPD of parotid gland was made. Cystic lesions in the parotid gland may represent an array of diverse entities with

distinct biological behaviour and other cystic lesions must be considered in the differential diagnosis. DPD is a unique entity that resembling other polycystic diseases that affect the kidneys and pancreas, however there seems to be no association between them. Long-term follow-up is required to rule out recurrence and to screen for the involvement of other salivary glands.

PS-11-022

Human papilloma virus type 16 expression in pleomorphic adenomas and adjacent tissue of salivary glands

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Background & objectives: Pleomorphic adenoma (PA) is one of the salivary gland (SG) tumours. The role of human papilloma virus (HPV) in this tumour development is ambiguous. The objective is to determine the HPV type 16 expression in PA and SG adjacent tissue.
Methods: Two groups were formed. Group 1 (G 1) included 4 cases with an intact SG (autopsy material). Group 2 (G 2) included 30 cases (surgical material) with SG PA of mesenchymal (n=15), mixed (n=15) and epithelial (n=5) histological variants. Immunohistochemical reaction (IHCR) was performed, using mouse monoclonal antibody (MCA) to HPV type 16 (clone CAMVIR-1, «Diagnostic BioSystems», USA).
Results: IHCR was negative in G 1 and positive in G 2 in 26 cases (86.7%). In G 2 nuclear expression of MCA to HPV type 16 was found in tumour parenchyma (epithelial cells formed nests and cords, solid, trabecular, cystic, glandular, ductal, tubular structures; myoepithelial cells) and stroma (vascular endotheliocytes; immune and fibroblastic cells; myxoid and mucoid zones cells). In adjacent SG tissue, the ductal epithelial cells, myoepithelial cells expressed this MCA. IHCR in PA and SG adjacent tissue was the most pronounced, pronounced, moderately pronounced, respectively, in epithelial, mixed, mesenchymal tumour variants. In all PA variants, IHCR was less pronounced in SG adjacent tissue compared to PA tissue.
Conclusion: The positive expression (in 86.7% of cases) of MCA to HPV type 16 in pleomorphic adenomas tissue and adjacent tissue of salivary glands indicates that HPV type 16 may be one of the causes of such tumour development. The results obtained by the authors are of great therapeutic and prognostic significance.

PS-11-024

SALL4 expression in oral squamous cell carcinoma and its possible involvement in oral carcinogenesis

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Background & objectives: SALL4 plays important roles in cancer. This study analyses the expression of SALL4 in oral squamous cell carcinoma (OSCC), link it to characteristics of OSCC patients and assess the expression of a closely-linked protein, Beta-catenin, in the same population.
Methods: This study analysed the expression of SALL4, using immunohistochemistry, in a tissue microarray of 50 oral squamous cell carcinomas (OSCCs) and 10 normal oral mucosal tissue from the oral cavity. Clinic-pathological parameters of the patients were assessed in relations to SALL4 expression in those tissues. Moreover, an Epithelial-Mesenchymal Transition (EMT) phenomenon-linked protein, Beta-catenin's expression was analysed in the same microarray.
Results: A significant majority of oral squamous cell cancers exhibited positive expression of SALL4 protein. All of the OSCC tumours expressed SALL4 in their cytoplasm and nuclei. The overall majority of those same tumours exhibited an aberrant expression of Beta-catenin, where a shift of expression of Beta-catenin from their membranes to the cytoplasm and nuclei was noted. This study presents evidence of an aberrant co-expression of SALL4 and beta-catenin in OSCC cells. With the current findings and with past evidence of SALL4 modulating the Wingless/Wnt/Beta-catenin pathway in other tumours, it suggests a similar regulatory role for SALL4 in OSCCs.
Conclusion: SALL4 is a uniquely qualified candidate for therapeutic intervention in OSCCs, first because it is missing in normal adult cells, and secondly because of its triple involvement in OSCC development, EMT phenomenon in OSCCs and tumour's stemness. This may provide a rare opportunity to roll back the dismal course of this disease.

PS-11-025

The role of mu (μ) and kappa (k) opioid receptors in the carcinogenesis and prognosis of oral squamous cell carcinoma: an immunohistochemistry retrospective study

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Background & objectives: Squamous Cell Carcinoma (SCC) is the mouth's most prevalent tumour. Opioids may be involved in carcinogenesis while helping symptoms management in advanced cases. The objective is to analyse the influence of opioids receptors in the progression of oral cavity carcinomas.
Methods: Cross-sectional, observational and retrospective study which considered 25 samples of oral mucosa from healthy patients, 25 samples of squamous dysplasia and 50 samples of SCC. Tissue Microarray was performed for immunohistochemistry with anti-receptor μOpioid and kOpioid antibodies. Immunostaining was evaluated with ImageJ® software. Socio-demographic and survival data were analysed from medical records.
Results: There was an increase in immunoexpression of both μOpioid and kOpioid receptors in dysplasia and SCC. A lower expression of μOpioid was observed in T1 tumours when compared to the other T stages. Patients who died showed a more prominent immunodetection of kOpiod in the cytoplasm, suggesting that the survival rate of patients with low cytoplasmic expression for κOpioid is greater than in those with high expression. Clinical characteristics such as sex, age, smoking history, alcohol consumption and site of the primary tumour didn't influence the immunoexpression for opioid receptors.
Conclusion: This was the first study to characterize the immunoexpression of opioid receptors in the healthy mucosa compared to dysplasia and oral SCC samples. The study demonstrated an increase of the receptors in SCC and the influence of the Kappa receptor on patients' survival expectations. Therefore, it is necessary to study the mechanisms by which these receptors act in carcinogenesis and tumour progression.

PS-11-026

Sialolithiasis: biophysical studying of calculi

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Background & objectives: The aim is to study the biophysical features of stone formation in structurally altered tissues of the salivary glands.
Methods: In our investigation 20 tissue samples of SG with biomineral formations were used in the study by histological method, scanning electron microscopy, statistical analysis.
Results: Sialolites of the salivary glands had an elongated oval shape, ranging in size from 0.3 to 2.0 cm in the largest dimension. Biomineral formations often had a whitish-grey colour, although there were stones of yellowish-brown and brown shades. Some small stones were found in the parenchyma of the salivary gland. The average mineral content in sialolites averaged 64.33%. The study of the relief of the sialolites section surface showed a circular deposition of mineral matter on the periphery of the calculus and a complex pattern of mineralization layers in its core. The

following composition of sialolites was determined by electron microscopy: Ca-11.66%, P-6.39%, Na-0.47%, Mg-0.23%, S-0.14%.
Conclusion: Formation of SG stones occurs on the background of chronic inflammation and structural rearrangement of glandular tissue.
According to the results of factor analysis, the connection between the presence of benign or malignant tumours and the process of calcification (0.83) in structurally altered tissues of the salivary gland was defined. The stoichiometric ratio of calcium and phosphorus is 1.82.

PS-11-027
Malignant salivary gland tumours in South Tunisia: a clinicopathological study of 40 cases
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Background & objectives: Malignant salivary gland tumours (MSGTs) are very rare representing 3% of all cancers of the head and neck. They greatly vary in origin, subtype, and behaviour. The purpose of this study is to review the clinicopathological features of MSGTs.
Methods: Forty cases of MSGTs diagnosed in our department of pathology, were collected from January 2010 to December 2020. These tumours represented 20.9% of the total number of salivary gland tumours. An analysis of the clinical and histological data was carried out in all cases.
Results: The mean age of patients was 52.72 years (16 - 86 years). The parotid gland was the commonest location (21 cases, 52.5%). The submandibular and sublingual glands accounted for 3 cases (7.5%) each, and minor salivary glands for 8 cases (20%). On histological examination, adenoid cystic carcinoma was the most frequent type accounting for 9 cases (22.5%) followed by acinic cell carcinoma in 8 cases (20%), mucoepidermoid carcinoma in 7 cases (17.5%), carcinoma ex pleomorphic adenoma in 6 cases (15%) and polymorphous carcinoma in 5 cases (12.5%). Adenocarcinoma NOS, lymphoepithelial carcinoma and poorly differentiated carcinoma were found each in 2 cases (5%) and salivary duct carcinoma in 1 case (2.5%).
Conclusion: Malignant salivary gland tumours are one of the most difficult areas of diagnostic pathology, with significant morphological diversity and many overlapping features. The principal hurdle in the management of these tumours is the difficulty in distinguishing them from benign tumours. They demonstrate an unpredictable clinical course marked by frequent locoregional recurrence and distant metastasis.

PS-11-028
Clinicopathological features and mutation of BRAFV600E in papillary thyroid carcinoma
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Background & objectives: Identifying pathogenic variants in the BRAF gene is important in various ways. Therefore, we aimed to study the V600E mutation of the BRAF gene among patients with papillary carcinomas in the Mongolian population.
Methods: A total of 46 patients with PTC collected from 2017 to 2019 at the National Cancer Center of Mongolia. DNA extractions from Formalin-Fixed Paraffin-Embedded and fresh thyroid tumour tissue were extracted using a genomic DNA kit. ABI 3730xl genetic analyser was used to identify DNA sequencing.
Results: Out of the PTC cases, 38 (82.6%), 6(13%), 1(2.2%), and 1(2.2%) cases were classic, follicular, oncolytic, and tall-cell variants, respectively. BRAFV600E alteration was found in 9(19.6%) of 46 cases that were diagnosed as classic papillary variants, histopathologically. The mutation was not relative to the patients' age or gender (p>.005). In terms of clinicopathological features such as tumour stage, capsular and vascular invasion, histological type, lymph node metastasis, extra-thyroid invasion, and tumour location were not different between 2 groups (with or without BRAFV600E mutations)(p>.005).
Conclusion: BRAFV600E mutation was detected in 19.6% of PTC cases in our study. There was no correlation between BRAFV600E mutation and increased PTC aggressiveness in the study.

Funding: This study funded by a research grant from the Division of Science and Technology, Mongolian National University of Medical Sciences (MNUMS).

PS-11-029
Sinonasal intestinal-type adenocarcinoma showing contralateral intestinal metaplasia: a morphological and immunohistochemical study
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Background & objectives: Intestinal metaplasia (IM) can be present in the sinonasal mucosa adjacent to intestinal type adenocarcinoma (ITAC), possibly being a step in the development of these neoplasms. Herein we examined the mucosa contralateral to the tumour to identify areas of IM.
Methods: Nineteen patients (17 males, 2 females), age ranging between 44 and 89 years (mean 63.7), affected by unilateral ITAC treated with bilateral surgical approach were enrolled. The series included 3 well differentiated, 12 moderately differentiated, 1 poorly differentiated and 3 mucinous ITACs. Ethmoidal mucosa contralateral to the tumour site was morphologically and immunohistochemically analysed using cytokeratin 20 and CDX2.
Results: In 3 cases (15,7%) we observed foci of IM in the sinonasal mucosa of the opposite side of the tumour, with no evidence of dysplasia. Metaplastic areas involved both the surface and glandular epithelia.
Conclusion: A subset of sinonasal ITAC patients simultaneously shows foci of IM in the contralateral ethmoid mucosa, suggesting that IM could be associated with chronic environmental exposure and supporting the idea that the concept of "field cancerisation" could be applied to the development of ITAC in the sinonasal tract.

PS-11-030
Epidemiological and histopathological features of eyelid tumours: a 20-years retroprespective study at a tertiary university hospital in South-Western Greece
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Background & objectives: The aim of this study is to describe the epidemiology of primary eyelid tumours over a 20-year period, based on patient data derived from a Tertiary University Hospital in Greece.
Methods: A computerised retrieval system was used to identify all patients who underwent eyelid mass excisions with histological reports, encountered during the years 2000-2019. The demographical (age, gender), clinical and histological features along with the pathological diagnosis of each patient were documented. Descriptive statistical analyses were performed on the data. A total of 157 eyelid tumours comprised the study sample.
Results: Sixty-five (41.4%) malignant cases and 92 (58.6%) benign cases were identified. The most frequent benign diagnoses included cyst (25%), nevus (19.6%), squamous papilloma (11,96%) and seborrheic keratosis (8.7%). Malignant tumours included basal cell carcinomas (92.3%), squamous cell carcinomas (4.62%) and melanomas (3.08%). The main variants

of the basal cell carcinomas were: nodular (41.7%), nodular cystic (15%), ulcerative (15%), infiltrative (13.5%) and basosquamous (6.7%). Benign eyelid lesions occurred with equal frequency in the upper and lower eyelids (43.5%). Malignant lesions were more frequently located in the lower eyelid (61.5%) compared to other areas. The mean age at diagnosis was 70 (38-86) years for malignant and 50 (4-96) for benign lesions.
Conclusion: In this Greek cohort, benign eyelid lesions affected mostly working-age individuals, and malignant lesions occurred predominantly in elderly patients. Te majority (60%) of the patients with malignant tumours were females. Males and females were equally affected by benign lesions. Among the malignant lesions, basal cell carcinoma was the most common type, with lower eyelid involvement in the majority of cases. The clinical and histological features of the tumours varied among the different variants.

PS-11-031
Features of TIMP1 expression for different types of periodontitis
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Background & objectives: Periodontitis is an inflammatory disease, leading to progressive destruction of the tooth-supporting apparatus and to tooth loss. The dysregulation between an activity of matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMP) plays an important role in progression of inflammation.
Methods: Objective. To study features of TIMP1 expression in patients with different types of periodontitis.
A gingival biopsy was analysed from patients with aggressive (AgP, n=16), chronic simplex (CSP, n=3), chronic complex (CCP, n=23) periodontitis, and a control group (n=6). Morphometric and statistical analysis of the TIMP1 expression was performed using AperioImageScope v12.4.0.5043, Statistica10, $p<0.05$.
Results: The expression of TIMP1 in the biopsy was obtained in all patients with different forms of periodontitis, both in the gingival epithelium and stroma. There was a statistically significant increase of epithelial and stromal levels of TIMP1 in all groups of periodontitis compared to healthy tissue ($p<0.05$). At the same time, the lowest levels of both epithelial and stromal expression were found in the CSP group, increased in the AgP ($p<0.01$) and were highest in the CCP group ($p=0.001$). In the AgP group, compared with the CCP, there were lower levels of intensity and the proportion of strong and moderate intensity pixels ($p<0.03$) of epithelial and stromal expression of TIMP1.
Conclusion: A increase in epithelial and stromal expression of TIMP1 with a dysregulation of MMPs expression in different types of periodontitis compared to the healthy tissue supports its importance in the pathogenesis of periodontal inflammation. At the same time, an even greater decrease in TIMP1 expression in the group of aggressive periodontitis compared to chronic complex periodontitis may explain the high aggressiveness of its course and can be used in the differential diagnosis of these forms at the disease manifestation stage.

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PS-12 | History of Pathology Posters

PS-12-001
Pathological findings of the 1918-1919 “Spanish” influenza from the autopsy reports of the Santi Giovanni e Paolo Hospital in Venice
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Background & objectives: The ancient autopsies reports are kept at the Santi Giovanni e Paolo Hospital in Venice. An archive search was carried out to valuate the pathological findings of the Spanish flu from autopsy descriptions.
Methods: The cases reporting diagnosis named as “flu bronchopneumonia” have also been selected since 1918. In Venice, between 1918 and 1919, 1669 autopsies were performed, respectively 807 in 1918 and 862 in 1919. The autopsies were performed only on deceased in the hospital, not on people deceased in their own home.
Results: The first case of Spanish flu in Venice dates back to 26th September 1918. The autopsy was performed on a 46-year-old male who died at Santi Giovanni e Paolo Hospital. The last was reported on 19th January 1920, remarkably associated with Encephalitis lethargica. The cases reporting flu bronchopneumonia are 169. The reports describe a haemorrhagic bronchopneumonia, splenic reactive hyperplasia and blood congestion of kidneys and liver. These pathological findings were similar to those already described in a similar archive research performed at the Pathology Department of the University of Turin.
Conclusion: The autopsy reports of Santi Giovanni e Paolo Hospital of Venice confirm the temporal distribution of deaths following the pandemic trend of Spanish flu. The pathological findings are comparable to those described in literature, confirming the relevance of old autopsy reports as historical documentation for the history of pathology.

PS-12-002
A unique museological display of antique urologic stones
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Background & objectives: 'Urologic Lithiasis' affects mankind since Antiquity. Currently, despite multiple therapeutic measures, incidence is rising with high recurrence rate, even in transplanted kidneys. Authors aim to draw attention to study the resources kept in the "Museum of Anatomical Pathology" in Coimbra.
Methods: Retrospective study of specimens kept in the Coimbra Museum was performed, searching for the different characteristics of urological calculi. Photographs were taken and comparison with literature was applied.
Results: Ninety (n=90) sets of calculi corresponding to single stones or aggregates of calculi gathered in containers or hangers, varied in their form, colour and consistency. Topography was registered: renal (n=14), bladder (n=64), urether (n=3); as well as composition: calcium (n=2), cistine (n=2), uric acid (n=3), struvite (n=2).
Conclusion: Etiopathogenic factors underlying urolithiasis are multiple, ranging from infection, dehydration, diet to metabolic syndrome and genetic background. Increased longevity and alimentary habits change, among other risk factors, favour higher incidence, both in adults/elderly and children. During lithiasic patients’ clinical workup evaluation, consensus studies have shown the importance of crystalluria and calculi morphoconstitutional analysis. This XIXth century Museum collection is available for Medical Students and Residents to review urologic calculi and correlate with patients symptoms. Other areas of Science are welcome.

PS-12-004
Clinical and morphological analysis as a tool for finding diagnostic errors: traditions laid down by N.I. Pirogov in the "Annals of the surgical department of the clinic of the Imperial Dorpat University"
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Background & objectives: The world-famous scientist Nikolai Ivanovich Pirogov made an important contribution to the development of pathological anatomy. In 1837 N.I. Pirogov published a work: "Annals of the surgical department of the clinic of the Imperial University in Dorpat".
Methods: In "Annals" N.I. Pirogov, included a collection of case histories, arranged in sections depending on the type of diseases, summarizing articles. There were also forty-eight topics related to the pathological anatomy of surgical pathology. The Annals revealed the features of the operative technique, they became the basis for clinical and morphological analysis, which is currently a tool of pathological anatomy.
Results: N.I. Pirogov wrote: "It is my sacred duty to tell the readers frankly about my medical activity and the results of it, since every conscientious person, especially a teacher, should have a kind of inner need, perhaps, rather to publicize his mistakes in order to warn other people against them." Pirogov considered self-criticism to be a method that could improve the results of clinical practice.
According to Pirogov's Annals, doctors should analyse their professional mistakes, enriching their experience and the cumulative experience of medicine.
Pirogov compared the data of clinical examinations with the data of autopsies, in fact, it was about clinical anatomical conferences.
Conclusion: Pirogov's attitude to medical errors prompts us to deepen the meaning of this maxim in moral and ethical terms. Anyone who stops at the pessimistic and apathetic statement "medical errors are inevitable" is in the position of ethical surrender, which is immoral and unworthy of the title of a doctor.

PS-12-005
Prognosis and prediction in medicine and pathology in a historical context
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Background & objectives: Prediction and prognosis (forecast) are two overlapping and coexisting terms in modern medicine. Notions about the prognosis of a disease primarily imply the nature of its natural course, and the term «predicate» reflects rather the probability of response to treatment.
Methods: The scientific works devoted to prognostics and predication (prediction) are analysed, starting with Hippocratic's «Prognostic» and ending with modern works dedicated to 4p and 5 p-medicine. Scientific articles, philosophical definitions, data of dictionaries were analysed according to basic definitions about prognosis as the nature of the current and the outcome of the disease and prediction as possibility of «predict» pathologies.
Results: The evolution of the predictive approach in medicine from ancient times to modern research is considered. It has been established that the prognosis existed from the very beginning in two directions: as a prediction of the outcome of a disease and as an assessment of the risk of a disease, the ability to anticipate and prevent its development. The modern prognostic approach is based on individualized conception of the person and his individual reaction to the treatment, which is especially relevant in the development target treatment of tumour diseases. It is in this context that prediction seems to be considered in modern times.
Conclusion: Prognosis in medicine is a specific historical concept that evolves together with the development of the principles and values of medical discourse: from a general understanding of human, disease and organism to maximum individualization. The relevance of the term prediction, related to the breakthrough in individualizing the treatment of tumour pathologies, characterizes one of the stages of development of prognostics approach.

PS-12-006
The pathways that defined the construction of pathology's history in Ceara, state in the Northeast of Brazil
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Background & objectives: The History of Pathology has guiding principles shared with all other medical specialties. In Ceara, the pathways that defined it were marked by challenges and important achievements. This study seeks to review the History of Pathology in Ceara.
Methods: The present study consists of a literature review. The search for articles was conducted in the PubMed, Scielo and Lilacs databases. Literary works on the subject were also considered. The descriptors History, Pathology, Medicine and Ceará were applied, utilizing the boolean operator and. The period from 2010 to 2021 was set as the search limit.
Results: In Ceara, the evolution of medical care has been marked, for a long time, by the lack of means to prevent diseases. At first, the introduction of studies focused on Pathological Anatomy faced challenges, which included rudimentary equipment and inadequate facilities. In 1949, the first Pathological Anatomy laboratory was set up, beginning the task of providing anatomopathological diagnoses. The first systematic research in Pathological Anatomy was on visceral leishmaniasis, during an endemic period. The introduction of routine necropsy services allowed a rapid change in the quality of the services provided. In early 2021, the first autopsy using the Minimally Invasive Autopsy (MIA) technique was performed in the state.
Conclusion: It is indisputable that anatomopathological reports, obeying pathogenetic and chronological aspects, are instruments for a better understanding of the diseases. It is necessary to promote the training of pathologists with professional qualifications who, inspired by the pioneers of the past, can contribute to the development of Pathology in Ceara.

PS-12-007
Questionnaire portrait of the Russian pathologist, scientist and educator, academician of the Academy of Medical Sciences of the USSR, Professor Vladimir Georgievich Garshin (19.12.1887–20.04.1956)
A. Zubritsky*
*Russia

Background & objectives: Born in Novgorod in the family of a forensic investigator. He graduated from the Medical Faculty of the Kiev Imperial University of St.Vladimir (1913) and was awarded the degree of "doctor with honours".
Methods: As a student, he showed interest in pathological anatomy and was left at department "to prepare for title of professor" in this subject. He was sent to Berlin to improve his knowledge, but in view of outbreak of First World War, he was arrested and placed in concentration camp, a month later, according to decision of Berne Convention, was released.
Results: In 1935, based on the totality of his works, he was awarded the academic degree of Doctor of Medical Sciences. Assistant of the Pathology Department (PD) at the Kiev Women's Medical Courses (1913); Assistant Commissioner of the Red Cross General Directorate, was wounded in fighting on the San River (1914). Head of the Growth Laboratory of the PD of the Institute of Experimental Medicine, etc. (1933–52); forced to leave work due to the progression of stroke (1952);
Conclusion: creator of fundamental research on aseptic inflammatory growths and epithelial metaplasia; he made a great contribution to the study of the pathology of starvation and the wound process, as well as hyperplastic changes, their biological potential in refraction to malignancy; man of high erudition, culture, and intelligence; he loved, knew poetry and was a close friend of the poetess Anna Akhmatova. He died at the age of 69 from cancer. He was buried at the Seraphim Memorial cemetery in St. Petersburg.

PS-12-008

Academician of the Academy of Medical Sciences of the USSR, honoured scientist of the RSFSR, Professor Mikhail Alexandrovich Skvortsov – the founder of the pathological anatomy of childhood diseases (02.10.1876–08.03.1963)

A. Zubritsky*
*Russia

Background & objectives: Born in Moscow. He graduated from the gymnasium (1894) and the Medical Faculty of Moscow University (1899). Zemsky, district and factory doctor in Kaluga province (1899–1902); Assistant of the Pathology Department (PD) at Moscow University (1902–11);
Methods: Prosector at the Morozov Children's Hospital (1911–53) and at the same time a Professor of the PD of the 1st and 2nd Moscow Medical Institute; Head of the Laboratory of Paediatric Pathological Anatomy at the Institute of Normal and Pathological Morphology (1945) and at the Institute of Pediatrics (1953).
Results: Awarded the 1st Prize of the International Anti-Rheumatic Committee for his works on rheumatism (1938); he created a unique and rich museum of macro-and micropreparations and a large school of children's pathologists; for the first time he developed the pathological anatomy of the superficial forms of pulmonary actinomycosis; he gave a new interpretation of allergic vascular pathology in early childhood, the significance of the inflammatory nonspecific reaction of the myocardium in rheumatism is shown, the pathological anatomy of umbilical sepsis has been developed in detail, one of the first to prove the viral (infectious) nature of liver cirrhosis in children, etc.
Conclusion: Author of 124 scientific papers on childhood pathology, including a textbook, manuals and monographs. Distinctive feature: crystal honesty, simplicity, modesty, high culture, great erudition, benevolence. Hobbies: literature, art, history, playing the piano, especially loved Grieg. He died in Moscow at the age of 87 after a serious and prolonged illness. He was buried at the Novodevichy cemetery.

PS-12-009

Shalva Iosifovich Krinitsky – well-known Russian pathologist, scientist, and educator (18.10.1884–02.02.1961)

A. Zubritsky*
*Russia

Background & objectives: He was born in Kutaisi in the family of a Georgian prince. Studying at the Kutaisi classical gymnasium (1894–1904) and at the Medical Faculty of the Imperial Novorossiysk University with the diploma of "Doctor with honours" (1904–10);
Methods: as a student, he studied pathological anatomy with interest; defense of the doctoral dissertation on the topic "Anatomical and histological changes in the organs of people who died from poisoning by asphyxiant gases" (1917). Prosector of the Pathology Department (PD) at the Imperial University of Warsaw (1910–13);
Results: Head of the PD, Central Anatomical and Bacteriological Laboratory of the Red Cross of the South-Western Front, where for the first time he performed autopsies of soldiers who died from the enemy's use of asphyxiant gases (1914–17); Head (1921–61), PD, Don University, then Rostov Medical Institute, etc. Organizer of the first Medical Society on the Don and the Pathoanatomical Museum; creator of the Rostov School of Pathologists. Author of 80 scientific works, including 4 textbooks for students and doctors, a three-volume "Guide to General Pathological Anatomy", 7 monographs.
Conclusion: Distinctive feature: Strict and demanding teacher, high integrity, brilliant lecturer, etc. Winged expression: A bad pathologist will do more harm than good. Hobbies: Loved to play chess, cards with friends exclusively for interest, in volleyball; he was fond of hunting and fishing, knew German, English, Polish. He died at the age of 76 from cardiac tamponade due to transmural myocardial infarction. He was buried at the Bratsk cemetery in Rostov-on-Don.

PS-12-010

Academician of the Academy of Sciences of the Ukrainian Soviet Socialist Republic, Professor Nickolai Fedotovich Melnikov-Razvedenkov – outstanding Russian pathologist, scientist, organizer and educator (24.12.1866–20.12.1937)

A. Zubritsky*
*Russia

Background & objectives: Born in Ust-Medveditskaya stanitsa (Serafimovich city, Volgograd region) in the family of a Don nobleman, a veteran of the Sevastopol defense. He graduated from the gymnasium with a gold medal (1884), the Medical Faculty of Moscow University (1889) and
Methods: was left at the Pathology Department (PD), as a promising person, where he was engaged in scientific, teaching and socio-political work; defense of the doctoral dissertation on the topic "On artificial immunity to anthrax" (1895); scientific trip to Germany (1898–1900); Private-Associate Professor (1897–1902), PD, Moscow University; Head, PD, Kharkiv Medical Institute (MI) (1902–20);
Results: Rector of the Kuban MI; Head of the PD and Forensic Medicine, Kuban MI (1920–25); director of the Ukrainian Pathology Institute, founded by him (1925–30), etc. Organizer of the pathoanatomical circle (1892), which later developed into the Moscow Society of Pathologists; creator of the Pantheon of the brain of outstanding people; he proposed a method of making and preserving of anatomical specimens while preserving the natural coloration of organs (1895); he developed a unique method of embalming, which was then used by scientists after the death of Vladimir Lenin and other state officials, including abroad;
Conclusion: He was awarded the Gold Medal and the Anatomical Prize by P.A.Zagorsky (1897, 1901). Research interests: Tumours, allergic processes, peculiarities of vascular-granulomatous nature, infectious pathology, history of pathological anatomy. Author of over 200 publications. Motto: "Movement is life". Distinctive feature: Outstanding mobility, a person of high duty, persistent and inquisitive, extraordinary mind, high professionalism. He died at the age of 70 from cancer after a complex operation on the bile tract. He was buried in the 13th cemetery of Kharkiv.

PS-12-011

Questionnaire portrait of the Russian pathologist, scientist and educator Honored Scientist of the RSFSR, Professor Vladimir Timofeevich Talalaev (29.05.1886–01.09.1947)

A. Zubritsky*
*Russia

Background & objectives: Born in the Nizhnekundryuchenskaya village,1st Don District of the Don Army Region, in the family of a Cossack officer of the border troops who retired with the rank of general.
Methods: He graduated from the Medical Faculty of the Odessa (Novorossiysk) University with the title of "doctor with honours" (1912); as a student, he performed a very valuable scientific work on the pathological anatomy of gout, for which received a prize. Assistant professor (1926–30), Pathology Department (PD), Moscow University (MU); Head, PD, Moscow City Old Catherine Hospital (1912–47);
Results: Head (1930–41), PD, Central Institute for Advanced Medical Training (1932–47) and Head, PD, Moscow Medical Institute. He described the histogenesis of rheumatic granuloma (the so-called Aschoff-Talalaev granuloma), a clinical and anatomical classification of rheumatism was created, he performed a re-autopsy of the body of V.V.Mayakovsky in the morgue of the MU due to the fact that rumors spread about the poet's alleged venereal disease, on the basis of which it was concluded that there were no signs of venereal diseases (1930); organizer of the PD of the Central Institute for Advanced Medical Training; chief pathologist of evacuation hospitals, Moscow (1943);

Conclusion: awarded the 1st prize of the International Anti-Rheumatic League for the monograph "Acute rheumatism" (1936). Author of over 70 scientific works. His favorite phrase: "We all know this very well". Distinctive feature: Simplicity, availability etc. He died suddenly at the age of 62. Buried at the Novodevichy cemetery. Talalaev's name was assigned to the pathological building of the Moscow Regional Research Clinical Institute, and his bronze bust was installed at the entrance to it.

PS-13 | Infectious Diseases Pathology Posters

PS-13-001

Fortuitous discovery of ganglionar tuberculosis in systematic lymph node dissection for thyroid carcinoma: about 05 cases

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Background & objectives: Cervical lymphadenopathy in case of neoplasia primarily suggest metastatic extension. However, the diagnosis of tuberculosis should be sought in our population. We aim to study cases of subclinical lymph node tuberculosis discovered during lymph node dissection in surgical management of thyroid carcinoma.
Methods: This is a descriptive retrospective study of all the cases of cervical lymph node dissection performed as a part of surgical management of Thyroid carcinoma(TC). We included lymph node dissections of patients with TC and no suggestive symptoms of tuberculosis. This study, carried out at Habib-Thameur's hospital, collected all the cases of TC operated on with neck dissection between 2016 and 2020.
Results: We collected 133 samples of lymph node dissections performed on 133patients. In five cases (3%), we have noted the presence of epithelioid and gigantocellular granulomas suggesting the diagnosis of ganglionar tuberculosis. They were 5 women aged between 40 and 65 years with a mean age of 51.8+/-8.98 years. The histological type of TC was papillary carcinoma in all of the five cases. The total number of lymph nodes removed ranged from 5 to 87 with a mean number of 38.4+/-30.02.
Metastatic lymph node involvement was diagnosed in two patients among this 5 patients.
Conclusion: Ganglionar tuberculosis (GTBC) is the first extrapulmonary localisation of tuberculosis in Tunisia. Its incidence is constantly increasing in our country. Our study prouved that GTBC was incidentally diagnosed in 3% of lymph node dissection performed for TC. Therefore, we have to keep this diagnois in mind and systematically seek the presence of GTBC in all the lymph node dissection performed.

PS-13-002

Acute myocarditis associated with SARS-CoV-2 infection in a child: a post-mortem case study

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Background & objectives: SARS-CoV-2 infection in children is usually asymptomatic or milder than in adults. However, severe forms of the disease can occur. To report a case of acute myocarditis in a child with SARS-CoV-2 infection.
Methods: Report a case of Acute myocarditis associated with SARS-CoV-2 infection in a child.
Results: A seven-year-old female child started asthenia, adynamia and weight loss with about a month of evolution. Two days before death, persistent dry cough, difficulty breathing, odynophagia and refusal to eat followed by low fever, two episodes of vomiting and anasarca. She had cardiopulmonary arrest and died. The autopsy revealed skin paleness, mild anasarca and evident pediculosis. Macroscopy: slight diffuse cerebral atrophy and thrombi in the sigmoid sinuses; cardiac chambers with dilated cardiomyopathy and intracavitary thrombi, swollen lungs with small thrombi, shock kidneys. Microscopy: myofibrillar myocardial atrophy and myocarditis with liquefactive necrosis of microabscesses. The lungs had interstitial pneumonitis, diffuse alveolar damage. Kidneys with tubular injury, spinal congestion. Nasopharynx (RT-PCR) screening for SARS-CoV-2 was positive.
Conclusion: SARS-CoV-2 infection in children can cause acute myocarditis with variable degree of cardiac dysfunction. Pre-existing heart diseases, such as congestive heart failure, contribute to an unfavourable outcome.

PS-13-003

SARS-CoV-2 and placenta: new insights and perspectives

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Background & objectives: This case-control study aimed to report the analysis of a large series of placentas from SARS-CoV-2 positive mothers observed and to compare them with a control group in order to highlight any histopathological alterations attributable to SARS-CoV-2.
Methods: Study was made of 83 placentas from 81 pregnant mothers followed at the Gynaecology and Obstetrics Operative Unit from 15 September 2020 to 31 January 2021, identified through electronic clinical records. The SARS-CoV-2 group was compared with a Control group of 142 placentas, selected from a population of pregnancy with physiological outcome, matched by gestational age and maternal age.
Results: Prevalence of maternal vascular malperfusion were not significantly different between cases and controls (54.3% vs 43.7% p=0.19), whereas the differences in regard to foetal vascular malperfusion (21.1% vs 4.2% p<0.001) resulted significant. More frequent in cases respect controls were decidual arteriopathy (40.9% vs 1.4% p<0.0001), decidual inflammation (32.4% vs 0.7% p<0.0001), perivillous fibrin deposition (36.6% vs 3.5% p<0.0001) and foetal vessel thrombi (22.5% vs 0.7% p<0.0001). The Anti-SARS-CoV-2 spike-S1 glycoprotein antibody results were significantly different, with 33/51 cases (65%) of diffuse positivity throughout the examined section and 18/51 cases (35%) of localized positivity, the expression being prevalently in the cytoplasm of the villi trophoblasts.
Conclusion: Our study demonstrates some more frequent aspects in the placentas of infected women, in particular maternal thrombosis and deciduous, increased intervillous fibrin and, in rare cases, foetal thrombosis. The immunohistochemical investigation demonstrates the positivity for the Anti-SARS-CoV-2 spike glycoprotein antibody both among maternal cells (including inflammatory intervillary cells) and in the trophoblast and rarely in the endothelium. The ultrastructural investigation demonstrated both the suffering of foetal endothelia and the presence of particles attributable to SARS-CoV-2 in the trophoblast.

PS-13-004

Entamoeba hystolitica and COVID-19: a potentially fatal synergy

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Background & objectives: Entamoeba Hystolitica is a protozoon, predominantly found near the equator, which infects the gastrointestinal tract of approximately 10% of the world's population. Most patients are asymptomatic, but a few suffer from fulminant colitis. At this stage, mortality is high.
Methods: SARS-CoV-2 is a thrombogenic virus and has been shown to lead to large bowel ischemia in certain patients. 75 year-old man, formerly emigrated to Venezuela, presenting at our emergency department with severe dyspnea. He had a history of hematochezia and no other relevant

priors. The patient was diagnosed with severe COVID-19, admitted to intensive care and treated with dexamethasone.
Results: During his hospitalization he developed signs of large bowel perforation and underwent total colectomy, dying in the post-op.
Grossly, large, serpiginous ulcers could be seen throughout the entire bowel, amidst sections of preserved mucosa. Histologically, the mucosa was extensively ulcerated. Some of these ulcers were "flask-shaped" and others associated with areas of transmural necrosis and perforation. In these areas and at the bottom of the ulcers, countless histiocytoid organisms could be seen. These stained with PAS and Masson's Trichrome and were negative for CD68 by immunohistochemistry. Hemophagocytosis was observed. The remaining mucosa was mostly preserved, but focal ischemic changes were seen, as well as transmural congestion and numerous fibrin thrombi.
Conclusion: A diagnosis of fulminant amebic colitis (FAC) was made, associated with ischemic changes probably secondary to SARS-CoV-2. We describe the first case, to our knowledge, of FAC in a SARS-CoV-2 patient showing large bowel changes consistent with involvement by COVID-19. These changes and steroid therapy, a well know trigger of FAC, might have had a synergic effect in this patient, enabling the development of fatal fulminant amebic colitis. Clinicians should be aware of this possible complication.

PS-13-005
Peritoneal tuberculosis: a restrospective study of 43 cases
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Background & objectives: Peritoneal tuberculosis is one of the most challenging forms of extrapulmonary tuberculosis to diagnose. Its poses a public health problem in endemic regions of the world. The aim is to analyse the epidemiological and histopathological characteristics of this entity.
Methods: A retrospective study was conducted in our pathology department at CHU Habib Bourguiba of Sfax over 11 years period, between 2010 and 2020. During this time, 43 cases of Peritoneal tuberculosis were reviewed.
Results: Peritoneal tuberculosis accounts for 5,23% of all cases of tuberculosis in our department. Mean age was 45,85 years old (extreme: 10-79 years); with female predilection (F:34 /H:9). In microscopic examination, granulomatous reaction was composed of epithelioid cells and multinucleated giant cells with variable number of lymphocytes. These granulomatous lesions were centred by caseous necrosis in 34 cases overs 43 (79%), the rest were non caseating (21%).
Conclusion: Peritoneal tuberculosis is rare, more common in young women. Microscopic finding are variable and sometimes slight and uncertain, especially with non-caseating granulomatous reaction. The histological examination must be completed with bacteriological studies, mainly when the clinic presentation suggest the diagnosis.

PS-13-006
Histological features of SARS-CoV-2 infection in placenta
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Background & objectives: The placental pathology in pregnant women with SARS-CoV-2 infection seemed quite nonspecific, describing signs of maternal and foetal vascular malperfusion, intervillus fibrin deposits, or inflammation. Recently, trophoblast necrosis has been associated with SARS-CoV-2 placental infection.
Methods: The sampling of 71 placentas from pregnant women with active SARS-CoV-2 disease was done according to the Amsterdam consensus. Immunohistochemistry (IHC) for SARS-CoV-2 was performed in all of them. In SARS-CoV-2 IHQ positive cases, in situ hybridization (ISH) and real-time prolimerase chain reaction (RT-PCR) of the placental tissue were also tested.
Results: 90% of placentas were negative for SARS-CoV-2 IHC, while 10% were positive, as well as for ISH and RT-PCR. Regarding the infected placentas, 6/7 showed a stiff appearance with white deposits between 20 and 90% of the disc and 1/7 had only a chorangioma. Trophoblast necrosis, increased intervillous fibrin deposition, collapse of the intervillous space and variable histiocytic intervillitis were observed. IHC and ISH showed granular trophoblast staining. In 5/7, this lesion affected 80-90% of the disc and was associated to stillbirth. In 2/7, one showed a focal lesion and the other a 20% involvement of the disc, and babies were born premature without SARS-CoV-2 infection.
Conclusion: Trophoblast necrosis with collapse of the intervillous space, increased fibrin deposition, and variable histiocytic intervillitis is characteristic of SARS-CoV-2 placental infection. According to these results, only diffuse damage to the placental disc is associated with stillbirth. The histological study of the placentas of pregnant women with active disease for SARS-CoV-2 in delivery is essential to know the mechanism of placental transmission and the probable foetal infection.

PS-13-007
Concomitant diseases pathology in fatal COVID-19 cases
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Background & objectives: The pathogenesis of a severe course of the acute respiratory syndrome due to viral COVID-19 infection is not yet fully understood. Therefore, the aim of the study was to analyse the role of concomitant diseases in lethal cases of COVID-19.
Methods: Postmortem investigations of the 47 dead bodies performed in cases of the COVID-19' fatal outcome. Medical records and clinical data were studied. The length of hospital stay before death was analysed. Gross pathology of the lungs, internal organ and brain were examined and tissue samples were taken for histological examination. Microscopy of H&E stained slides performed at x10, x20, x40.
Results: Most of the deaths in the study group were men (57,44%). Hospitalization for less than a day and within 1-3 days accounted for 23,4% of cases each. 21,3% of patients stayed in hospital for 4-10 days before death. The autopsies have shown characteristic COVID-19-induced pathological changes in the lungs. Pre-existing chronic disease included: ischemic heart disease pathology (89,3%), chronic pancreatitis (61,7%), arterial hypertension (31.9%), diabetes mellitus (21,27%), cerebrovascular diseases were (17,0%) chronic nephritis (14,9%) and others. The main histological findings were: alveolar injuries due to microcirculation disorders accompanied with microthrobi formation, systemic inflammatory infiltrates, dystophies and necrosis of the parenchymal organs cells, mainly cardiomyocytes.
Conclusion: Autopsy studies of patients with fatal COVID-19 due to severe acute respiratory syndrome revealed concomitant multiple features of cardiac pathology: ischemic and metabolic injury, myocardial inflammatory cellular infiltrates, myocyte destruction and microvascular thrombi in myocardial tissues, stromal oedema, capillaries hyperaemia. Chronic pancreatitis, hypertension, and diabetes mellitus occurred with decreasing frequency. Clinicopathological correlation revealed COVID-19 is considered to be primary cause of death, however, further research would clarify the role of comorbidities in the pathogenesis of deaths from this infection.

PS-13-009
Ultramicroscopic features of erythrocytes in splenectomised people affected by attacks of Ixodes ticks infected with Babesia spp
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Background & objectives: Babesiosis is a Ixodes ticks (IT) transmitted disease caused by Babesia spp. (Bs). It is characterized by severe course, frequent death in splenectomised people (SEP). The objective is to determine erythrocytes ultramicroscopic features in SEP affected by Bs infected IT.
Methods: The study material was blood from 19 SEP. Splenectomy was performed due to spleen trauma, its rupture and bleeding. Group 1 (G 1) included 8 people without IT attacks. Group 2 (G 2) included 11 people affected by Bs infected IT attacks. Slides were stained by Romanovsky-Giemsa method. Scanning electron microscopy was also performed.
Results: In G 1 and G 2 in blood there were found normocytes, regenerative forms and degenerative forms among erythrocytes. In G 1, the relative numbers (RN) of normocytes, regenerative forms and degenerative forms were (69.6±2.13) %, (1.5±0.07) %, (28.9±1.16) %, respectively. In G 2, the RN of normocytes, regenerative forms, degenerative forms were (64.5 ±2.18) %, (1.3±0.09) %, (34.2±1.96) %, respectively. Comparative analysis of the obtained data in G 1 and G 2 did not reveal significant differences between the indicators. In both groups, intra-erythrocytic and extra-erythrocytic forms of Bs were not detected, and erythrocytes were characterized by anisocytosis (microcytes and macrocytes were determined) and poikilocytosis (echinocytes, degmacytes, schistocytes were determined).
Conclusion: Erythrocytes of splenectomised people exposed to Babesia spp. infected Ixodes ticks do not differ from erythrocytes of splenectomised people without Ixodes ticks attacks. They are characterized by the presence of normocytes, regenerative and degenerative forms with predominating normocytes and degenerative forms; changes in size (anisocytosis) and shape (poikilocytosis); absence of intra-erythrocytic and extra-erythrocytic forms of Babesia spp. despite the detection of pathogens in the Ixodes ticks.

PS-13-010
Rhinosporidiosis in north-eastern Brazil: a series of five cases
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Background & objectives: Rhinosporidiosis affects humans through stagnant water, affects usualy the nose. It is curable through surgery and prophylaxis, but is aggravated if left untreated. Similar diagnoses include polypoid vascular lesions in unusual locations. This series reports five cases in northern Brazil.
Methods: A total of five cases with Rhinosporidiosis suspicions were analysed, by the clinical information and the microscopy of each lesion, which were obtained by biopsy. It is important to add that two biopsies were obtained by nose lesions, two were from conjunctival injury and a single one was a urethral lesion. All of the cases originated in Maranhao, in Brazil.
Results: Three cases were about infants. The first case was of a 5-year-old male, with a papillomatous tumour in the right nostril. Another case showed a 4-year-old female, with a conjunctival injury. The third one was an 11-year-old male, was a papillomatous lesion in the left nasal mass, implanted in the anterior nasal vestibule. The last two were adults, a 36-year-old and 69-year-old, both male. The first one had a papillomatous conjunctival lesion in the right eye, and the second had a urethral injury, with the suspected Human Papillomavirus (HPV).
Conclusion: Rhinosporidiosis is an uncommon infection and when presented is seen as nasal cavity lesion. However, in this present study, nasal mass corresponds to 40% of the cases, and the other 60% of the less common clinical manifestations include a conjunctival injury (40%) and a urethral lesion (20%). Histopathological diagnosis is straightforward, although, since it is uncommon, ample awareness is essential, as typified by this report.

PS-13-011
Pathomorphological features of tuberculosis pleurisy
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Background & objectives: Tuberculosis (TB) is an infection disease with high level of fatal outcomes worldwide. TB commonly presents with systemic involvement of various patient's organs and tissues. Extrapulmonary TB often affects pleura, but clinical diagnosis of TB pleurisy may be misdiagnosed.
Methods: We reviewed needle biopsy specimens of the parietal pleura in 87 patients who had tuberculous pleurisy (TBP) diagnosed in 2015-2019 at Lugansk Anti-Tuberculosis Dispensary and The Thoracic Department of the Republican Clinical Hospital. The histological slides of the pleura stained with hematoxylin, and eosin were studied under microscope. All accompanying medical documentation with clinical information analysed.
Results: The TBP diagnosed in 67 male and 20 female patients. The average age of patients in 2014-2015 was 45, in 2016-2017 - 55, in 2018-2019- 37 y.o. It was also noted that TBP in people 18-30 years old(y.o.) was diagnosed in 21 cases, 31- 50 y.o.- in 44, 51 - 70 y.o.- in 20, and in people older than 70 y.o. in 2 cases. Acute onset of TBP was detected in 80% cases and the latent course- in 12%. Main variants of pleura biopsies' pathology presented by classic epithelioid-giant cell granulomas with caseous necrosis; epithelioid-giant cell granulomas without caseous necrosis; lymphocytic-epithelioid cell granulomas; granulomas with nonspecific acute purulent inflammation.
Conclusion: TBP is the most common cause of the pleural exudate, however, to reveal the aetiology of disease may be difficult due to the lack of adequate clinical symptoms and possible misinterpretations. Present study revealed the majority of TBP cases within 31-50 y.o. age group. Histological examination of pleural biopsies specimens has shown various pathomorphological changes characterizing the tuberculous process. In order to improve early diagnosis and substantiate the adequate treatment further evaluation of clinical and pathomorphological TBP' features are needed.

PS-13-012
Placental pathology findings after SARS-CoV-2 infection
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Background & objectives: The placenta is an immunoprivileged organ with attenuated immune response. Several viruses can cross the placental barrier and be associated with placental morphological changes and foetal diseases. Our objective has been to evaluate the placental histopathological changes related to SARS-CoV-2.
Methods: We present a series of seven placentas of SARS-CoV-2-positive women, who had been diagnosed by PCR on nasopharyngeal swabs, before birth. We provided a detailed histopathological description of morphological changes found, comparing them with those found in six placentas from women without infection. Extended immunohistochemical analysis has been carried out to identify the presence of SARS-CoV-2 in the placental tissue.
Results: The mother's age ranged between 29 and 42 years old. 4 out of 13 placentas were below 40th gestational week. Histomorphological findings range from signs of poor perfusion to inflammatory changes. 3 out of 7 cases with historial of viral infection showed inflammatory changes like chorionitis, chorioamnionitis and vasculitis, 5 presented signs of malperfusion such as infarction, subcorionic thrombi and intervillous thrombosis and 1 did not show any morphological change. Control placentas showed overlapping findings, 5 out 6 presented subcorionic

thrombi, intervillous and subcorial thrombosis and central and peripheric infarcts. The immunohistochemical analysis to demonstrate the presence of the virus in the placental tissue are pending of study.
Conclusion: The morphological response to viral infections of the placenta is variable and in some cases well known. In our study, no differences in findings could be demonstrated between SARS-CoV-2 infected and uninfected women. In both groups there are data of poor perfusion and inflammatory changes, which could be attributed to infection of the placenta and an altered coagulation state induced by the virus; however, the data are not conclusive and more studies are needed.

PS-13-013
Hydatid disease of the central nervous system: a report of 9 cases in South Tunisia
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Background & objectives: Hydatid disease is an endemic parasitic infection especially around the Mediterranean, caused by Echinococcus granulosus. Central nervous system (CNS) involvement is unusual and represents 2% of all hydatid locations. In this work is will analyse clinicopathological features of CNS hydatidosis.
Methods: This work is a retrospective and descriptive study of 9 cases of CNS hydatidosis registered at the department of pathology of the university hospital of Sfax in Tunisia, during a period of 11 years from 2010 to 2020. Their epidemiological, clinical, therapeutic and pathological characteristics as well as their outcome were retrospectively reviewed.
Results: The mean age was 29,6 years [4 - 66 years]. The sex ratio was 1/2. The cysts were located in cerebral hemisphere in 4 cases and spinal cord in 5 cases. For spinal location, lumbar and sacral regions were involved in respectively 3 and 2 cases. Bifocal cerebral involvement was observed in one patient. No other systemic locations were associated. Histopathological diagnosis was made on surgical specimens in all cases. Microscopically, the presence of eosinophilic laminated and non-nuclear layer which was positive for PAS confirmed the diagnosis of hydatidosis. All patients received perioperative albendazole treatment with good recovery. A local vertebral recurrence was noted in one patient after 8 years.
Conclusion: Hydatidosis usually affects liver (60-70%) and lung (20-30%). The passage of the larva through the first filters (liver and lung) before hematogenous dissemination explains the rarity of CNS involvement. CNS hydatidosis should always be considered when encountering cystic lesion especially in endemic areas. It is more common in children and young adults. Brain involvement is more frequent than the spinal one. Histological examination is the key to confirm the diagnosis. Recurrences are observed in 30% of cases despite adequate therapy.

PS-13-014
Clinical and pathomorphological characteristics in fatal COVID-19 cases
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Background & objectives: The COVID-19 disease, declared by the WHO as a pandemic, is still an urgent problem of modern medicine. Despite the fact that many laboratory data have been well characterized, clinical and pathology data correlation needs to be investigated.
Methods: Autopsy records of 47 fatal cases of COVID-19 disease were reviewed. Demographic characteristics and clinical peculiarities were noted. Gross pictures and histopathology of lungs and other organs were studied.
Results: Most deaths were recorded in the 61-75 age group(46,8%).The second age group with frequent fatal outcomes ranged 76- 90 years(31,9%).10.6% were in the 18-44 age group. 8.5% of cases were aged 45-60 years. One man was 90yo. Postmortem investigation revealed COVID-19-induced pathological changes in the lungs in most patients:76,5% of them had interstitial pneumonia and the development of acute respiratory distress in the most severe cases (72,3%). Our study also has shown the tracheitis with epiglottitis (44,6%), gastroenteritis (21,3%), bacterial bronchopneumonia (19,1%) and other pathologies (myocarditis, pleurisy, nephritis, meningitis, thromboembolism) with a male predominance among patients. The main histological peculiarities were presented in lungs as alveolar damage accompanied with widespread microscopic thromboses.
Conclusion: COVID-19 viral infection contributes to heterogeneous lung damage and has been associated with other internal organs injury and dysfunction. Capillary microthrombi and inflammation, as well as macrothrombi, areas of dystrophy and necrosis revealed in organ's tissues. Multiple manifestations of the accompanying pathologies may contribute to disease progression and fatality. Further study of the COVID 19 morphology with clinical–pathologic correlations is needed to develop effective therapies and preventive countermeasures.

PS-13-015
Small bowel ischemia and SARS-CoV-2 infection: Immunohistochemistry positivity in endothelial and inflammatory intestinal cells: case report
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Background & objectives: SARS CoV-2, in addition to affecting the respiratory tract, can cause thrombogenic ischemia in various organs including the gastrointestinal tract. The cause is multifactorial: hypercoagulability, endothelitis, coagulopathy leading to thromboembolic complications, the use of vasopressors in patients with hemodynamic compromise.
Methods: A 39-year-old male, without previous pathologies was admitted to the intensive-care unit due to bilateral COVID-19 interstitial pneumonia. On the 13th day of hospitalization, he presented paralytic ileus. In abdominal tomography, acute mesenteric ischemia in jejunum-ileum was observed. The patient had an emergency laparotomy with evidence of segmental small bowel ischemia with faecaloid peritonitis. A small bowel resection was performed.
Results: Small intestine resection specimen of 164 cm long, externally it presented reddened serous and fibrin plaques. Histologically, massive acute intestinal ischemia was observed, with trans-mural necrosis, thrombosis in arterial and venous vessels of small and medium calibre in all the intestinal wall including adipose tissue. In addition to images of vasculitis, fibrinoid necrosis, and serositis with perforation. An immunohistochemical technique was performed for SARS CoV-2 (GeneTex), which was positive in endothelial and inflammatory cells. The patient presented septic shock secondary to faecaloid peritonitis; intestinal failure secondary to short bowel syndrome; multi organ failure and finally death 58 days after surgery.
Conclusion: Severe COVID-19 pneumonia should be considered a hypercoagulable state, maintaining a high level of suspicion of intestinal ischemia. In the literature, there is only one case (Norsa et al.) where they described small bowel ischemia that confirmed the presence of SARS CoV-2 in the intestinal mucosa by ISH RNA. These findings suggest a direct viral role in the ischemic process and not just a consequence of the hypercoagulable state; more studies are needed to clarify it.

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PS-14-001

Artificial intelligence-based mitoses counting in gastrointestinal stromal tumours

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Background & objectives: Mitotic activity is one of the prognostic parameters in Gastrointestinal Stromal Tumours (GIST). We aimed study the role of Artificial intelligence (AI) based counting mitosis and to search interobservance agreement between human eye and AI counting in GISTs.
Methods: Slides belong to 18 GIST cases were scanned at 40x magnification by 3DHistech Scanner. Two-stage deep algorithm was used to detect mitotic cells. Nucleus centres was detected using RetinaNet architecture. Prediction was performed to determine mitosis using VGG-11 architecture. Mitosis was also counted by 3 pathologists in light microscopy. The agreement analysis was performed using Intraclass correlation coefficient (ICC) test.
Results: Mean age:54; Female/Male ratio:1,2/1 Tumour size range:3,4-28cm ; 38% of cases were in high risk, 38% in moderate and 22,2% of cases were in low risk group. In AI program; 246 patches (size of 512x512 pixels) extracted from the slides and annotated 21237 nuclei. Dice(F1) score; 0.96, a true positive rate:0.97; true negative rate:0.97; validation accuracy:0.97. ICC results showed an excellent level of agreement between the pathologists, with an ICC point estimate of 0.909 (95% CI [0.814, 0.962]). Inclusion of the AI rater led to a moderate level of agreement with an ICC of 0.682 (95% CI [0.479, 0.846]). Agreement was significantly higher in cases show <2 mitosis/5 mm2.
Conclusion: This is the first study which analysing AI-based mitotic counting in GIST, as we know, so far. The agreement was found better in larger tumours compare to small one (trucut, endoscopic biopsy) in this preliminary study. Our study continue with larger series later.

PS-14-002

Computer-assisted immunohistochemical (IHC) scoring of erb-b2 receptor tyrosine kinase 2 (HER2) protein expression in breast cancer

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Background & objectives: The uPath HER2 (4B5) image analysis for breast algorithm aids in scoring breast cancers stained with the VENTANA HER2 (4B5) assay. We present data comparing manual scoring to computer-assisted scoring using the uPath HER2 (4B5) image analysis for breast algorithm.
Methods: Three study pathologists scored 180 FFPE breast cancer cases independently by both manual and HER2 (4B5) image analysis methods. Scoring results from both manual read (MR) and computer-assisted scores (image analysis, IA) were compared against the ground truth (GT) scores generated by consensus panel pathologists. The differences in agreement rates for HER2 IHC status between scores were determined.
Results: Agreement rates* (PPA: positive percent agreement; NPA: negative percent agreement; OPA: overall percent agreement) between MR, IA and GT were:
PPA- MR vs GT-95.5% [95% CI: 92.9, 97.8]; IA vs GT-95.5% [95% CI: 92.9, 97.4]
NPA -MR vs GT-95.0% [95% CI: 92.3, 97.5]; IA vs GT-95.4% [95% CI: 93.1, 97.7]
OPA -MR vs GT-95.3% [95% CI: 93.5, 97.2]; IA vs GT-95.5% [95% CI: 93.6, 97.2]
Further, inter-reader agreement rates were observed for the image analysis method with point estimates of at least 95.6%.
*-2-sided 95% CI
Conclusion: Comparison of agreement rates demonstrated that the lower bounds of the difference of PPA and NPA 95% CIs were -0.0% and -1.1%, respectively, and met the pre-specified study's acceptance criteria. Overall, the studies demonstrated that the uPath HER2 (4B5) image analysis for breast algorithm is equivalent to the manual pathologist scoring method in determining HER2 IHC status in breast cancer.

PS-14-003

Immunohistochemical (IHC) scoring of programmed death-ligand 1 (PD-L1) protein expression in non-small cell lung cancer (NSCLC) using an automated digital pathology algorithm

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Background & objectives: The uPath PD-L1 (SP263) image analysis (IA) algorithm functions as an aid in the interpretation of the VENTANA PD-L1 (SP263) Assay in NSCLC. We present data comparing manual scoring to computer-assisted scoring using the uPath PD-L1 (SP263) IA algorithm.
Methods: Using a supervised machine learning approach, the uPath PD-L1 (SP263) IA algorithm was trained on NSCLC cases scanned on VENTANA DP 200 scanners and annotated by pathologists. Equivalency at the 50% cut-off between pathologists' manual read (MR) and computer-aided scoring using the uPath PD-L1 (SP263) IA algorithm was compared using 180 NSCLC cases stained with VENTANA PD-L1 (SP263) Assay.
Results: The computer-aided interpretation (image analysis, IA) using the uPath PD-L1 (SP263) IA algorithm displayed equivalence to manual interpretation at the 50% cut-off with a positive percent agreement (PPA) rate of 96.7% (95% CI: 94.0, 98.9), and a negative percent agreement (NPA) of 93.1% (95% CI: 90.2, 95.6). Inter-reader agreement rates for the computer-aided interpretation were concordant with a PPA rate of 95.1 % (95% CI: 92.5, 97.5) and a NPA rate of 98.5 % (95% CI: 97.1, 99.7). Intra-reader agreement for the computer-aided interpretation were also concordant with a PPA rate of 98.4% (95% CI: 95.1, 100.0) and a NPA rate of 100% (95% CI: 96.8, 100.0).
Conclusion: Overall the study met the expected goals and shows that computer-aided interpretation using the uPath PD-L1 (SP263) IA algorithm is reproducible among readers and is equivalent to the manual scoring method at the 50% cut-off in NSLC.

PS-14-004

Computer-assisted scoring of erb-b2 receptor tyrosine kinase 2 (HER2) gene amplification status in breast cancer

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Background & objectives: The uPath HER2 Dual ISH image analysis, Breast algorithm aids in determining HER2 gene status using the VENTANA HER2 Dual ISH DNA Probe Cocktail assay. We compared manual to computer-assisted scoring using the uPath HER2 Dual ISH image analysis algorithm.
Methods: Pathologists reviewed 220 FFPE breast cancers using manual and uPath HER2 Dual ISH image analysis methods. Manual read (MR) and computer-assisted scores (IA) were compared against the ground truth (GT) scores generated by consensus panel pathologists. Differences of agreement rates of HER2 gene status between manual, computer-assisted, and GT scores were determined, as well as inter-reader reproducibility of computer-assisted scores.

Results: Agreement rates* (PPA: positive percent agreement; NPA: negative percent agreement; OPA: overall percent agreement) between MR, IA and GT were:
PPA- MR vs GT-96.9% [95% CI: 94.2, 99.0]; IA vs GT-97.2% [95% CI: 95, 99.3]
NPA -MR vs GT-97.6% [95% CI: 95.8, 99.4]; IA vs GT-94.3% [95% CI: 90.8, 97.3]
OPA -MR vs GT-97.2% [95% CI: 95.7, 98.6]; IA vs GT-95.7% [95% CI: 93.8, 97.5]
Further, inter-reader agreement rates were observed for the IA method with point estimates of at least 96.7%.
*-2-sided 95% CI.
Conclusion: Comparison of agreement rates showed that the lower bounds of the difference of PPA and NPA 95% CIs were -0.9% and -6.2%, respectively, and met the study's pre-specified acceptance criteria. Overall, the validation studies demonstrated that the uPath HER2 Dual ISH Image Analysis method is equivalent to the manual scoring method in determining HER2 gene status in breast cancer.

PS-14-005
Validation and concordance study on digital pathology for the primary histopathological diagnosis of routine dermatopathology specimen
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Background & objectives: The Pathology Department in Aalborg, Denmark, is currently in the process of implementing digital pathology. Our aim was to train and validate three dermatopathologists using digital pathology for primary dermatopathological diagnoses and to assess concordance, safety and to identify pitfalls.
Methods: The validation model was inspired by guidelines for implementation (by The Royal College of Pathologists), with a few modifications to local circumstances. The cases were reviewed digitally and then immediately reviewed by conventional light microscopy. Diagnoses, discrepancies, technical qualities and challenging areas were noted for each case. All specimen types were covered and included a representative mix of different diagnoses.
Results: Each pathologist reviewed 20 cases in the training phase and all three reviewed a total of 434 cases in the validation phase between May 2020 and January 2021. The diagnostic concordance rate was 99.28 %, excluding deferrals. Three discordant cases were identified; two were associated with poor focus quality and one with difficulties in identifying cell morphological details. The total mean level of confidence when diagnosing was 6.63 digitally and 6.79 microscopically, based on Likert scale (ranging from 1-7). Common pitfalls observed were related to morphological details associated with inflammatory cells, dysplasia and carcinomas, and to a lesser extent, adnexae, microorganisms and mitoses.
Conclusion: The concordance of 99.28% and the pitfalls observed are similar with those of other contemporary studies. It indicates that digital review is a safe alternative to conventional microscopy, but more work is needed to improve the focus quality at a cellular level.

PS-14-007
3D reconstruction of kidney with tumour based on histopathological macroscopic imaging
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Background & objectives: The histopathological macroscopic examination of kidney is performed to conclude the presence of lesions in kidney and metrical description. The transverse kidney slicing, photographing and 3D reconstruction procedure can be useful to visualization and quantification of the kidney and cancer.
Methods: The serial slicing of kidneys were performed on the special table with the row of needles and comb guide for a knife with 10mm distances. The sections were photographed, initially pre-agreeded and the kidney and cancer outlined by a pathologist. The 3D reconstruction was performed by mesh generation, its smoothing and step-parallel optimication with the different aim functions.
Results: The set of 20 kidneys were 3D reconstructed based on the macroscopic imaging. It was observed that the main problem to obtained the smooth, anatomically concordance reconstructions was the large spacing of the data. The coarse pre-agreeding of sections effects the unwanted surface unevenness which was minimized on the optimization procedure. The step-parallel procedure of sections transposing in the X and Y directions, and rotation was applied in the gradient-descent manner due to high computational cost. The aim function based on the maximization of volume gives a better results than criteria of concordance between the sections and mesh intersections. The visualization and volume counting is a final step of procedure.
Conclusion: The 3D reconstruction of kidney and their lesions based on the macroscopic imaging can be done with the expert's annotations and the proposed optimization procedure. The maximization of object volume can be used as the aim function in fine agreed of sections. The high computational cost can be reduced by the parallel computing and gradient-descent manner instead of the whole parameter grid examination. In such a way, the volume quantification and visualization can be done.

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PS-14-008
Workplace evaluation in the practice of a digital pathologist: an ergonomic approach
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Background & objectives: Along with all the benefits of digital pathology this area also escalates some issues we usually have to deal with. Workspace ergonomics becomes extremely important factor due to even more prolonged immobility comparing to traditional non-digital pathology.
Methods: A number of criteria were adapted from analysed articles for assessment work-related discomfort (WRD). The ergonomic comfort index (ECI) reflecting the grade of ergonomic discomfort was offered, varying from 1 to 24. Each studied workstation (n=32) was categorised into 1 of 3 groups according to the level of compliance with the recommendations for ergonomics: complete discrepancy, part-agreement and relative agreement.
Results: A questionnaire was also developed to assess the clinical symptoms as subjective part of WRD. Results of the pilot study showed that 62,5% of respondents complain about head & neck discomfort by the end of the day with second most popular complain of carpal tunnel syndrome. ECI varied from 8 to 11, and none of the workstations were deemed appropriate to complete discrepancy. Interestingly, senior pathologists tend to gain more points than younger ones.
Conclusion: The study showed the need for systematic approach when dealing with bad workspace ergonomics. As we move forward to the digital pathology, we will require more comfortable supplies. The proposed algorithm of workplace evaluation and the questionnaire would be helpful for self-assessment to reveal the ergonomic problems and for a standardized assessment after appropriate validation.

PS-14-009
N/C ratio developing software/program as an assisting tool for pathologist in daily life
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Background & objectives: To develop the software/applicable program to validate N/C ratio in ascites fluid cytology.

Methods: 1. Retrospective collection of ascites cytology specimen prepared with liquid base cytology during the year 2019-2020 2. Development of interpretation software/program to validate the N/C ratio 3. Apply the software/program to the selected cases at highest magnification (x40) 4. Interpretation and validation (compare to measurement from scan slide Aperio Image Scope)
Results: N/C ratio plays the major role to help diagnosis in most of the cases, but this parameter is vary from person-to -person. To cut off the discrepancy of diagnosis from human error, the computing programmed would be beneficial. The program is developed as a research project for students at Faculty of Computer Science, Chulalongkorn University, Thailand. Preliminary testing results aim for validate the N/C ratio measured from newly developed program and the standard commercial program (Aperio Image Scope). Among testing 40 cells at different coordinates, the different measurement value is ranging from 0.000380166947 to0.124475444 (mean at 0.393864932). The study will apply more cases and will be added during the presentation.
Conclusion: N/C ratio plays the major role to help diagnosis in cytology cases, but this parameter is vary from person-to-person. To cut off the discrepancy of diagnosis from human error, the computing programmed would be beneficial. The software/developing program from our students gives hope and premise to reduce loads of routine cytology screening for pathology. This helps to validate the influential parameters, reduce human errors, and easily access from smartphones.

PS-15 | Molecular Pathology Posters

PS-15-001
Rapid detection of microsatellite instability in non-colorectal cancers
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Background & objectives: We now need to detect microsatellite instability (MSI) to all of the patients included to immunotherapy protocols. This study was designed to assess robustness of the Idylla™ MSI Test to detect MSI in non-CRC.
Methods: 64 cases from archived specimens, including 32 gynaecological carcinoma, 26 digestive carcinoma and 6 sebaceoma, were retrospectively analysed using Idylla™ MSI Test. The results were compared to those previously determined by the Promega™ MSI assay or to the expression of the 4 mismatch repair proteins detected by immunohistochemical staining.
Results: Out of 64 cases, 15 were classified as MSI by the Idylla™ MSI Test. Among the 15 MSI tumours, the number of altered MSI biomarkers ranged from 2/7 to 6/7. MSI status were detected, whatever the tissue origin, sebaceoma, cholangiocarcinoma, endometrial carcinoma, gastric or small intestine carcinoma. Compared with the Promega™ MSI assay, sensitivity and specificity of 87.5%, and 100% was reached, respectively. The lowest sensitivity was found in the endometrial carcinoma.
Conclusion: The novel Idylla™ MSI Test showed high concordance in determining MSI status in non-CRC, with a good concordance in all the various tissue tested. The findings in our study support the use of this Test as an alternative method to detect MSI in non-colorectal cancers.

Funding: This work was supported by Biocartis who provided the Idylla™ platform and the Idylla™ MSI Tests cartridges used in this study.

PS-15-002
Study of transcriptomics in colon cancer patients of the Consensus Molecular Subtype 2/3.
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Background & objectives: Tumour location and IHC-based Consensus Molecular Subtype (CMS) are essential in prognosis and treatment of colon cancer (CC), characterized by its heterogeneity. The aim is to identify differentially expressed mRNA in CMS-2/3 patients classified by tumour location and health status.
Methods: Formalin-fixed-paraffin-embedded tissue was selected from 24 CC patients, including 12 at right colon (6 alive/6 dead) and 12 at left colon (7 alive /5 dead); all the cases were CMS-2/3, pT3/pT4, regional positive lymph-nodes and unmethylated CDX2. Up- and down-regulated genes were detected by whole-transcriptome analysis. Libraries were sequenced in the HiSeq1500 (Illumina). The bioinformatic analysis was performed by SARTools (FDR<0.05).
Results: 215 genes were differentially expressed in more aggressive tumours compared to less aggressive ones, including genes involved in epithelial-to-mesenchymal transition. There also differences in the expression of key genes between right and left-sided tumours.
Conclusion: The application of Transcriptomics is feasible in archived paraffin samples.
This high-throughput technology allows the detection of differentially expressed mRNAs with potential clinical value in the study of CMS-2/3 patients, characterized by its clinical and pathological heterogeneity.

PS-15-003
Development and validation of a prognostic molecular cell cycle progression signature for decentralized testing of men with localized prostate cancer
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Background & objectives: The Prolaris cell-cycle progression (CCP) test is a validated 46-gene assay which informs risk of disease progression for men with localized prostate cancer. This study developed and validated a 16-gene kit-based version of Prolaris for use in decentralized testing laboratories.
Methods: RNA was extracted from formalin-fixed, paraffin-embedded prostate cancer biopsy tissue. CCP scores were calculated as the expression of CCP genes normalized to housekeeper genes. Amplification efficiency, minimum tumour content, repeatability and reproducibility were evaluated. Scores from the 46- and 16-gene tests were compared to verify the 16-gene test could be applied in a similar clinical manner to the 46-gene test.
Results: The 16-gene test performed across a range of RNA input concentrations. Amplification efficiency for all CCP and housekeeper genes in the 16-gene test fell within the allowable range (90-110%). Samples with at least 60% tumour content were determined to be appropriate for testing with the 16-gene kit. Test results were highly repeatable (SD in CCP score 0.085) and reproducible (SD 0.115), with instrument used, test operator, and kit lot all having minimal impact on test result variation (SD 0.000, SD 0.016, and SD 0.114, respectively). The CCP scores generated from the 46- and 16-gene tests were correlated.
Conclusion: The 16-gene test, which consists of 10 CCP and 6 housekeeper genes, results in similar scores to the 46-gene test. Kit lot, test instrument, and operator had minimal impact on the CCP score results from the 16-gene test, indicating it is appropriate for use in a decentralized testing setting. This will allow access to a version of the Prolaris test for patients in areas where testing in local laboratories is required or desired.

Funding: This study was funded by Myriad Genetics, Inc.

PS-15-004

A clinical practice assessment educational activity to evaluate the knowledge of pathologists and oncologists regarding their understanding of NGS

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Background & objectives: Next generation sequencing (NGS) can simultaneously evaluate multiple genetic alterations and is becoming more important for individualizing cancer therapy. This activity was designed to understand the gaps in knowledge haematologists/oncologists (hem/oncs) and pathologists have regarding the use of NGS.
Methods: A continuing medical education (CME)-certified clinical practice assessment comprising 29 multiple-choice questions that measured knowledge, attitudes, and perspectives regarding NGS was developed. The self-assessment was available online to physicians without monetary compensation or charge. Respondent confidentiality was maintained, and responses were de-identified and aggregated prior to analysis. The activity launched Jan 9, 2020; data through March 12, 2020 are presented.
Results: At the time of this analysis, between 180 hem/oncs and 94 pathologists answered some to all questions in this activity.
Only 44% of hem/oncs and 26% of pathologists regularly use NGS in their clinics. Around 80% of hem/oncs and 62% of pathologists indicated that the approximate turnaround time for NGS results is 10 or more working days, and cost was the most important barrier to using NGS in their practice.
Of the 20 questions assessing the knowledge of clinicians regarding the use of NGS, the percentage of hem/oncs answering correctly ranged from 18% to 77%, while 23% to 81% of pathologists answered these questions correctly.
Conclusion: NGS is becoming more important in guiding and driving treatment decisions for various cancers in clinical practice, however only 20% of hem/oncs and pathologists felt moderately or very confident in their ability to explain to their colleagues how to apply NGS in clinical practice. This educational activity illustrates that there are clear knowledge gaps regarding how to optimally implement NGS in clinical practice, indicating the importance of developing educational activities on this topic.

Funding: The educational activity was supported by an independent educational grant from Thermo Fisher Scientific.

PS-15-005

Next generation sequencing based targeted panel analysis in advanced non-small cell lung cancer (NSCLC)

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Background & objectives: Multigene mutation analysis is getting more important in NSCLC, in terms of multidrug treatment. We aimed to identify druggable genomic variants using targeted gene panel in NGS platform.
Methods: RNA was isolated via "RNEASY FFPE KIT" from paraffin blocks containing 80 Tumour tissue with NSCLC. Archer® FusionPlex® Comprehensive Thyroid & Lung (CTL) was used to create cDNA libraries. Illumina NextSeq next generation sequencing platform was used. All Analysis performed in Archer Analysis Ver.6.0.3.2 software.
Results: Mean age was 51: M/F:1,2/1: Analysis included: Fusions for ALK, AXL, BRAF, CCND1, FGFR1,FGFR2, EGFR, FGFR3, MET, NRG1, NTRK 1-2 ve 3, PPARG, RAF1, RET, ROS1, THADA; and Single Nucleotide Variants (SNV), INDEL: BRAF, CCND1, CTNN1B, EGFR, ERBB2,DDR2, FGFR1, FGFR2, FGFR3, GNAS, IDH1, IDH2, HRAS, KRAS, NRAS, MAP2K1, PIK3CA, RET, ROS1. Genomic variations found: EGFR-mutation (15.8%), EML4-ALK Fusion (3.75%), KRAS codon 12mut (22.5%), BRAF (7.5%) ERBB2 mut(2.5%), MET mut (2.2%), exon 14 skipping MET (3.75%, CD74-ROS1fus (3.75%), KIF5B-RET fus (1.25%), FGFR3-TACC3 fus (2,5%) were treatable alterations in study group. There is no SNV, indel, fusion or expression 25 % of cases.
Conclusion: Our study support that NGS based targeted panel is useful to detect druggable mutations in Lung Carcinomas. This method can be used also for small biopsies.

PS-15-006

Inter-laboratory evaluation of somatic BRCA mutations in clinical practice: a ring trial of the Spanish Group of Research in Ovarian Cancer (GEICO)

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Background & objectives: PARP inhibitors have shown efficacy in BRCA-mutated ovarian cancer (OC) patients. The aim of this study is to perform an inter-laboratory ring-trial to compare and evaluate different analytical approaches to identify and classify BRCA variants in formalin-paraffin-embedded (FFPE) tumours.
Methods: Five independent clinical diagnostic and two reference laboratories tested 9 specimens, including commercial synthetic human FFPE (n=3) and OC tumour tissue DNA (n=3) and FFPE (n=3) samples. Each centre performed their routine next-generation-sequencing (NGS) workflow and report. To estimate the concordance rate 17 variants were evaluated: 10 pathogenic, 1 likely pathogenic, 3 variants of unknown significance (VUS) and 3 wild-type.
Results: Five different commercial NGS panels were employed, two based on hybridization-capture and three on target PCR/amplicons, on two NGS instruments (MiSeq-Illumina and Ion S5™ System-Thermo Fisher Scientific). Different NGS bioinformatic pipelines were used to identify and annotate variants.
The median concordance detection rate was 64.7% (35.3-70.6%). Most of non-reported results correspond to variants within homopolimeric regions, bioinformatic issues, low variant allele frequencies or low coverage. One laboratory reported no results for one commercial specimen due to insufficient DNA; another laboratory reported a false positive variant within a commercial sample.
Discrepancies in variant classification affected four alterations, three of them with clinical relevance (VUS vs likely pathogenic).
Conclusion: This ring-trial showed a wide range of concordance rates in the identification and interpretation of BRCA somatic analysis. It highlights the relevance of establishing standard criteria for detecting, interpreting and reporting BRCA somatic variants. Validation of both NGS methodology and bioinformatic pipelines are required. Standardization in analytical criteria is also mandatory. Regarding interpretation, discrepancies affecting non-reported variants in databases remain a challenge with relevant clinical implications.

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PS-15-007

Immunohistochemical screening for microsatellite instability in sebaceous gland neoplasms

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Background & objectives: Muir-Torre syndrome is a Lynch syndrome variant, characterized by the presence of sebaceous gland neoplasms. It is caused by a germline mutation in the mismatch repair system. Currently, there are no well-established guidelines for universal screening in these neoplasms.
Methods: Patients with a histological diagnosis of sebaceous gland neoplasia in our hospital in the last 10 years were included in the study. Immunohistochemical techniques for the expression of MMR proteins were performed. The protein expression results, and the expression loss pattern were collected. The percentages of type of neoplasia, expression loss and patterns were calculated.
Results: The sample consisted of 32 patients with sebaceous gland neoplasms, 15 (46.8%) of which were sebaceous epitheliomas, 14 (43.7%) sebaceous adenomas and 3 (0.9%) sebaceous carcinomas. Eight neoplasms (25%) had loss of expression of MMR proteins. The most common pattern was the loss of MSH2 and MSH6, corresponding to 7 neoplasms (87'5%), whereas one of them (12.5%) lost expression of MLH1 and PMS2.
Conclusion: Universal immunohistochemistry screening for microsatellite instability in sebaceous gland neoplasms shows remarkable percentages in this and other studies. However, in other publications, it has been pointed out that immunohistochemistry may be less specific for these neoplasms, compared to the same screening performed in other organs. Therefore, more studies are needed to determine the need for universal screening for sebaceous gland neoplasms.

PS-15-008
The mutational burden in the genes encoding elements of Hedgehog signalling pathway in paediatric germ cell tumours
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Background & objectives: Pathogenesis of Germ cell tumours (GCTs), especially in children, is not fully understood. Hedgehog (Hh) signalling pathway controls cellular migration and specification during embryogenesis and affects gonadal formation and sexual differentiation. Hh pathway molecular changes participate in GCTs pathobiology.
Methods: The molecular changes in Hedgehog pathway genes in 70 childhood germ cell tumours were examined. The mutational analysis of the Hh pathway associated genes and chosen non-HH network genes in GCT was performed in FFPE tumour samples using the next generation sequencing technique (NGS) with a custom designed QIAseq Targeted DNA panel comprising 25 genes of the pathway (Qiagen).
Results: Analysis of 70 GCTs revealed somatic molecular changes in 52 (74%) of tumours, mostly dysgerminomas and mixed tumours. The most common were activating pathogenic changes in KIT gene (33%, n=23) and KRAS (9%, n=6). 25 (36%) tumours had at least one sequence variant in the genes encoding canonical elements of the Hh pathway. These included likely pathogenic loss-of-function variants in PTCH1 (n=3), PTCH2 (n=5), SMO (n=5), DISP2 (n=5), HHIP (n=1), ZIC2 (n=1) and SUFU (n=1). Also, a number of missense variants of unknown significance were described including rare single nucleotide variants in LRP2 gene present in 23 tumours.
Conclusion: The observed selective activation of individual pathway elements implies that Hh pathway may be involved in GCT pathogenesis, although may rather through to dysregulation of physiological maturation processes than being a trigger factor that activates oncogenesis. Due to the individual nature of the changes found and the limited number of tumours studied a comprehensive assessment of the complex molecular changes in Hh pathway loci associated with the GCTs pathogenesis is not possible at present stage of the study.

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PS-15-009
Differentially expressed genes associated with ETS-fusion-positive PC
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Background & objectives: There are seven molecular subtypes of prostate cancer (PC), four were characterized by gene fusion between *TMPRSS2* and *ETS*-family member, which is 65% PC cases. In this work, we aimed to identify differentially expressed genes (DEGs) associated with ETS-fusion-positive PC.
Methods: This study included RNA-Seq data of PC samples of The Cancer Genome Atlas (TCGA-PRAD project). The cohort was divided: patients with ETS-fusion and ETS-fusion-negative. Differential expression analysis was performed in statistical environment R using the EdgeR package was used. The Mann-Whitney test, and quasi-likelihood method (QLF) were used for statistical analysis. To exclude false positive results FDR method was used.
Results: We identified at list 93 differentially expressed genes (based on QLF FDR and Mann-Whitney FDR < 0.05) between the studied groups (38 genes were upregulated and 55 – downregulated). The following genes showing overexpression in ETS-fusion-positive PC samples are marked: *ALOX15B* (fold change – 4.8), *GNMT* (4.1), *MIPEP* (4.4), *PCOTH* (5.1), *TFF3* (8.2), and as downregulated: *CDH7* (-5.5), *KCNN4* (-5.1), *LINC02418* (-8.1). STRING Network analysis shown enrichment for several GO-term: arachidonate 15-lipoxygenase activity (GO:0050473), acetylgalactosaminyltransferase activity (GO:0008376), and glucuronylgalactosylproteoglycan 4-beta-N-acetylgalactosaminyltransferase activity (GO:0047237).
Conclusion: We found out 93 differentially expressed genes, which were involved in acetylgalactosaminyltransferase and arachidonate 15-lipoxygenase activity. The highest changes we observed in ALOX15B, CDH7, GNMT, KCNN4, LINC02418, MIPEP, PCOTH, TFF3 genes.
This work was performed using the equipment of EIMB RAS "Genome" centre (http://www.eimb.ru/ru1/ckp/ccu_genome_c.php).

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PS-15-010
MicroRNAs profile associated with Gleason score in locally advanced prostate cancer
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Background & objectives: Prostate cancer is the second leading cause of cancer death among men worldwide. The aim of our study was to identify changes in the miRNAs expression profile associated with Gleason scores and to identify miRNAs with prognostic potential.
Methods: miRNA-Seq on Illumina platform was performed for 44 prostate cancer specimens taken from Russian patients. Bioinformatic analysis of relative expression was performed in the R statistical environment using the edgeR package. Additionally, a correlation analysis was carried out using the Spearman test. The results were considered statistically significant at p-value QLF-test and p-value Spearman test < 0,05.

Results: As a result, we identified a profile of 21 miRNAs, in which an increase in relative expression was noted with the highest Gleason score for miR-183-5p, miR-615-3p, miR-106b-3p, miR-342-5p, miR-182- 5p, miR-25-3p, miR-7-5p, miR-409-3p, miR-432-5p, miR-1275; and is marked by a decrease in relative expression for miR-455-5p, miR-582-3p, miR-143-5p, miR-221-5p, miR-221-3p, miR-1-3p, miR-29c-3p, miR-222 -3p, miR-133a-3p, miR-499a-5p, miR-224-5p, respectively. The greatest correlation with an increase in Gleason scores was noted for miR-183-5p (rs = 0.47), miR-615-3p (rs = 0.47), miR-455-5p (rs = -0.47), miR-582-3p (rs = -0.47).
Conclusion: We found a miRNA expression profile associated with an increase in Gleason scores, in particular, in a cohort of Russian patients. Many of the identified miRNAs are well known as participants in various cancer associated events. Further experimental studies with extended sampling are required to validate these results.

This work was performed using the equipment of EIMB RAS "Genome"center (http://www.eimb.ru/ru1/ckp/ccu_genome_c.php).
Funding: This work was funded by the Russian Science Foundation grant no.18-75-10127.

PS-15-011
Liquid biopsy and lung cancer
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Background & objectives: Cell-free tumour DNA (cfDNA) found in blood plasma has been applied for the detection of EGFR mutations in lung cancer. The objective of study was examination of EGFR mutation frequency in liquid biopsy and its correlation with clinical characteristics.
Methods: This study, conducted at the Institute for Lung Diseases of Vojvodina, in the period from October 2016 to October 2019, included 75 patients with advanced non-small cell lung cancer, who underwent liquid biopsy and EGFR testing. cfDNA was isolated using the Cobas®cfDNA Sample Preparation Kit. The target DNA was amplified and detected using real time PCR Cobas®EGFR Mutation Test v2.
Results: Average age in the investigated population was 63.4 years. There were 74.7% men and 25.3% women. Overall EGFR mutation rate was 9.3%. The most common EGFR mutations were deletions in exon 19 and single-point mutation L858R in exon 21. Majority of patients were active and former smokers; 60.0% and 29.0% respectively. There were only 11% non-smokers. We found statistically significant correlation between positive EGFR mutation and former smoking status (p=0.030). Association between females and EGFR mutation was statistically significant (p=0.042).
Conclusion: Although histological and cytological specimens should be the first sample choice for EGFR testing in lung cancers, liquid biopsy is a promising minimal invasive diagnostic approach.

PS-15-012
MiRNAs hypermethylation in gliomas
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Background & objectives: MiRNAs expression has been frequently deregulated in many cancers. This deregulation can be induced by epigenetic modifications, such as hypermethylation. Few studies have investigated miRNAs hypermethylation in gliomas. Herein, we aim to evaluate miRNAs methylation status and DNMTs overexpression in gliomas.
Methods: The methylation status of 15 tumour suppressor miRNAs was evaluated by specific PCR-methylation technique after DNA modification with sodium bisulfite in 112 cases of adult gliomas. DNA methyltransferases enzymes expression was assessed by immunohistochemistry. The association of miRNAs hypermethylation with DNMTs overexpression and tumour features was evaluated using SPSS.
Results: MiRNA methylation profile analysis showed an hypermethylation of miR-9, miR-34, miR-124, miR-107, miR-127, miR-137, miR-148, miR-193 and miR-203. Expression of DNMT1, DNMT3a and DNMT3b was detected in 45,5%, 21,4% and 7,1% adult gliomas, respectively. The association between miRNAs hypermethylation and DNMTs expression revealed a significant correlation between the overexpression of DNMT1 and the methylation of the miR-9 family, miR-34 family and miR-193a. For DNMT3b, its overexpression was significantly associated with miR-9-1, miR-9-3 and miR-34b/c. However, expression of DNMT3a showed a statistically significant association with hypermethylation of promoters of all miRNAs studied except miR-203a.
Conclusion: Our results suggest that miRNAs hypermethylation constitutes an epigenetic event that could be involved in gliomas pathogenicity.

PS-15-013
RET fusion testing in papillary thyroid carcinoma patients: a comparison of break-apart FISH and RNA-based NGS
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Background & objectives: After the approval of RET inhibitors for RET fusion-positive papillary thyroid carcinoma (PTC), we hypothesized that a comparison of testing assays is needed. Moreover, the sensitivity of FISH has been challenged, mainly driven by the presence of NCOA4-RET fusions.
Methods: A retrospective search of consecutive PTC cases with tumour size larger than 0.5 cm between January 2007 and December 2020 from the pathology archives was performed. All tumours underwent break-apart RET FISH (Vysis) with an automated scanning system (BioView). All the identified RET-positive PTCs were subsequently studied by targeted RNA-based NGS (Oncomine Comprehensive Assay v3, OCAv3).
Results: Analyses by FISH was successful in all 191 tumours. Sixteen RET-positive PTC (8.4%) were identified. The conventional and follicular histological variants accounted for the majority of RET-positive PTCs (37.5% each). A predominant conventional split signal pattern (≥2 signal diameter) was present in 15 tumours (94%). The percentage of tumour cells with this pattern ranged from 30-80%. Interestingly, isolated red signals (atypical pattern) were only absent in one case. The percentage of tumour cells with atypical pattern ranged from 0-42%. The RNA-based NGS confirmed the presence of a RET fusion in all 16 FISH positive PTCs. The most common partner was CCDC6 (94%). The remaining positive-PTC contained the ERC1-RET variant (6%).
Conclusion: The most frequent partner in this retrospective series of consecutive PTCs was CCDC6. Accordingly, the concordance between FISH and RNA-based NGS was perfect, with a 0% failure rate. The interpretation of RET FISH was straightforward in all cases due to the absence of subtle split signals or complex patterns.

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PS-15-014
p53 immunohistochemical staining and correlation with TP53 status
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Background & objectives: Strong and diffuse immunohistochemical staining of p53 at some carcinomas is interpreted as likely indicating a TP53 missense mutation. However, the significance of completely negative immunostaining is controversial. We analysed the correlation of p53 immunostaining and mutations in colorectal cancer.
Methods: A total of 99 cases of colorectal carcinoma were studied. Immunohistochemical procedures were performed according to Roche Ventana (anti-P53 (DO-7)) protocol. TP53 exons 5 to 8 were analysed by Sanger sequencing using the primers described by Asai et al (Asian Pac J Cancer Prev, 2014). In case of mutation, normal tissue was studied to confirm/discard the presence of germline variants.
Results: 69 samples presented strong immunostaining (positivity higher than 90% of cells) and in 30 tumours staining was absent or less than 1.5%.
Altogether, 62.7% (62/99) of samples carried a TP53 mutation. Among 69 IHQ positive samples, 48 (69,6%) had missense mutations. One sample presented a double mutation, which is unusual. Regarding negative staining samples, 14 out of 30 (46,7%) had protein-truncating mutations. Loss of heterozygosity (LOH), as a manifestation of chromosomal aneuploidy, was present in 51/62 samples with TP53 mutations (37 with missense and 14 with truncating variants); eight of the patients were homozygous (non-informative) for the analysed microsatellites. Among non-carriers, 24/37 presented LOH.
Conclusion: As described in the literature for other tumours, immunohistochemical staining for p53 can be used as a surrogate for mutational analysis also in colorectal cancer, with strong staining being associated with missense mutations and absent staining with protein-truncating variants in our series.
The higher frequency of chromosome alterations in tumours associated with TP53 mutations confirms its role in the chromosomic instability pathway. We cannot discard that the three TP53-mutant tumours carry other type of genomic alterations as translocations or amplifications.

PS-15-016
Categorization of medulloblastoma of childhood using genome-wide methylation assay
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Background & objectives: Precise diagnosis of childhood medulloblastoma is of critical importance to ensure delivery of tailored therapy, limiting side-effects of treatment. The goal was to assess genome-wide methylation assays in correctly categorizing these tumours in one of the four known molecular groups.
Methods: cDNA microarray methylation analyses were performed using combination of bisulfite conversion of DNA samples and the Infinium HD Assay (Illumina) for methylation. Microarray signals were detected using the Illumina iSCAN System. Genome Studio V2011.1 analysis software was used to analyse the raw data.
Results: Using bisulfite conversion followed by the Infinium HD methylation assay (Illumina) provided us with data files (iDAT) which were uploaded on a public domain classifier, a bioinformatic analysis tool provided online (courtesy of the German Cancer Research Center), this study was able to categorize all 7 samples attempted. The majority of the samples fell into two categories, either the "methylation class medulloblastoma, subclass groups 3" or the "methylation class medulloblastoma, subclass groups 4".
Conclusion: The Infinium HD methylation assay is a robust molecular technique that is able to categorize medulloblastomas of childhood compared to plain histomorphology, immunohistochemistry or both. Furthermore, the technique provides a genetic profile of each tumour by providing the copy number variations derived from the same assay.

PS-15-017
Evaluation of BRCA1 promoter hypermethylation (B1PHM) in ovarian carcinomas (OC)
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Background & objectives: B1PHM is observed in 10-30% of OC. This epigenetic event is associated with low BRCA1 protein expression and, therefore, it is considered as a mechanism of BRCA1 loss of function. Studies are needed to clarify its importance in clinical settings.
Methods: OC patients who underwent germline/somatic BRCA testing between 2015-2020 were selected (n=86). Both debulking or biopsy surgery specimens were analysed. Only FFPE specimen was used and the most significant block was selected. B1PHM was evaluated with MS-MLPA on selected samples (three CpG sites). A pyrosequencing assay, considering the most investigated CpG sites in literature, was also designed (fourteen CpG sites).
Results: MS-MLPA was applied in 54 cases. B1PHM was detected in all three CpG sites in 10/54 cases (18.5%). Methylation was confirmed in another tumour area and excluded in healthy tissue. In addition, 4/54 cases were partially methylated (18% to 23% of methylation in only one CpG site). Pyrosequencing was performed on entire OC cohort and MS-MLPA positive methylation status was confirmed (10/86, 12%). No other methylated cases were identified. The methylation percentages were comparable to those obtained by MS-MLPA and linear in all CpG sites analysed. The partial methylation status was confirmed only in one case (11% to 31% of methylation reproducible in all CpG sites of the CpG island).
Conclusion: B1PHM was observed in 12% of OC, according to literature reports, and both assays are robust in identifying B1PHM. The accurate selection of tumour areas/healthy tissue was essential for the correct interpretation of results. Given the low number of observations presented here, studies are needed to better define the "partial methylation" status. Furthermore, the analysis of therapeutic profile of these patients will help to better clarify the role of B1PHM as a predictive biomarker in OC.

PS-15-018
Technical reliability of PD-L1 laboratory developed test compared to companion diagnostic test in urothelial carcinoma: experience of a university hospital
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Background & objectives: In the last years, urothelial carcinomas (UC) have been tested to novel immune checkpoint inhibitors (ICI).
The main goal of this study is to compare the IHC expression of PD-L1 in UC by using SP 142, SP263 and 22C3 clones.
Methods: Forty-three samples of high-grade UC diagnosed in 2019 and 2020, corresponding to 34 males and 9 females, were selected from Centro Hospitalar e Universitário de Coimbra and tissue microarray (TMA) were constructed. Two commercial Kits (Ventana SP142 and Ventana SP263) and DAKO 22C3 Laboratory Developed Test (LDT) data were analysed using the SPSS.
Results: No statistic technical issues were found between different PD-L1 clones, especially when comparing LDT and Companion Diagnostic Test (CDT).
There were neither technical issues in our samples, or with antibodies.
Differences were not found between female and male taking into account the histological grade and stages at the time of diagnosis.
Female patients have higher PD-L1 22C3 ($p=0.051$) and SP263 positivity ($p=0.06$) compared with male.

Conclusion: Anti PD-L1 treatment has been associated with an increase of survival rate. Several studies show different agreement between tests comparing LDT and CDT, reinforcing the importance of ongoing quality control, laboratory personnel training and competency assessment. In our study no relevant technical issues differences were found between PD-L1 clones. It might be explained by improved skills and technical formation of the professionals. Therefore, our LDT protocol is optimized, since we achieved the same IHC quality when compared with CDT protocols.

PS-15-019

Analysis of the SARS-CoV-2 virus variability causing the COVID-19 disease among the inhabitants of the Świętokrzyskie Voivodeship

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Background & objectives: The main aim of the research is to analyse the degree of variability of the SARS-CoV-2 virus occurring in the Świętokrzyskie Voivodeship within one year from the outbreak of the global COVID-19 pandemic.
Methods: The material used for the research is RNA isolated from swabs taken from the nasopharynx of patients reporting symptoms of SARS-CoV-2 infection. The RNA was prepared for sequencing with the Illumina® RNA Prep, Tagmentation (L) with Enrichment kit. Then sequencing using the MiSeq Illumina.
Results: Analysis of the sequencing results of patient samples revealed many different lineages of SARS-CoV-2. The samples collected from patients in November were characterized by a variety of variants like B.1.1.258, B1.1. or B.1.1.595. For samples obtained in March, all analyses showed the presence of only variant B1.1.7. Additional KI polyomavirus Stockholm 60 virus infection was observed in one patient during sample analysis. The presence of the Human adenovirus C2 was detected in another patient.
Conclusion: The obtained results indicate the dominance of the British variant of the SARS-CoV-2 virus in 2021. It also causes much more severe symptoms. The study group will be enlarged to finally confirm the obtained results. The rapid development of the pandemic forces the search for new variants and the observation of the spread of the current ones. Therefore, we plan to analyse at least 150 samples.

PS-15-020

Copy number variation detection for the indication of targeted therapy in a lung cancer patients series. Next-Generation Sequencing panel vs fluorescent in-situ hybridization

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Background & objectives: Driver genes copy number variation (CNV) detection is crucial for treatment management in NSCLC. The aim of this study was to validate and compare CNVs detected by NGS panel with those obtained by a FISH assay.
Methods: This retrospective study included NSCLC patients evaluated at our institution from 2019 to 2020. All FFPE samples underwent routine ERBB2 and MET FISH amplification study and a complete morphomolecular diagnostics, CNV, fusions and gene mutations analysis using a 52 genes NGS panel. A comparison analysis based on the number of copies of each gene detected by each technique was performed.
Results: Series included 201 NSCLC patients. In 31 (15,4%) patients a CNV was detected by NGS in genes not tested by FISH (MYC, FGFR1, CCND1, NF1, EGFR, CDK6 and KRAS). FISH analysis for MYC, FGFR1, CCND1 and EGFR confirmed the 100% of these alterations. Considering FISH testing as the gold-standard for ERBB2 and MET CNV, only 2 ERBB2 and 2 MET CNVs, respectively, were identified by NGS. These 4 CNVs detected by both techniques presented more than 10 copies of each gene by FISH signal counting. In the discordant ERBB2 FISH positive-NGS negative tumours an average of 4.3 to 7.8 ERBB2 copies were detected by FISH probably due to CNV heterogeneity.
Conclusion: NGS panel increases the percentage of NSCLC patients suitable for a target therapy as it screens 52 genes in one single assay.
ERBB2 and MET FISH assay performs better than the NGS panel as it is capable to detect CNV when less than ten copies of the gene or when heterogeneity of CNVs are present in tumour cells.
NGS and FISH assay have the same accuracy in the detection of CNVs of MYC, FGFR1, CCND1 and EGFR.

PS-15-021

Validation of the Biocartis Idylla System for BRAF and KRAS mutations in formalin fixed tissues

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Background & objectives: A retrospective, single-centre study validating the use of the Biocartis Idylla v-raf murine sarcoma viral oncogene homolog B (BRAF) and Kirsten rat sarcoma viral oncogene (KRAS) mutation tests for use in pan tumour types, particularly, non-small cell lung cancer (NSCLC).
Methods: Archived formalin-fixed paraffin embedded tissue samples from resection specimens were sourced from deceased patients, following approval from Blackpool Teaching Hospitals Research and Development Department. Samples include those with known mutations in the BRAF and KRAS genes. All tests were provided by and performed using the Biocartis Idylla system which uses real time PCR to detect mutations in extracted DNA.
Results: The KRAS study tested samples from NSCLC patients with unknown KRAS mutation status. Of 75 samples tested for KRAS mutations 46% (n=35) of these have been found to have a KRAS mutation within exons 2, 3 and 4 of the KRAS gene. Of these, 5.7% (n=2) have been G12A; 20% (n=7) G12D; 28.6% (n=10) G12C; 5.7% (n=2) Q61H; and 40% (n=14) G12V mutations.
112 (n=75 NSCLC; n=23 skin; n=6 lymph node; n=2 bone; n=6 of each of rectum, jejunum, thyroid, trachea, pleura, FNA) samples were tested for mutations in codon 600 of the BRAF gene. 24 samples carried a mutation (n=20 V600E; n=4 V600K) and 88 samples had no mutation.
Conclusion: The study has shown a 46% mutation rate for KRAS mutations in NSCLC samples, and with a KRAS G12C inhibitor on the horizon we have shown that it is feasible to use KRAS testing as a screening tool and for treatment stratification purposes in parallel. Results from the BRAF validation demonstrate the ability to detect mutations in the BRAF gene in a number of tissue types.

Funding: Biocartis have provided all test cartridges for the study.

PS-15-022

Evaluation of microsatellite instability in colorectal cancer samples by the ddPCR microsatellite instability assay in comparison to immunohistochemistry and fragment length analysis and in correlation to the tumour mutational burden (TMB) status

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Background & objectives: Alongside prognostic value microsatellite instability (MSI) is a predictive biomarker for immune checkpoint therapy response.

This study evaluates MSI in colorectal cancer by ddPCR (Bio-Rad) in comparison to immunohistochemistry (IHC), fragment length analysis and correlates results to the TMB status.
Methods: Eleven colorectal cancer samples with known MSI status estimated by IHC and MSI-PCR were tested with the ddPCR MSI Assay on the QX200 Droplet Digital PCR System (BioRad). TMB was evaluated with the Oncomine Tumour Mutation Load Assay on the Ion S5 Sequencing System (Thermo Fisher Scientific). TMB was calculated on the Ion Reporter 5.10 (Thermo Fisher Scientific).
Results: The MSI status of the eleven colorectal cancer samples were successfully estimated by the ddPCR MSI assay. Six of the eleven samples were microsatellite instable (MSI) and five of the eleven samples were microsatellite stable (MSS) as previously classified by IHC and fragment length analysis. Further, the six MSI samples were all TMB high and the five MSS samples were all TMB low. In sample 5 the MSI status could not be determent by fragment length analysis as no normal tissue was available. In this sample another DNA-based parallel sequencing approach confirmed MSI.
Conclusion: This study showed that the ddPCR Microsatellite Instability Assay can be used reliably for MSI assessment in colorectal cancer samples and demonstrated a good correlation between MSI and TMB status.

PS-15-023
Molecular biomarkers of glioblastoma according to the latest WHO's classification "2016"
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Background & objectives: Glioblastoma is the most common and aggressive primary brain tumour in adults despite therapeutic management. The WHO classification established a diagnosis based on histological and molecular criteria. The objective is to detect the molecular alterations in order to improve patient survival.
Methods: A retrospective study was conducted on 106 patients with glioblastoma
Histological and immunohistochemical study (antibodies used: anti-p53, anti-ki67, anti-ATRX and anti-IDH1) were performed.
Codon 132 of the IDH 1 gene and codon 172 of the IDH 2 gene were amplified and sequenced.
Amplification of exon 20 of the EGFR gene was identified by qPCR and confirmed by FISH.
Results: The patients included in the study were 72 men and 34 women, aged 10 to 83 years with an average age of 46 years.
P53 expression is positive in 44 cases of glioblastoma patients. Immunostaining for ki67 was positive in 88 cases. ATRX expression was conserved in 27 of 32 cases.
The use of the anti-IDH1 antibody shows cytoplasmic and diffuse positivity in 13.2% of glioblastoma cases.
The substitution Arginine-Histidine R132H (IDH1) was detected in 14 cases marked positively by immunohistochemistry. While the substitution Arginine-lysine R172K (IDH2) was absent in all glioblastoma cases.
EGFR has been amplified by qPCR in 17 cases. Nevertheless, only 14 glioblastomas were confirmed by FISH.
Conclusion: Glioblastomas are heterogeneous tumours. A systematic search for molecular alterations, in particular those of IDH and EGFR, to distinguish primary from secondary glioblastomas and should be imposed in order to establish a good
diagnosis and better management of patients with glioblastoma. The IDH mutation characterizes secondary glioblastomas while the EGFR gene amplification strongly suggests the diagnosis of primary glioblastomas.

PS-15-024
Microsatellite instability status using a next-generation sequencing assay and Anchored Multiplex PCR chemistry
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Background & objectives: Microsatellite instability (MSI) is high in tumours with DNA mismatch repair gene deficiencies. Here we evaluate a DNA-based Anchored Multiplex PCR (AMPTM) next-generation sequencing (NGS) assay designed to support parallel MSI detection and somatic variant profiling in various tumour types.
Methods: Our VariantPlex® MSI assay examines the abundance of repeat lengths at 114 microsatellite loci after collapsing PCR duplicates using molecular barcodes. The diversity of lengths is used to determine stability at each locus. The proportion of microsatellite loci called as unstable relative to an unmatched normal cohort enables categorization of samples as microsatellite instability high (MSI-H) or microsatellite stable (MSS).
Results: Our assay and prototype algorithm perform very well on previously characterized FFPE samples from multiple tissue types. When tested on a set of 200 samples (50% MSI-H, 50% MSS as defined by polymerase chain reaction (PCR) and capillary electrophoresis (CE)), we were able to call MSI-H status with 97% sensitivity (95% binomial confidence interval of 91.5-99.4%) and 100% specificity (96.4-100%) using a threshold of >23% unstable sites for MSI-H and ≤23% for MSS. Performance was consistent under sub-optimal conditions (low input mass, tumour purity, and read depth) and in the context of multiple panel sizes.
Conclusion: Using tumour only FFPE-derived inputs, our assay makes MSI status calls that are strongly concordant with a PCR and CE assay without requiring a matched normal. Molecular barcodes incorporated into our AMP chemistry enable unique molecule deduplication and error correction, which support robust assay performance across a range of conditions. Our design also functions modularly, meaning it can be used as a stand-alone MSI solution or as part of a larger customized VariantPlex panel.

PS-15-025
Genetic alterations detected in metastatic cutaneous malignant melanoma cases, single centre experience
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Background & objectives: Genetic alterations disrupt key signalling pathways in cutaneous melanomas. Alterations, which are known to be associated with various types of melanomas and UV radiation exposure, can help to predict targeted therapy, drug resistance, and provide insight about progression and prognosis.
Methods: Next generation sequencing method was performed on paraffin tissue blocks of 89 metastatic cutaneous melanomas which had been diagnosed between 2017 and 2020 cases in our department. One of the cases was insufficient. The patients' ages were between 22 and 92 (median 67). Primary tumour blocks of 53 cases and metastatic tumour blocks of 36 cases were used.
Results: Pathogenic variations in BRAF, NRAS, EGFR, c-KIT, KRAS, MET genes were detected in 41 (46,59%), 5 (5,68%), 4 (4,55%), 2 (2,27%), 2 (2,27%), 1 (1,14%) of the patients, respectively.
Uncertain significance were detected in EGFR, c-KIT, KRAS, PIK3CA, NRAS, PDGFRA, ERBB2, ERBB4 gene in 13 (14,77%), 7 (7,95%), 7 (7,95%), 6 (6,82%), 2 (2,27%), 2 (2,27%), 2 (2,27%), 2 (2,27%) of the patients, respectively and 1 (1,14%) of the cases were detected for each of the genes of BRAF, MET, GNAQ, FBXW7, RAF, MAP2K1, MAP2K2, FGFR3, FGFR2, NOTCH1.
Also, likely benign alterations of 2 (2,27%) PDGFRA, 1 (1,14%) KRAS were detected.
There was no pathogenic variation in 21 (23,86%) cases.

Conclusion: The discovery of the molecular features of melanomas continues to reveal predictive therapeutic markers, treatment approaches and prognostic markers. Next generation sequencing methods pave the way for advancing the knowledge about the pathogenesis of melanoma and new treatment strategies.

PS-15-026

The landscape of NTRK fusions detected by comprehensive genomic profiling in patients with advanced cancer in a large healthcare system

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Background & objectives: NTRK gene fusions are pan-cancer predictive diagnostics for TRK inhibitors. This study employed tumour comprehensive genomic profiling (CGP) using RNA and DNA hybrid capture sequencing to investigate NTRK alterations in a large patient cohort from a community health system.
Methods: Patients in the Providence St. Joseph Healthcare system diagnosed with advanced cancer from July 2019 through March 2021 received reflex CGP testing of FFPE tumours using the TruSightTM Oncology 500 or 170 assays (Illumina, Research Use Only) as part of their clinical care. Using deidentified electronic medical record data and CGP results, NTRK1, NTRK2, and NTRK3 fusion transcripts were assessed.
Results: 5,263 patients received CGP testing. 22 of 5263 (0.4%) tumours were found to harbour an NTRK gene fusion; 3(14%) of these involved novel fusion partners (SFPQ-NTRK1, C1orf54-NTRK1, SOX6-NTRK2). The most frequently observed fusions were MYO5A-NTRK3 (6 cases), TPM3-NTRK1 (3), EML4-NTRK3 (2) and ETV6-NTRK3 (2). Tumour types where >1 NTRK fusions were observed included melanocytic lesions (8 of 69 cases), non-small cell lung carcinoma (4 of 1788), papillary thyroid carcinoma (2 of 45), and colorectal adenocarcinoma. (3 of 522). Co-occurrences of NTRK fusions with other targetable alterations included high MSI and TMB in 2 colorectal cases and IDH1 R132H in a glioma case.
Conclusion: While many assays have technical limitations that disallow the detection of all relevant fusion partners, hybrid capture RNA sequencing can identify novel as well as known partners, permitting a more complete evaluation. The low frequency of NTRK fusions in most tumour types suggests that routine screening may be the most effective approach for identifying patients who are candidates for TRK inhibitor therapy. CGP provides a complete assessment of actionable gene alterations to inform the routine clinical care of cancer patients.

PS-15-027

The first experience of NTRK testing in Russia. Multicentre research

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Background & objectives: The first NTRK multicentre research in tumours of different localisation started in Russia in March of 2020. More than 40 cities from all 8 regions were included in research. All tumour samples have been analysed by 5 hospitals in Moscow.
Methods: IHC staining was made by Ventana pan-TRK (EPR17341) antibody and OptiView DAB IHC Detection Kit in Ventana BenchMark Ultra Slide stainer. An appendix was used as normal tissue control.
Results: For one year (from 01.03.2020 to 01.04.2021) 799 FFPE specimens were tested. Broad range of tumour types was included: breast and salivary gland secretory carcinoma, papillary thyroid carcinoma, colorectal carcinoma, lung adenocarcinoma, squamous cell carcinoma of the head and neck, skin melanoma, infantile fibrosarcoma, mesoblastic nephroma, soft tissue sarcomas and other.
There was 70/799 (8.7%) IHC pan-TRK-positive tumours. Cases were assessed for staining intensity and localization. Staining of variable intensity was noticed in nuclear, cytoplasm and membrane of tumour cells. 6/39 (15.3%) specimens were NTRK-fusion positive via NGS (2 cases with FMI) and FISH (4 cases).
Conclusion: The first NTRK multicentre research have found 8.7% IHC panTRK-positive tumours. Positive staining with confirmed NTRK fusion was seen in thyroid carcinoma, breast and salivary gland secretory carcinoma and infantile fibrosarcoma and mesoblastic nephroma.

PS-15-028

An economic approach of preanalytical variables on quality assessment of Silver In Situ Hybridization in Albania

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Background & objectives: Considering the importance of SISH, his involvement in routine examinations is an important key of success. Highlighting problems, optimizing and reducing the average cost are challenges to standardization of this method at NUHC "Mother Teresa" as only centre in Albania.
Methods: 70 patients from the University Hospital Center "Mother Teresa" with Ad.Ca of gastrointestinal tract, who were already proved as HER2 (2+) by immunohistochemistry were taken in exam. HER2 gene amplification for these patients was assessed by silver in situ hybridization method (SISH) with Ventana Benchmark XT using Single SISH, Dual SISH and SISH Cocktail assay kit.
Results: In a cohort of 60 patients analysed with SISH method, 25% (15) of them showed problems in implementation and unable to be assessed. Among the problems encountered included the presence of black and red haze, the presence of peripheral signal, poor staining, lack of signal, etc. After repeated examinations within a short time frame, some of these problems were resolved. Switching to SISH cocktail kit reduced time but included higher costs. Single SISH results were comparable with Dual SISH. HER2 gene amplification after recurrence was observed in 35% (21) of cases.
Conclusion: Preanalytical phase preparation of samples is an essential factor to be taken into consideration before using SISH for further review of HER2 status in gastrointestinal Ad.Ca. Tissue fixation on 10% neutral buffered formalin for no more than 48 hours and continuous operational status of VENTANA Benchmark XT are essential conditions that must be met to avoid false positive/negative results and large losses in the cost of realization. Single SISH is a good, more economical alternative to Dual SISH and SISH cocktail.

PS-16 | Nephropathology Posters

PS-16-002

The lesional kaleidoscope in glomerulopathies: experience of a Romanian referral nephropathology centre

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Background & objectives: Renal biopsy provides relevant data for glomerulonephritis (GN) diagnosis. However, identical patterns are shared by different diseases or mechanisms. We aimed to analyse the GN diagnosed in a Romanian referral nephropathology centre, based on their histological and clinical features.
Methods: The study group comprised 442 biopsies performed between 2011 to 2019. The biopsy specimens were examined in immunofluorescence and light microscopy (hematoxylin and eosin, periodic acid Schiff,

Masson trichrome, Jones silver methenamine stains, Congo red stains). The baseline clinical characteristics included nephrotic syndrome (NS), acute nephritic syndrome (ANS), asymptomatic urinary abnormalities, acute kidney injury (AKI), and chronic kidney disease (CKD).
Results: Primary GN represented 59.5% of cases, secondary GN – 12.7%, vascular nephropathy – 7.5%, tubulointerstitial nephropathy – 1.1%. Among primary GN, membrano-proliferative GN (24.4%; 41% of primary GN) and membranous GN (21.9%; 36.9% of primary GN) were the most frequent diagnoses, followed by idiopathic crescentic GN (6.1%; 12.2% of primary GN), IgA nephropathy (3.8%; 6.5% of primary GN), FSGS (2.9%; 4.8% of primary GN). Secondary GN included lupus nephritis (7.5%; 58.9% of secondary GN), amyloid nephropathy (2%; 16% of secondary GN), infection-related GN (1.4%; 10.7% of secondary GN). Associated clinical features were NS (35.3%), ANS (21.9%), AKI (20.1%), CKD (16.5%), persistent haematuria (6.1%).
Conclusion: Our study revealed the GN distribution model in the population with renal pathology in NE Romania. The rate of biopsies was constant. The comparison to other world renal reports showed a higher frequency of membrano-proliferative GN and membranous GN, with an upward trend, a lower incidence of minimal change disease and mesangial GN, with a downward trend, a higher frequency of infection-related GN; vascular nephropathy and tubulointerstitial occur in an important proportion of patients with NS and AKI.

PS-16-003
Clinicopathological correlation of paediatric Alport syndrome
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Background & objectives: Alport syndrome is a hereditary disorder which is characterized by haematuria, sensorineural hearing loss and ocular abnormalities. In this study, 14 Alport syndrome cases were re-evaluated by clinicopathological findings to define the clues of morphological features.
Methods: Totally 14 paediatric Alport syndrome patients were enrolled into this study. All cases were diagnosed in a single centre between 2006-2020. Clinical, and laboratory data were obtained from medical records; light microscopy, immunofluorescence and electron microscopy features were correlated with clinicopathological features.
Results: Nine male and 5 female patients' mean age was 10 years old. Familial renal failure was seen in 57,1% of all patients. The most common clinical symptom was macroscopic haematuria (64,2%). The glomerular filtration rate was >90 ml/min/1.73m2 except two cases had chronic renal failure (p=0.08) at the time of diagnosis. Predominantly, patients had mesengial proliferation (71%); fibrosis, tubular atrophy were observed in 41% of all patients and six patients showed normal morphology under light microscope. Immunofluorescence microscopy lacked staining except two individuals exhibited weak C3 and weak IgM staining. Ultrastructurally all patients had thinning, thickening and lamellation of basement membrane (min:125-max:1000)
Conclusion: This study evaluates 14 paediatric cases with pathological and clinical features. Particularly patients were in early stage of Alport syndrome. Nonspecific morphology make the diagnosis difficult thus Alport syndrome should be kept in mind in patients which have features of concordance of haematuria and mesengial proliferation.

PS-16-004
Application of direct stochastic optical reconstruction microscopy (dSTORM) to the histological analysis of human glomerular disease
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Background & objectives: Electron microscopy (EM) is used for diagnosis in human glomerular diseases Single molecule localisation microscopy (SMLM) can extend conventional immunofluorescence to resolution near EM. We are exploring the diagnostic value of dSTORM in frozen and paraffin-embedded clinical kidney samples.
Methods: "histoSTORM": Immunofluorescence was carried out on frozen and formalin-fixed paraffin embedded (FFPE) tissue from renal biopsies with Membranous glomerulonephritis (MGN); Lupus nephritis and Minimal change disease. IgG and the Glomerular Basement Membrane (GBM) was documented with ifluor-647 and Laminin-AF555 respectively. using antibodies in routine clinical use. SMLM was undertaken on these tissue sections using an opensource platform for dSTORM.
Results: histoSTORM was applied to immunofluorescence of both FFPE and frozen histological sections using standard clinically approved antibodies. dSTORM images rendered at 25 nm per pixel reveal well-defined subepithelial deposits in MGN and enlargement of the GBM that are consistent with those observed by EM. In a case of stage IV lupus nephritis, mesangial, subendothelial and subepithelial IgG deposits are readily observed with dSTORM and recapitulate the distribution of electron dense immune complex deposits documented with EM. dSTORM also enables GBM thickness measurements on paraffin-embedded tissue with resolution below diffraction in a case of Minimal change disease.
Conclusion: While this study does not establish that histoSTORM can fully replace EM in renal diagnosis, it does provide evidence of added value relative to Light Microscopy and IF. The large dSTORM field of view (120 μm square) and standard sample preparation make it more convenient than EM. However, prospective studies of large case series are required to establish its clinical utility. histoSTORM may have potential for wide clinical impact, especially in less well-resourced settings where EM is not available.

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PS-16-005
Possible role of cell adhesion genes in the development of IgA nephropathy
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Background & objectives: The pathogenesis of IgA nephropathy (IgAN) isn´t yet fully understood. Previous GWAS studies have related the development of IgAN to several gene mutations, but the potential role of cell adhesion gene mutationsin in its pathogenesis has not been previously explored.
Methods: We included 22 patients, 14 males and 8 females, aged 18-74 years, with IgAN, from 2004 to 2019, with clinical follow-up of at least 2 years. The histological findings of all renal biopsies were reviewed, and a total of 29 genes of cellular adhesion molecules were studied. The rate of mutations in our IgAN patients were identified using UnifiedGenotyper.
Results: All patients have mutations. Of the 29 genes studied, we found mutations in all of them, except for the RHOA and LPAR5 genes.
There are two genes that present mutations in all cases: TNC and FN1, and they are non-silent. Furthermore, among the mutations found, there are mutations that do not occur in all cases, but these mutations found are non-silent, as are the cases of the SELE, ELN, ITGB3, LPAR3 and LPAR4 genes.
On the other hand, there are many genes in which mutations are found, none of them are non-silent, such as the ITGA5, ITGB1, RHOC, LPAR1, TPM1, VCAM1, ARHGDIA, TRAM1, ACTB and CDC42 genes.
Conclusion: The molecular study of adhesion molecules in IgAN could allow us to identify molecular markers that allow us to obtain clear

differential mutational patterns of other primary glomerulopathies, in addition, we could classify it into subgroups and select specific therapies.

PS-16-006

Clinical relevance of C4d-positivity in the different compartments of transplanted kidneys

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Background & objectives: Antibody mediated rejection commonly deteriorates transplanted kidneys causing graft-loss. C4d-positivity in peritubular capillaries proved to be important, but other kidney-compartments are less investigated for C4d-staining. We aimed to evaluate the clinical relevance of arteriolar and glomerular C4d-positivity and graft survival.
Methods: Biopsies from transplanted kidneys (n=122) and explanted allografts (n=30) from 135 patients were involved in the study based on any C4d positivity. The specimens originated from the archive of 1st Department of Pathology and Experimental Cancer Research, Semmelweis University, Budapest, Hungary. Presence of C4d-positivity in any kidney compartment was correlated with laboratory and clinical data of the graft-function and graft-survival.
Results: We found C4d staining in the glomeruli in 69 cases, in the arteries in 39 cases and in the PTCs in 114 cases. We found a significant correlation between C4d-positivity in the arteries and graft loss. Furthermore, we also found significant correlation between the C4d staining of the glomeruli and decrease in long-term eGFR levels, graft function, and a correlation between PTC staining and an initially elevated serum creatinine and urea level. However, we couldn't find association between C4d staining in the PTCs and long-term graft survival, which is contrary to some literature data,
Conclusion: Our results suggest that C4d positivity in the biopsies outside the peritubular capillaries might have clinical relevance regarding graft-survival and graft function, and thus may have prognostic value for graft survival and deterioration of graft function. As our study involved a relatively small number of cases, it should be further investigated in larger studies.

PS-16-007

Crescents in glomerular diseases: evaluation of 243 kidney biopsies with crescents

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Background & objectives: Crescentic glomerulonephritis (CrGN) is a morphologic reflection of severe injury of glomeruli rather than a specific disease. On the basis of immunopathologic features it can be classified into three major categories: pauci-immune, anti-glomerular basement membrane (anti-GBM), and immune complex glomerulonephritis.
Methods: Kidney biopsies with any crescents (cellular/fibrocellular) evaluated in our department between June 2014 and March 2021 were included in the study. Crescents were defined as extracapillary hypercellularity of >2 cell layers involving >10% of the capsular circumference composed of cells and fibrous matrix. Demographic data and final diagnoses according to histopathological and immunofluorescence findings were recorded and classified.
Results: The mean age of patients was 45 years (range 1 - 85 years). There were 141 males and 102 females. The aetiology of CrGN was immune complex mediated in 135 (56%), pauci-immune in 95 (39%), and anti-GBM glomerulonephritis in 11 (5%) cases. Among immune complex glomerulonephritis cases the most common diagnosis was IgA nephropathy (n=82) followed by membranoproliferative glomerulonephritis (n=15), IgA vasculitis (n=12), lupus nephritis (n=7), C3 glomerulopathy (n=4), postinfectious glomerulonephririts (n=3), and diabetic nephropathy (n=2). The number of cases with >50% crescents was 45 (19%). Among these, 33 (73%) cases were pauci-immune, 7 (16%) cases were anti-GBM, and 5 (11%) cases were immune complex glomerulonephritis.
Conclusion: Crescentic glomerulonephritis could be caused by many different aetiologies. Although some crescents can be seen in immune complex glomerulonephritis, many studies have shown that majority of the cases with diffuse crescents are pauci-immune glomerulonephritis, especially in older ages. In our series when any number of crescents are taken into account the most common diagnosis was IgA nephropathy. However, in biopsies with more than 50% crescents the most common diagnosis was pauci-immune glomerulonephritis compatible with previous studies.

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PS-17-001

Methylation profiling as a molecular diagnostic tool in neuropathology: a lesson from two cases

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Background & objectives: In the past, the diagnosis of central nervous system (CNS) tumours was based mainly on histology. In the 2016-WHO classification, the integration of molecular and histological features is recommended. Many reports revealed this integration is achieved by methylation profiling (MP).
Methods: Two cases were evaluated histologically, and the histology was unclear or unexpected. Therefore, MP was performed. The first case, 5-year-old boy diagnosed as a case of AT/RT. The second case, a 7-year-old boy had a glioma with atypia and anaplasia although the Ki-67 was low.
DNA extracted and followed by 450K/EPICS array hybridization. Automated reports are then generated by MolecularNeuropathology.org.
Results: The first case was re-evaluated after the MP, and the histopathological diagnosis was not correct. The result of the MP suggested the diagnosis as diffuse midline glioma H3 K27M mutant. The copy number variation profile revealed a normal status of INI-1 indicating the IHC results that showed loss of INI-1 was not conclusive.
The second case showed atypical glioma with anaplastic features histologically. However, the results of MP concluded the diagnosis as a low-grade pilocytic astrocytoma. The later observation is consistent with the low expression of Ki-67.
Conclusion: In this study, two cases are presented to show how is effective to implement MP as a diagnostic tool. The MP in diagnostic neuropathology is highly useful mainly when the tumour has unexpected/unclear histology, affecting children, or need detailed molecular subclassification.

PS-17-002

Rare thyroid transcription factor 1 (TTF-1) staining posterior pituitary tumours: twenty-year experience in a single institution

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Background & objectives: Tumours of the neurohypophysis (pituicytoma, granular cell tumour, spindle cell oncocytoma) are low-grade tumours with TTF-1 immunoreactivity. They represent a daunting

diagnostic challenge. We analyse their frequency in our hospital along with clinical, radiologic and histologic characteristics and treatment outcome.
Methods: We conducted a retrospective review of histologically diagnosed pituitary tumours in our institution from January 1999 to January 2021. Five cases of tumours arising in neurohypophysis were found. In addition to the histopathological information, we collected data relating to age, gender, initial radiological diagnosis, cancer treatment and clinical follow up.
Results: From an average of 700 pituitary surgeries per year, 0, 7% resulted in posterior pituitary tumours (three females, two men). Mean age at diagnosis was 62 years. Clinical symptoms were related to mass effect. One case was an incidental finding in a clinical autopsy and four cases were endoscopic resection specimens, with and initial pathological diagnosis of hypophyseal adenoma and craniopharyngioma. Tumour subtypes analysis included two pituicytomas, one spindle cell oncocytoma and two granular cell tumours. All cases expressed nuclear TTF-1. During follow-up two cases showed tumour persistence, one despite radiation therapy.
Conclusion: The limited number of confirmed cases in our series is consistent with studies in the literature. Histopathological findings are essential for the diagnosis of posterior pituitary tumours due to the lack of specific clinical signs and radiological features. Despite a low proliferation index relates to a benign behaviour, an appropriate clinical monitoring and close follow up is advisable.

PS-17-003
Comorbid Alzheimer's and Creutzfeldt–Jakob disease: micromorphology of colocalizing extracellular protein aggregates and neuronal dystrophy
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Background & objectives: Alzheimer's disease (AD) and sporadic Creutzfeldt–Jakob disease (sCJD) are characterized by extracellular pathologically conformed aggregates of amyloid proteins. The aim of our pilot study was to simultaneously visualize Aβ-, PrP- and AT8-immunoreactive structures, to describe the micromorphology of plaques.
Methods: To investigate the potential morphological colocalization of Aβ with PrPSc aggregates, and AT8-positive dystrophic neurites, we examined the hippocampal regions (archicortex and neocortex) of 20 subjects with confirmed comorbid AD and sCJD using neurohistopathological analyses, immunohistochemical methods, and confocal fluorescent microscopy.
Results: Our data showed that extracellular Aβ and PrPSc aggregates tended to be, in most cases, located separately, and "compound" plaques were relatively rare. We observed PrPSc plaque-like structures in the periphery of the non-compact parts of Aβ plaques, as well as in tau protein-positive dystrophic structures. Our data showed that PrPSc aggregation could dominate during co-aggregation with non-compact Aβ in the periphery of Aβ plaques. The main types of Aβ and PrPSc plaque colocalizations identified were: (1) non-compound and minimal compound plaques, (2) central core deposits, and (3) diffuse plaques.
Conclusion: The results as presented indicate that a specific subset of Aβ, in particular the non-compact component of Aβ plaque, where Aβ42 predominates, exhibits higher levels of interaction with PrPSc and, thus, in certain circumstances, could be assumed to act as the PrPSc seeds within the brain. The AD score, and prion protein subtype with codon 129 methionine–valine (M/V) polymorphisms in sCJD, while representing key characteristics of these diseases, did not correlate with the morphology of the Aβ/PrPSc co-aggregates.

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PS-17-004
Epidermoid cysts of the brain: clinicopathological report of 4 cases
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Background & objectives: Epidermoid cysts are rare benign lesions of the central nervous system that accounts for approximately 1 – 2% of all intracranial tumours. They arise from entrapped cells of the mesectoderm that originate from the neural crest during foetal development.
Methods: This is a retrospective study of epidermoid cyst of the brain diagnosed between 01 January 2014 – 31 December 2020. Clinical information, radiological investigations and hematoxylin and eosin-stained sections were retrieved and reassessed.
Results: The four patients had mean age of 30,8 years (range: 3 – 63), one male and 3 females. All four patients presented with headache and one associated with seizures. On CT and MRI of the brain, two patients had posterior fossa, one occipital and one extra-axial tumours. Two patients with posterior fossa tumours had associated hydrocephalus. All tumours were successfully removed, and histopathological assessment confirmed epidermoid cysts. All patients showed clinical improvement and were discharged home.
Conclusion: Epidermoid cysts of the brain are rare and still remain a preoperative clinico-radiological conundrum as they may be indistinguishable from other intracranial tumours. Therefore, collaboration with histopathologists is advised in the management of these cases.

PS-17-005
Histopathological spectrum of paediatric central nervous system tumours seen at a single academic centre in South Africa
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Background & objectives: Central nervous system tumours are the most common solid tumours in paediatric population with associated increased morbidity and mortality. However, few studies regarding paediatric central nervous system has been undertaken in the African continent including South Africa.
Methods: This is a retrospective histopathological analysis of paediatric central nervous system tumours diagnosed between 01 January 2012 – 31 December 2020. Clinical information and hematoxylin and eosin-stained sections were retrieved and reassessed.
Results: The study consisted of 24 patients with mean age of 5,45 years (range: 1 - 18), 19 males and 5 females. The histopathological diagnosis consisted of 6 pilocytic astrocytoma (25 %); 4 medulloblastoma (16,7 %); 2 meningioma WHO grade I, embryonal tumour, atypical teratoid rhabdoid tumour, craniopharyngioma and pineoblastoma, each (8,3 %); 1 gliosarcoma, primitive neuroectodermal tumour (PNET), choroid plexus papilloma and arteriovenous malformation (4,2 %).
Conclusion: Our study had equal distribution of benign and malignant tumours. In accord with existing literature, pilocytic astrocytoma and medulloblastoma were the common benign and malignant tumour, respectively.

PS-17-006
SARS-CoV-2 and skeletal muscle. Autopsy case series
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Background & objectives: Early studies have indicated that there is also considerable musculoskeletal dysfunction in some COVID-19 patients, although long-term follow-up studies have yet to be performed. The

objective of this work is to identify histopathological lesions in patients who died from COVID19.
Methods: There have been 13 autopsies of patients who died by COVID-19, (4 deaths were occurred due to another circumstance not related to COVID19). Samples were taken for study in freezing, paraffin, electron microscopy and microbiology of deltoid and psoas muscles, and the quadriceps anterior muscle in some times. The clinical history was analysed to identify neuromuscular signs and symptoms.
Results: The muscles analysed showed non-specific degenerative-regenerative processes. And no nuclear internalizations were seen. Angulated fibres and atrophy were found in two psoas muscles of two patients with> 3 months of admission, with isolated target-type fibres, probably related to critical patient myopathy. No vasculitic or thrombotic findings were identified. Immunostaining for this virus was negative, a fact that was confirmed with RT-PCR.
Conclusion: With the data available in our series, it cannot be stated that skeletal muscle presents lesions typical of SARS-CoV-2 infection, nor has the presence of the virus been demonstrated by immunohistochemistry or RT-PCR, despite the fact that 8 patients had PCR positive in the naso-pharyngeal exudate.

PS-17-007
Tumoral recurrences and anaplastic transformation of ganglioglioma: a 9-year study from a single neuropathology unit
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Background & objectives: Ganglioglioma represents a benign mixed neuronal-glial tumour, occurring most commonly in the paediatric population and frequently located in the temporal lobe. Anaplastic transformation of gangliogliomas has been reported in less than 35 cases in the scientific literature.
Methods: This is a retrospective study including all gangliogliomas, benign or atypical, that recurred or underwent anaplastic transformation during a period of 9 years (2012-2020). Nine cases were identified and clinical and imaging data was retrieved from the virtual database and from the clinical charts. We thoroughly re-examined all Hematoxylin-Eosin, aiming to establish correlations that could predict the poor outcome.
Results: Clinically, 44.4% were located in the parietal lobe, while 22.2% affected the temporal lobe and only 55.5% presented with epileptic seizures. Atypical features, suggestive for the diagnosis of atypical ganglioglioma were present in 55.5% of the initial cases. 44.4% of cases have had anaplastic progression, 75% of these cases evolving towards an anaplastic ganglioglioma and 25% towards a glioblastoma. Mean follow-up was 53 months, period in which 75% of those who had anaplastic transformation have had a fatal outcome. Histologically, rare neuronal mitoses were identified in 44% of cases and, correlating with those cases that have had an anaplastic transformation. Perivascular inflammation was present in only 55.5% of cases.
Conclusion: Our study shows that the presence of recurrences and anaplastic transformation is more often encountered in adults with a mean age of 39 years and in cases with an atypical location. From a histological point of view, only the presence of atypical neuronal mitoses correlated with progression to anaplasia, while those who showed recurrences, only rarely showed this feature. Close follow-up of these cases can lead to early detection of those cases that have the potential to progress histologically.

PS-17-008
Cerebral tuberculoma: a challenging diagnosis
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Background & objectives: Tuberculosis of the central nervous system is rare. Tuberculomas may be solitary or multiple and may be indistinguishable from cranial abscess or primary brain tumour. We report 4 cases of cerebral tuberculoma and discuss their histological differential diagnosis.
Methods: We retrospectively analysed a clinical series of 4 cases of intracranial tuberculoma treated between 2012 and 2021 in the department of neurosurgery of Habib Bourguiba University Hospital of Sfax Tunisia. Analysis comprised medical records, clinical imaging, surgical management, histological findings and adjuvant strategies. A review of the current literature was performed.
Results: There were 3 females and a male patients with age range from 9 to 63 years (mean 32.5). The serological test for HIV was negative in all patients. A long term fever was described in 2 cases. Headache was the most common symptom. We did not found an extra cerebral location of the disease in all cases. CT scan and MRI were performed with all patients, showing a unique supra tentorial lesion with a mean size of 4.5 cm. The lesion was totally removed in 2 cases. A biopsy was done in the other cases. The patients were discharged from the hospital and treated with multi-drug anti tuberculous therapy.
Conclusion: Cerebral tuberculomas are a rare and serious form of tuberculosis due to the haematogenous spread of Mycobacterium Tuberculosis. Symptoms and radiologic features are nonspecific, leading sometimes to misdiagnosis. Differential diagnoses depend on the stage of lesion and can include cysticercosis, brain abscess, gliomas, toxoplasmosis, etc. Surgical excision helped to establish the histological diagnosis. Negative results from the bacterial examination do not eliminate the tuberculous infection. Multidrug chemotherapy is highly efficacious in the management of intracranial tuberculomas.

PS-17-009
Place of histological examination in the diagnosis of central nervous system infections: Experience of a centre in southern Tunisia
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Background & objectives: A variety of microorganisms can cause infections in the central nervous system (CNS). Although less invasive testing is preferred, surgical biopsy may be necessary. The aim of this study is to discuss histologic features of CNS infections.
Methods: We retrospectively reviewed the epidemiological and histologic features of CNS infections diagnosed at Habib Bourguiba's Hospital from 2010 to 2020.
Results: Twenty-eight cases were collected. Patients were aged between 2 and 73 years (mean age: 31.9). The sex ratio was 1.5. The study included 9 immunocompetent and 19 immunocompromised individuals. Pathological examination identified the pathogen in 10 cases. The aetiology of CNSI was echinococcosis in 4 cases, tuberculosis in 3 cases, toxoplasmosis in 2 cases and cryptococcosis in 1 case. Special stains were used in 78% of cases. The colouring used were Periodic Schiff Acid (PAS) stain in 20 cases, Gomori-Grocott stain in 18 cases and Ziehl Nielson staining in 2 cases. All these stains were carried out manually. An immunohistochemical study was not used in any case.
Conclusion: Standard histopathologic evaluation of tissue, including special stains, can provide a great deal of information about infections through identification of characteristic inflammatory patterns and by direct visualization of organisms. Further characterization can be achieved by immunohistochemistry and molecular assays.

PS-17-010
Glial cell density in epileptogenic focus of brain tissue from adult patients with drug-resistant epilepsy
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Background & objectives: Current theories of epileptogenesis include neuronal dysfunction and glial cell activation as a reason of seizures development. The aim of this study was to analyse glial cell density in epileptic focus of brain tissue from patient with drug-resistant epilepsy.
Methods: We analysed glial cellular density of cortex brain slides from 14 patients who underwent surgical resection of epileptogenic focus. The immunohistochemistry antibody as a GFAP, IBA-1 and Olig-2 were used. Count glial cell was done in 8-10 non-overlapping fields at high power magnification (x400, HPF). The area of HPF was 66585.8 μm2. Cellular density (CD) was presented as a cell/mm2.
Results: Foci of "active" and "non-active" gliosis were found in analysed brain tissue from all patients. The "active" gliosis was identified as a foci of increased glial cell density compare with all surrounding brain tissue in specimen from each case. The median of CD of astrocytes was 148.96 (119.16;178.74) cells/mm2 in "active" gliosis and 74.48 (44.69;89.37) cells/mm2 in "non-active" gliosis (p=0.000). The median of CD of microglial cells was 178.74 (104.27;223.43) cells/mm2 in "active" gliosis and 74.48 (44.69;119.16) cells/mm2 in "non-active" gliosis (p=0.000). The median of CD of oligodendrocytes was 685.19 (446.87; 968.21) cells/mm2 in "active" gliosis and 528.79 (283.01;722.44) cells/mm2 in "non-active" gliosis (p=0.000).
Conclusion: Epileptogenic focus of patient's brain with drug-resistant epilepsy was characterized by "mosaic" glial changes with foci of "active" and "non-active" gliosis. An "active" gliosis was detected as a local focus of glial cell (astrocytes, microglial cells and oligodendrocytes) proliferation.

PS-17-011
Deposition of phosphorylated alpha-synuclein in kidney and endocrine organs of patients with neurodegenerative diseases
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Background & objectives: Patients with Parkinson's disease (PD) develop motor symptoms but also suffer from non-motor symptoms. These latter symptoms may be caused by pathological deposits of phosphorylated alpha-synuclein (PAS) in the peripheral nervous system or in other organs, we´ll study this hypothesis.
Methods: We have reviewed 171 autopsies to study by immunohistochemistry the deposition of PAS in kidneys, adrenal, thyroid and pituitary. The sample includes 36 patients with synucleopathies [PD, dementia/incidental Lewy bodies (DLB/ DLBD), 85 patients with Alzheimer's disease, and 50 patients without histological alterations in the central nervous system. We evaluate the presence/absence of this protein in the aforementioned locations.
Results: In all the organs evaluated, alpha-synuclein deposition was higher in patients with CNS pathology than in the control group. If we compare the diseases grouped together, the synucleopathies are the ones in which the most deposits of PAS were observed, and within them PD. Of note is the thyroid gland in PD patients, where it increases from 21% in the control group to 75%. This finding is also observed in the other organs studied (adrenal 13% vs 31%, adenohypophysis 4% vs 10%, neurohypophysis 3% vs 29% and kidney 17% vs 54%).
PAS deposition has been observed within epithelial cells except in the neurohypophysis, which is in neural cells.
Conclusion: PAS deposition is observed in epithelial cells outside the central and peripheral nervous system in all the organs studied, with a greater accumulation of this protein in PD patients than in the rest of the pathologies or in the control group. The accumulation of Pas in kidney and endocrine organs may be responsible for the appearance of non-motor symptoms in patients with neurodegenerative diseases. The increase in the thyroid in PD patients is particularly striking.

PS-17-012
Immunodeficiency-associated lymphoproliferative disorders affecting the central nervous system
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Background & objectives: Immunodeficiency-associated lymphoproliferative disorders (IALD) is an uncommon entity observed in immunocompromised. It is a challenge for the neuropathologist due to not suspect affectation of central nervous system (CNS). We describe the frequency of CNS pathology IALD related in our hospital.
Methods: Retrospective review of histological diagnosis of IALD in CNS from 1993 to 2021. The following parameters were recorded: age, gender, clinical-radiological findings, histopathological disorder, type of immunodeficiency and their outcome.
Results: 12 cases were find with a median age at diagnosis of 53 years with a male predominance. All cases were caused by secondary immunosuppression: 6 HIV related, 1 post-transplant and 5 were iatrogenic. Initial clinical diagnosis were: brain tumour, infection or inflammation. Histologically the most common IALD was diffuse large B cell lymphoma (DLBCL) and positivity for EBV was more than 80%. One patient had radiological improvement, two remains in complete remission five years after diagnosis and eight patients died. There is no outcome information available from one patient.
Conclusion: IALD are a differential diagnosis to consider in immunocompromised patients with a radiological image of brain tumour. Our study shows the importance of neurological follow-up in patients under immunosuppression treatment. In HIV positive patients the IALD most frequent was primary CNS lymphoma as it is described in the literature.High prevalence of EVB infection is associate with IALD in immunocompromised patients.

PS-17-013
Molecular profile of lung carcinoma and their matched central nervous system metastasis
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Background & objectives: Advances in predictive biomarkers for targeted therapy have increased therapeutic options in brain metastasis. We describe clinical-pathological features in CNS metastasis from lung carcinomas and compare the difference between their molecular profiles, if available.
Methods: We performed a retrospective review of histological diagnosis in nine cases of metastatic lung carcinoma to CNS. Gender, age and histopathological data of both metastasis and primary tumour tissue were collected. In metastatic tissue, molecular analysis was done by panel-based next generation sequencing (NGS), fluorescent in situ hybridization (FISH) was used for diagnosis of the primary tumour when available.
Results: We found 9 patients (7M/2W) with CNS metastasis from pulmonary tumours; the median age at diagnosis was 62 years. 6 patients debuted with brain space-occupying lesions. 2 patients had recurrent CNS metastasis after surgical resection. 8 adenocarcinomas and 1 squamous lung carcinoma were found. In 8 cases molecular analysis of metastatic tissue with NGS resulted in pathogenic allelic variants (KRAS, BRAF, CCND1, androgen receptor and ROS gene), in 65% there were a double gene alteration. BRAF mutation was not actionable whereas ROS fusion is crucial for ROS1-targeted TKIs. FISH technique was available for molecular analysis in 5 samples from the primary tumour, resulting in the absence of ALK fusion gene.
Conclusion: Although CNS metastasis from primary lung tumours are frequent, pathological and molecular data are not always available, especially in old previous cases. It is challenging to analyse CNS lesions by

high-throughput sequencing technologies (NGS) for detection of new molecular findings in metastatic tissue not present in the primary tumour when the initial diagnosis was made. In contrast to classic molecular techniques like FISH, NGS provides the possibility to identify pathogenic allelic variants, many of them actionable by approved drugs.

PS-18 | Ophthalmic Pathology Posters

PS-18-001
Ocular melanoma; a five-year single institutional experience and the need for novel therapy

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Background & objectives: Ocular melanoma (OM) is the second most common type of melanoma after cutaneous melanoma. It is divided into uveal and nonuveal. Uveal melanoma consist of choroid, ciliary body and iris melanoma. Prognosis is based on mutational status of BAP1 genes.
Methods: This is a five-year prospective study of OM in our institution. Data of Patients were documented and followed for 8 months. Specimen collected were fixed in 10% buffered formalin, cut at 3μ and stained with routine H&E stain. Immunohistochemical stains used were S-100 and HMB 45. Data was analysed using SPSS version 24.
Results: Twelve cases of OM were seen during the study period with a mean age of 47.6±18.3 and male female ratio of 1.4:1. Uveal melanoma consists of 7(17.1%) choroid, 2(4.9%) ciliary melanoma and 3 (7.3%) conjunctival melanoma. All cases were positive for S-100 and HMB 45. Two cases of choroidal melanoma had early metastasis to the liver while only a single case was seen in the paediatric age group. High mortality was seen in five patients with choroidal melanoma after surgery and chemotherapy.
Conclusion: OM is gradually becoming common in our environment with choroidal melanoma having a dismal prognosis. Exploring novel therapies like targeted and immunotherapy may give hope in the future for our patients especially those with metastatic disease.

PS-18-002
The role of macrophages in the angiogenesis of uveal melanoma and its metastasis

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Background & objectives: Vascular-like mimicry of melanoma cells increases the risk of metastasis. Data on the creation of pseudovascular network by macrophages are scant. The aim is to assess macrophagal pseudovessels in uveal melanoma.
Methods: 299 enucleated eyes with uveal melanoma from 145 males and 154 females were studied in 2013-2018; exposure Group 1 - tumours without metastases (n = 258), exposure Group 2 - verified distant metastases in liver (n = 24). Immunohistochemical (CD68, CD 34, D2-40, CD31) testing was performed on tissue samples (Group1, N=28; Group 2, N= 17).
Results: In tumours of group 2, there are more macrophages than in non-metastatic melanoma: 202.5 (152.25; 254.5) versus 107 (67.23; 145.3) ($p = 0.007$), as well as a greater volumetric density of macrophage pseudovessels: 6.32 (4.9; 8.03) versus 3.22 (1.3; 3.7), $p = 0.05$) ($p = 0.007$), and lower volumetric density of blood vessels (3.95 (2.68; 5.09) versus 5.31 (4.43; 5.97), $p = 0.053$). There is an inverse, average strength correlation between the volumetric density of the vessels and the number of macrophages. There is a greater vascularization and smaller infiltration by macrophages in spindle cell melanomas.
Conclusion: It has been determined that macrophages in uveal melanoma are capable of vascular-like mimicry. The volumetric density of blood vessels and the number of macrophages in the experimental groups have statistically significant differences. Immunohistochemical markers were used in the study of blood vessels, tumour cell microenvironment and the pseudovascular spaces formed by them: the results obtained by them can be used to predict distant metastases of uveal melanoma.

PS-18-003
Morphological changes of Descemet' membrane and the disturbance of ocular immune privilege in eyes with chronic corneal oedema (Fuchs endothelial corneal dystrophy (FECD) and bullous keratopathy)

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Background & objectives: Chronic corneal oedema is associated with FECD or endothelial damage – bullous keratopathy (BK). The purpose is to explore morphological structure of Descemet' membrane (DM) and analyse aqueous humor (AqH) cytokine levels in patients with corneal oedema.
Methods: 29 patients with chronic corneal oedema (18 FECD and 11 BK), underwent endothelial keratoplasty. Intraoperatively obtained EDMs were stained with hematoxylin-eosin. A light microscopic morphometric analysis was performed (Leica DM-2500, ImageScope M). 37 AqH samples were collected from 29 patients during endothelial keratoplasty and from 8 patients with senile cataract (control). The AqH cytokine levels were measured with multiplex immunoassay.
Results: There was no difference in thickness of DM' prenatal anterior banded layer (2.27±0.61 μm) and postnatal posterior non-banded layer (11.0±2.14 μm) between BK and normal adult cornea. In FECD eyes DM was thickened due to additional collagen layer and guttate excrescences (postnatal layer thickness – 16.08±2.1 μm, $p<0.0005$), while prenatal anterior banded layer was similar to that zone in BK (2.89±1.38 μm, $p=0.134$). IL-6, IL-8, IFNγ, MCP-1 were elevated in FECD and BK groups compared to control ($p<0.01$). IL-13 was statistically lower in eyes with FECD and BK, than in the control ($p<0.05$). There was no significant difference in AqH cytokine levels between FECD and BK.
Conclusion: Chronic corneal oedema is related to different morphological changes of EDM in FECD and BK. The increased expression of IL-6 and IL-8 in the AqH of patients with chronic corneal oedema features severe local immunogenic inflammation. High preoperative levels of IFNγ, MCP-1 indicate Th1 immune response. The decreased expression of IL-4 and IL-13 shows the suppression of Th2 immunity. Thus, chronic corneal oedema is the condition associated with the disturbance of ocular immune privilege, leading to local inflammation and fibrosis.

PS-18-004
Inflamed juvenile conjunctival naevus: a case report and review of the literature on a challenging lesion

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Background & objectives: Inflamed juvenile conjunctival naevi (IJCN) constitute challenging lesions to diagnose because of their accelerated growth and atypical histological features, which raise the suspicion of malignancy for both patients and treating medical doctors.
Methods: We report the case of a 12-year-old boy who presented with a vascularized conjunctival lesion displaying fast growth during the preceding couple of months. The lesion was excised, and we received a fragment of conjunctiva measuring 8x6x2 mm and presenting a well-defined 5x4 mm grey macula.
Results: The histological analysis showed conjunctival mucosa with intraepithelial and stromal proliferation of melanocytes without significant atypia, associated with solid and cystic epithelial inclusions with preservation of goblet cells. Pleomorphism was scant and necrosis was not identified. In the stromal component there was 1 mitosis figure per 10

high-power fields. A moderate to intense inflammatory infiltrate containing numerous lymphocytes, plasma cells and eosinophils was observed associated with the melanocytic proliferation. Rare primary lymphoid follicles were also identified. Fibrosis or lesions of obliterative phlebitis were not evident. The immunohistochemistry study using double labelling with HMB-45/Ki-67 revealed a proliferative index below 5%.
Conclusion: This case illustrates the main features of this infrequent and unique lesion, which has features distinctive from the common compound conjunctival naevus. The recommended treatment is complete excision, and the prognosis is typically excellent. Currently, our patient remains well, without signs of lesional recurrence.

PS-18-005
An audit of outcomes for uveal melanoma patients treated with primary enucleation versus primary radiation therapy between 2011 and 2020
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Background & objectives: The one-year survival rate for metastatic uveal melanoma patients is approximately 15%. We aim to provide an examination of patient outcomes which compares uveal melanoma patients treated with enucleation versus plaque brachytherapy as their primary treatment modality.
Methods: From our database of over 1,000 uveal melanoma cases within the age range of 11 to 95 years, 257 relevant cases between the years 2011 and 2020 were extracted. Relevancy was determined based on patient primary treatment. Clinical information from charts and histopathology reports was analysed.
Results: The mean age of this cohort at time of treatment was 62 years. 145 patients were males and 112 females. 136 received primary enucleations, with mean age of 64. Mean largest tumour dimension (LTD) was 14mm [range 5-23]. 30% of which, metastasised. Using metastasis as a surrogate for death, all are assumed deceased. 121 received plaque brachytherapy, with a mean age of 60. Mean LTD was 9mm [range 1-19]. 8% recurred locally leading to enucleation. 15% metastasised. Metastasis was used as a surrogate for death. A subgroup of 94 choroidal tumour enucleation patients with no extra-ocular extension and an average LTD of 13mm [range 5-19], displayed a 22% metastatic rate.
Conclusion: Metastatic disease is linked directly to the mortality rate for patients with uveal melanoma. Approximately 50% of patients die due to metastatic disease. Of our cohort, there was a 46% metastatic rate, with 30% in the enucleation group and 15% in the brachytherapy group. When a subgroup of enucleated patients with size most similar to those of the brachytherapy patients was analysed, the metastatic rates for enucleation patients dropped to 22%. Further analysis of the two groups is currently underway.

PS-18-006
Signet-ring cell/histiocytoid carcinoma of the eyelid - clinicopathologic analysis of two cases
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Background & objectives: Signet-ring cell/histiocytoid carcinoma (HC) is a rare entity, with about 40 cases reported worldwide. It is considered aggressive and concerns mainly eyelids, seldomly axillae. The diagnosis is challenging; data on survival and optimal therapy are limited.
Methods: We report the clinical, histological, and immunohistochemical features of two novel eyelid-located HC cases: 71- and 66-year-old men. Patient 1 and 2, respectively, both with diffuse thickening of the involved skin. Patient 1 presented with ptosis and supraclavicular lymphadenopathy. By Patient 2, the swelling of the eyelid extended to the adjacent cheek.
Results: The eyelid thickening had been clinically misinterpreted as inflammatory/ infectious/ haematological disorders, delaying the correct diagnosis in both cases. Microscopy revealed diffuse infiltration of the dermis by single rows of signet-ring cells characterized by eccentric nuclei displaced by vacuolated cytoplasm. We differentiated the observations mainly with gastrointestinal-tract-derived adenocarcinomas and metastatic lobular carcinoma of the breast. Immunohistochemically, the cells expressed CK7, E-cadherin, CEA, EMA, and GCDFP15. In both cases, tumour cells expressed the androgen receptor (AR). Thorough clinical examination allowed for excluding metastases originating from the gastrointestinal tract and lobular breast carcinoma.
Conclusion: HC of the eyelid is a rare entity diagnosed by exclusion. One of our report's more significant findings is that AR might be expressed in the HC cells, constituting a possible therapeutic target in HC patients. The small sample size did not allow to assess the generalizability of the findings. Considerably more work will need to be done to determine whether AR expression modifies the survival and efficacy of implemented therapies.

PS-18-007
The evaluation of ocular melanoma based on pathologic prognostic factors: a 10-year experience of a single centre
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Background & objectives: Ocular melanoma is the second most common type of melanoma, with increasing incidence and limited therapeutic options. This study aimed to review the histopathological features with prognostic impact of ocular melanoma cases diagnosed in a single Romanian centre.
Methods: A retrospective analysis on all cases of ocular melanoma diagnosed between 2011-2020 in the Department of Pathology of the Mureş County Clinical Hospital was conducted. The following parameters were recorded: age and gender, tumour localization, histologic subtype, mitotic rate, ciliary body and optic nerve invasion, extraocular extension and immunohistochemical evaluation.
Results: There were 12 cases in 8 males (66.7%) and 4 females (33.3%), with a mean age of 61.75±12.85 years. 11 were localized in the uvea (91.7%) and one in the conjunctiva (8.3%). Retinal detachment was present in 5 cases (41.7%), the involvement of the ciliary body in 2 cases (16.7%), while in one case (8.3%) both optic nerve invasion and extraocular extension were identified. Most cases were mixed type (58.3%) and the mean mitotic rate was 1.23±0.77 mitoses/mm2 (range 0-3). The tumour cells stained positive for S100 (58.3%), SOX10 (50%), Melan-A (41.7%) and HMB45 (25%). Ki67 proliferation rate with a value of 1-2% was analysed in 3 cases (25%).
Conclusion: Most of the cases presented at least one poor prognostic factor such as ciliary body involvement, extraocular extension and epithelioid cell type, which implies a high risk for metastasis and shorter survival time. As recent data suggest that S100 is frequently weak in ocular melanoma, we should extend the use of SOX10, Melan-A, HMB45 and Ki67 proliferation rate, the last being an important prognostic factor.

PS-18-008
Clinicopathologic characteristics of ocular tumours: a retrospective analysis of 69 cases in a Tunisian institution
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Background & objectives: Ocular tumours are uncommon, divided into intraocular, adnexal (conjunctiva, eyelid), and orbital tumours. There are several types of benign and malignant tumours that can endanger functional and vital prognosis. We aim to analyse epidemiological and pathological features of these tumours.
Methods: This is a retrospective and descriptive study of 69 ocular tumours diagnosed at our department during a period of 12 years (from 2010 to 2021).
Results: Fifty-two adult cases and 17 paediatric cases were identified. The mean age was 43 years (2 – 94 years). The sex ratio was 1.22. The most common location was the conjunctiva (41.6%) followed by the orbit (33.3%), the eyelid (18.9%), and intraocular (7.2%). Malignant tumours represented 49.3%. Histological subtypes varied according to the location. Conjunctival tumours were dominated by nevi (9 cases) and squamous cell carcinoma (SCC) (6 cases). Orbital tumours were represented mainly by benign cysts (10 cases) and lymphoma (5 cases). Tumours of the eyelid were basal cell carcinoma (BCC) (8 cases) and seborrheic keratosis (5 cases). Intraocular tumours were uveal melanoma (3 cases) and retinoblastoma (2 cases).
Conclusion: Ocular tumours are very diverse and can affect all tunics. The most frequent primary intraocular tumours are uveal melanoma in adults and retinoblastoma in small children. Conjunctival tumours are dominated by melanocytic tumours especially nevi followed by epithelial ones. SCC is the most common carcinoma of the conjunctiva. Most frequent palpebral malignant tumours are BCC and SCC. Orbital malignant tumours are mainly represented by metastases, lacrimal gland tumours, and lymphomas in adults and rhabdomyosarcoma in children.

PS-18-009
Analysis of lumican expression in corneal dystrophies
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Background & objectives: Lumikan ensures corneal stroma transparency. Its expression can increase in epithelium upon regeneration activation. Aim: to establish the patterns of lumican expression in corneal explants of patients with corneal dystrophies and its changes 1% low molecular weight sodium hyaluronate application.
Methods: The prospective study included 37 patients: dystrophies in the outcome of keratitis (20 cases), endothelial epithelial dystrophy (EED) (17 cases). Patients were divided into 2 comparable groups. The first received 1% HA injections before keratoplasty. For immunohistochemical study primary monoclonal antibodies to lumikan applied. The proportion of pixels with high intensity (positivity) and the index of expression intensity calculated.
Results: In corneal dystrophies after keratitis after sodium hyaluronate application, the positivity of expression in the stroma decreased (72,5 [IQR 70,8-78,3] vs 94,2 [IQR 92,9- 94,6], p=0,004). While the intensity increased (139 [IQR 134-145] vs 93 [IQR 89-97], p=0,004). Epithelial expression positivity was higher after HA application in corneal dystrophy after keratitis (97,3 [IQR 96,6;98,1 vs 91,0 [IQR 69,9-94,7], p<0,001). In hereditary EED stromal expression positivity increased after treatment with HA (90,0 [IQR 88,2-91,0] vs 81,5 [IQR 10,9-86,7], p=0,06). While intensity decreased (95 [IQR 94-100] vs 125 [IQR 115-186], p=0,007). The same dynamics of changes in positivity and intensity of lumican stromal expression was observed in the group of acquired EED.
Conclusion: An increase of epithelial lumican expression after the use of 1% sodium hyaluronate indicates the activation of regeneration processes and correlates with clinical signs of an improvement in the condition and an increase in the transparency of the cornea. The study of the stromal expression of lumican showed that an important factor is its normal content in the corneal stroma, since both a sharp increase and low expression parameters are accompanied by a decrease in the transparency of the cornea.

Funding: To develop a method for the treatment of patients with dystrophic corneal diseases, based on the restoration of protective mechanisms of the eye surface

PS-19 | Other Topics Posters

PS-19-001
Forensic analysis of mortality in women of reproductive age
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Background & objectives: The unnatural death of women of reproductive age has a serious psychological, social impact on the family and society. Deaths among women of reproductive age were investigated in order to see trends in terms of causes and patterns of death.
Methods: The research team included 328 forensic autopsies of women of reproductive age conducted between 2016 and 2020 years in Central Kazakhstan. In the course of the study, the following methods were used: clinical and statistical, clinical and epidemiological, clinical and psychopathological, mathematical and statistical (using Student's t test for relative values and Pearson's association coefficient).
Results: The predominant method of suicide was poisoning in 42.3% cases, followed by hanging (34.9%), burns (11.4%), drowning (9.4%). These four methods are 98% of the total suicidal deaths in this study cohort. The married women were 63.1% of suicide victims. Among women who committed suicide attempts, persons with the following socio-demographic characteristics predominated: age under 40 (63.25%), secondary education (64.46%), social status of workers (43.37%), low income (91.57%). Among various social groups of the female population, the highest rates of prevalence of suicidal attempts noted in the group of unemployed able-bodied persons, where their frequency (330.57 per 100,000 population) is several times higher than similar indicators in all other groups.
Conclusion: The main features of the prevalence of suicidal attempts in women are: maximum rates among persons 20 - 29 years old with a gradual decrease in subsequent age groups; the highest rates are among non-working able-bodied women; the 1/3 part of suicidal attempts are under the alcohol influence; the predominance of poisoning among the methods of suicide. Women who have committed completed suicides and suicidal attempts have a number of typical socio-demographic characteristics.

PS-19-002
An internship programme in a pathology laboratory in the Northeast of Brazil: before and during pandemic
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Background & objectives: A pathology internship program was developed between UNIFOR (Brazil) and a local private pathology group to expose medical students to the daily routine of anatomic pathology as a medical specialty. In this report, we describe the experiences of these students.
Methods: The internship program was elaborated during the last semester of 2019. The group participating in the project was composed of 9 students between the 8th and 10th semesters of medical school. It started in January 2020 and took place in a private pathology laboratory in the city of Fortaleza, Brazil.
Results: The meetings were on Saturday afternoons and the students could monitor and carry out the macroscopic analysis of

specimens, as well as check the histological slides. They could also discuss the cases and findings with a pathologist present in the laboratory at the moment. After March 2020, some activities had to be carried out as online meetings because of the pandemic. During online meetings the interns developed the ability to create and organize projects on topics such as receiving specimens at a laboratory, slides making, microscopic and macroscopic analysis, preparation of histopathological reports and project management.
Conclusion: This internship presented opportunities of experiencing pathology face-to-face or at a distance the most appropriate modality in the current context without impairing the content. Medical school pathology has traditionally been restricted to the academic role pathology plays, as a bridge between basic and clinical sciences. Our initiative tries to decrease gap between pathology as an academic discipline and as a medical specialty. As a follow-up, we will measure the incidence of medical students that will apply to pathology as a residency.

PS-19-003
A tool to improve the teaching of pathology in times of pandemic
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Background & objectives: The COVID-19 pandemic showed the need to reinvent teaching methodologies. We seek to evaluate the applicability of profile games in the teaching-learning process of Pathology in pandemic.
Methods: A profile game using images of pathology was applied through Powerpoint about COVID-19 and death signs, respectively in students from the sixth and the seventh semesters of a medical school. The participants should have prior knowledge of the subject in order to play it. After applying the game, the students answered a questionnaire applied using the Google Forms platform.
Results: The game was applied to 180 students divided into 8 groups, 154 answered the questionnaire. When asked if the game helped them to fix knowledge, 100% answered yes, which shows that this teaching tool directly helped students learn the content. When asked what grade, from 0 to 10, students would give this teaching method, 66% answered that they would give a score of 10, 19% would give a score of 9, 11% would give a score of 8 and only 1 student would give a score of 0 to 5. All agreed that the game met the learning objectives and that this teaching method must be perpetuated.
Conclusion: In this work, it was noticed that an innovative and differentiated proposal of working with Pathology was important in the construction and consolidation of knowledge, since autonomy and interest in the subject were stimulated.

PS-19-004
A challenge for pathology undergraduate education during COVID-19 pandemic: is remote learning with digitized slides an option?
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Background & objectives: The outbreak of the new Coronavirus Disease (COVID-19) produced a global pandemic that affected pathology teaching. This study aimed to assess the teaching of this discipline during the pandemic context, highlighting the student's perspective.
Methods: A cross-sectional, descriptive, and semi-quantitative prospective study regarding medical students' perception on remote pathology learning during 2020 was performed. Students from 3rd to 7th terms from a Brazilian university (UNIFOR) were voluntarily assessed through a semi-qualitative five-point Likert scale online questionnaire focused on digital pathology employment during their undergraduate pathology course.
Results: 152 answers were obtained through the online questionnaire. Regarding the use of digitized slides, most of the students (69,7%) found “Excellent” or “Good” to learn from digital slides. Overall, 69% considered “Excellent” or “Good” to learn pathology in the remote pandemic scenario. Added to that, a relevant portion (44.7%) reported having, in the period of remote learning, more study time. 67.7% of the students reported worsening or felt indifferent about their performance in exams.
Conclusion: Most participants perceived the use of digital slides positively. Part of the participants, on the other hand, reported indifferent or worse exam performances. These can be attributed to the psychological and social impacts generated by the pandemic, as social distancing, and lack of adequate infrastructure to remote learning. Through the students’ perspective we conclude that remote and digital undergraduate pathology learning should be encouraged, although the human factor should be closely reinforced by mentoring and supervision.

PS-19-005
Teaching pathology at a private university in North-eastern Brazil
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Background & objectives: The methodology of Problem Based Learning (PBL) is useful to develop clinical reasoning, contributing to an integrated learning of Pathology. This study aims to describe the teaching of Pathology through the PBL method.
Methods: The present study consists of a report about the pedagogical strategies applied at Universidade de Fortaleza’s (UNIFOR) medical course in the teaching of Pathology. The university is located in the north-eastern region of Brazil. The institution considered the use of PBL as an active teaching methodology in theoretical and practice scenarios in five semesters.
Results: UNIFOR’s medical course includes Pathology in morphofunctional laboratories. The education starts at the third semester, with a six-hour week integrated curriculum approaching General Pathology alongside Radiology and Anatomy until the fourth semester. In the fifth, sixth and seventh semester we cover Special Pathology and Radiology. The students also study autopsy and learn how to fill death certificates in the seventh semester. In the classes, the students discuss clinical problems co-relating their findings and possible anatomic and clinical diagnosis. The methodologies used are socrative, kahoot, paint, cross-words, theater, memory games and profile games using microscopic slides and histopathological reports.
Conclusion: Considering the curricular analysis exposed with the experience of its application, we note the progressive evolution of knowledge in pathology. The curriculum was built in a spiral structure, evolving from introductory concepts to its applications in specific issues of pathology being applied through several active methodologies, ending with the filling out of the death certificate. Therefore, after five semesters of teaching pathology in the PBL curriculum, it also allows students to develop knowledge about the specialty.

PS-19-006

Tumour-to-tumour metastasis. case series and literature review

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Background & objectives: Less than 300 cases of tumour-to-tumour metastasis (TTM) have been reported, mostly as isolated cases. TTM may hinder the interpretation of radiological and histological images. We present four patients in whom this rare phenomenon was observed.
Methods: We reviewed the archives of the Pathology department. We identified four patients diagnosed with TTM. We collected and reviewed all the available clinical information, and pathological material.
Results: Patient 1: Female, 69 years-old. 2012: pT2N1 breast ductal carcinoma (IBDC). Autopsy in 2015: systemic spread, including metastases to a liver angioma, and uterine leiomyoma.
Patient 2: Female, 67 y.o. 1995: IBDC T4bN0M0. 2019: multiple metastases, and a Clear Cell Renal Carcinoma (CCRCC) with intratumoral IBDC.
Patient 3: Female, 60 y.o. 2015: CCRCC pT3a in left nephrectomy. 2020: right adrenal nodule diagnosed as adrenal cortical adenoma (ACA) with CCRCC metastasis.
Patient 4: Male, 72 y.o. 2014: pT3a renal cell carcinoma in right nephrectomy. 2021: right ACA with metastasis of RCC morphologically compatible with FH-deficient type.
Conclusion: Renal and breast tumours were the most frequently involved in this phenomenon, as tumour donors or recipients in our series. TTM, however rare, is expected to be increasingly seen in years to come. Atypical, dimorphic or evolving patterns in histological or image examinations should raise the suspicion of TTM. Pathologists and radiologists should be aware of this phenomenon in order to minimize diagnostic errors or delays.

PS-19-007

Inflammaging: the silicates seem to be the reason of this process in spleen

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Background & objectives: Early studies showed that silicon accelerates the thymus aging, its fatty transformation, a decrease in the number of macrophages, and a redistribution of the CD68 protein in macrophages. It is interesting to see how the spleen changes in this regard.
Methods: The spleens of white outbred male rats were studied. One group (n=10) received bottled water ad libitum, the other (n=10) received the same water containing 10 mg/l silica for during nine months. After 2 and 7 months (n=5 from each group) the rats were sacrificed. The immunohistochemical characteristics were detected. We made morphometric by the SigmaScan Pro V5.0 software.
Results: The first signs of aging appear in the spleen in 2 months: in rats treated with silicon, the number of large macrophages (Iba-1) increases in the marginal zone, and decreases in the red pulp. The average area of macrophages in the marginal zone in rats, in silicon treated rats, increases by 1.2 times, the thickness of the periarteriolar lymphoid sheath does not change. After 9 months, these changes are more noticeable: in silicon treated rats, the average size of macrophages (CD68+) in red pulp decreases 1.3 times, the thickness of the periarteriolar lymphoid sheath decreases 1.2 times.
Conclusion: It was revealed that in proportion to the silicon exposure period, the absolute area of the lymphoid nodules and their marginal zone decreases, but the relative area of the marginal zone increases. The Changes we have seems clearly emphasize that silicon accelerates the physiological aging of the spleen probably associated with the inflammatory process.

PS-19-008

The diagnostic impact of temporal artery biopsy in giant cell arteritis

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Background & objectives: The temporal artery biopsy (TAB) is the gold standard for the diagnosis of giant cell arteritis (GCA). However, its precision and limits remain controversial. Our study's aim was to assess the diagnostic accuracy of TAB in patients with suspected GCA.
Methods: We included retrospectively all patients with TAB performed for suspicion of GCA at Habib Thameur Hospital between January 2016 and December 2020. We compared the histological diagnosis of TAB with the clinical course and the definitive diagnosis made. Finally, we assessed the performance indices of the TAB which are sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy.
Results: Twenty-eight TABs were included (19 females and 9 males), with a mean age of 63.4 years. Positive results were found in 5 (18%) and negative in 23 (82%) patients. Epithelioid and gigantocellular granulomas were present in all TAB positive cases. The diagnosis of GCA was retained in 12 patients (43%), of which 5 patients (42%) had a positive TAB and 7 patients (58%) had a negative TAB. TAB was negative in all patients with no retained diagnosis of GCA. The specificity of TAB was 100% with a positive predictive value (PPV) of 100%. The sensitivity was 41% with a negative predictive value (NPV) of 69.5%. The diagnostic efficiency was 75%.
Conclusion: TAB has an excellent specificity for the diagnosis of GCA, but lacks sensitivity with a high number of false negatives. False negatives represent 13 to 32% of cases, according to studies (25% of the cases in our study). The focal and segmental nature of GCA may explain the frequency of false negatives. Therefore, a negative biopsy cannot exclude the diagnosis of GCA.

PS-19-009

Appendicitis pathology throughout the SARS-CoV-2 (COVID-19) pandemic: a single centre study

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Background & objectives: COVID-19 pandemic brought important changes in healthcare systems. In Greece during lockdown surgical procedures were limited to emergency conditions. The aim of this study is to evaluate the impact of COVID-19 pandemic in appendicitis' treatment before and after the lockdown.
Methods: We reviewed the pathology reports of appendectomy specimens from our department and divided them in different time periods before the beginning of lockdown (January 1st 2019-Martch 22nd 2020) and after the lockdown (March 23rd 2020-December 31st 2020)
Results: A total of 324 appendectomy specimens were studied. After March 23rd we observed a 49,4% decrease in the number of cases (mean number of cases during pre-Covid19 period 16,6/month to mean number of cases after lockdown 8,2/month). We also saw that the rate of negative appendectomies decreased significantly during Covid-19 period from 9,2% to 2,7%, while the rate of complicated appendicitis (gangrenous and perforated) was

notably increased from 30,8% to 44,6%. Six (8,1%) patients were diagnosed with Covid-19 and acute appendicitis.
Conclusion: Our study shows that the cases of acute appendicitis have decreased during the pandemic period, however the patients presented with more severe disease. Acute appendicitis is the most common emergency condition in children and delayed management correlates with increased complications. The limitations imposed during the lockdown, the fear of parents of an inhospital Covid-19 contagion and the increased occupation of emergency departments by Covid-19 patients has significantly affected the patient's behaviour regarding the utilization of emergency units.

PS-19-010
Concordance rates between frozen section diagnosis and final authorised diagnosis in University Hospital Galway from 2019 to 2020; an institutional audit
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Background & objectives: A frozen section is a pathological laboratory technique which allows rapid diagnosis of specimens and evaluation of disease margins. The objective of this audit was to assess the concordance rates between frozen section diagnosis and final authorised diagnosis in UHG.
Methods: A retrospective analysis of all frozen sections completed in UHG from 2019-2020 was undertaken using the internal APEX laboratory system, looking specifically at the concordance rates of frozen section diagnosis and final authorised diagnosis. The time to frozen section diagnosis was also measured, assessing if it was achieved within 20 minutes.
Results: A total of 45 frozen sections were performed in 2019, with a concordance rate of 100%. In comparison, 44 frozen sections were performed in 2020, with a slightly lower concordance rate of 97.7%. One case in 2020 which was suspicious for malignant involvement of the margin on frozen section showed no evidence of malignancy on the final authorised diagnosis.
In 2019, 82% of frozen section diagnoses were made within 20 minutes, compared to 75% in 2020.
Conclusion: These results show there were high concordance rates between frozen section diagnosis and final authorised diagnosis in UHG, however there is scope for improvement from a time-management perspective. Frozen sections are highly time-sensitive and effort should be made to answer the clinical question within 20 minutes of receiving the specimen.
In conclusion, this audit demonstrates that our institution's concordance rates align with international standards, however, there remains scope for improvement with regards to time taken for diagnosis to be completed.

PS-19-012
The influence of constant lighting on some haematological parameters of Wistar rats
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Background & objectives: The human undergoes the abundant exposure to an artificial lighting in the dark which leads to a shift in the circadian rhythms of the organism, or desynchronosis. Desynchronosis is a prolonged stress condition, which affects the blood results.
Methods: The study was conducted on 80 six-month-old male rats, divided into 2 groups, over 3 weeks. The first group was kept under the fixed regime "light-darkness" (10 hours / 14 hours) and the second group – under constant lighting. Subsequently, the haematological analysis was performed.
Results: As the result of the study it is established that staying under constant lighting within 3 weeks is accompanied by a decrease in the number of erythrocytes (RBC) and in haemoglobin level in the blood (HGB) with unchanged haematocrit (HCT). There is also a decrease in mean corpuscular haemoglobin (MCH) and an increase in red cell distribution width (RDWc) with unchanged mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC).
Conclusion: Exposure to constant lighting leads to a decrease in the number of erythrocytes and in haemoglobin level; against this background, an increase in RDWc indicates an increase in the number of reticulocytes in the blood.

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PS-20-001
Morphological and morphometrical characteristics of kidney in foetuses with Down syndrome
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Background & objectives: Data on prenatal kidney development in Down syndrome (DS) are scarce. Therefore, the aim of this study was to evaluate differences in nephrogenesis in foetuses with and without prenatally diagnosed DS.
Methods: Tissue of foetal kidneys with (DS group, n=17) and without (non-DS, n=17) prenatally diagnosed DS were analysed, using free image software Image J. We compared the thickness of the nephrogenic (NZ) and maturation (MZ) zone of the cortex, diameter and area of the glomerulus and glomerular tuft and presence of different nephron developmental forms.
Results: NZ was slightly thicker in DS samples. MZ in younger DS foetuses was significantly thicker than non-DS, but ate the 8th and 9th gestational month, MZ thickness of DS samples became significantly thinner, compared to non-DS. Glomerular diameter and area, and tuft area of DS group was smaller compared to non-DS, in juxtaglomerular zone of the renal cortex, while it was opposite in intermediate and superficial cortical zone. DS group had significantly higher percentage of more mature developmental forms of nephron, in all gestational ages.
Conclusion: Thinner MZ and higher percentage of more mature developmental forms of nephrons in all gestational ages, speak in favour of impaired nephrogenesis in DS group, as well as a possibility for lower nephron number in DS babies born with DS.

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PS-20-002
Liver adenomatosis in a 15-year-old-child
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Background & objectives: Hepatocellular adenoma is a rare benign neoplasm, representing <5% of all paediatric hepatic tumours. Liver adenomatosis is even more uncommon, described as multiple adenomas (usually>10) in a normal liver parenchyma. We report a case of hepatic adenomatosis in a child.
Methods: A 15-year-old girl presented with the history of chronic abdominal pain for 3 months. The patient did not have any history of hormonal use or significant medical history. Computed tomography

imaging revealed a multiple spontaneously hypodense liver masses of wish the greatest measure approximately 7 cm located at segment V. The patient underwent surgical resection of the largest mass.
Results: On gross examination, the specimen demonstrates a well-circumscribed, firm 7cm lesion. The cut surface of the lesion showed a tan-yellow colour with intratumoral haemorrhage. The nonlesional liver is noncirrhotic. Microscopically, the lesion was composed of multiple nodules separated by fibrosis septa within portal areas. The nodules consisted of benign-appearing hepatocytes arranged in one to two cell thick plates with marked steatosis and interspersed small blood vessels. The surrounding liver showed multiple well circumscribed millimetric lesions with the same histological appearance mentioned above.
Immunohistochemical stains revealed that the tumour was negative forβ-catenin. Intralesional steatosis and the multiple character of the lesions oriented towards to the subtypehepatocyte nuclear factor 1 (HNF-1A) inactivated liver adenomatosis.
Conclusion: Liver adenomatosis is an uncommon neoplasm, especially in the childhood age group. To our knowledge there is less than twenty cases in the literature. This is a rare case of liver adenomatosis HNF-1α inactivated in children. This subtype is defined by bi-allelic inactivating mutations of HNF1A. The diagnosis of this subtype can be confirmed by decreased or absent LFABP immunostaining in the lesional cells or by molecular test.

PS-20-003
Histopathological placental findings of the third trimester pregnant women COVID-19 positive: increased features of perfusion abnormalities
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Background & objectives: To determine the clinical and histopathological features of the placentas from women diagnosed with coronavirus disease-19 (COVID-19) during the third trimester of pregnancy.
Methods: We analysed 53 cases of COVID-19 positive patients admitted and delivered in the Obstetric Department of County Emergency University Hospital of Oradea, Romania, between July and December 2020. We compared the clinical and histopathological findings in this group with those from 55 placentas from Covid-19 negative cases delivered in the same period.
The mother's age in COVID-19 positive group ranged between 17 and 43 years (mean= 29.3). The majority were at term deliveries (94.3%) and had an asymptomatic Covid-19 infection (90.56%) and C-section was performed in 79.24% of the cases. We found no evidence of adverse foetal outcome due to the mother's positive COVID-19 status. Placenta's examination revealed increased features of maternal (villous infarction, decidual vasculopathy, accelerated villous maturation, distal vilous hypoplasia, retroplacental haematoma)(69.8% vs 49.1%)(OR=2.39; p=0.03) and foetal vascular malperfusion (umbilical cord abnormalities, avascular villi, villous stromal –vascular karyorrhexis)(50.9% vs 29.1%)(OR=2.53, p=0.03), with statistically significant differences.
Conclusion: Even though in COVID positive group was observed a slightly increased incidence regarding inflammatory/infectious processes (histologic acute chorioamnionitis, VUE, chronic vilitis, chronic histiocytic intervilositis)(45.3% vs 29.1%) we did not find statistically significant difference between the groups (p=0.11). The COVID-19 positive placentas showed a significantly higher prevalence of maternal and foetal vascular malperfusion, which possibly reflect an underlying hypercoagulable state, uterine underperfusion and subsequent hypoxic-ischemic injury induced by COVID-19 infection.

PS-20-004
Placental histology for predicting adverse outcomes in extremely premature neonates
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Background & objectives: Predicting complications of extremely premature birth (EP) is difficult and poses a major therapeutic challenge. We aimed to explore the placental characteristics of children born EP (< 28 weeks) and examine whether histopathological findings could predict neonatal outcomes.
Methods: Prospective observational study of EP singletons. The placentas were classified according to the Amsterdam Placental Workshop Group Consensus Statement. Logistic regression analyses were used to evaluate the associations between placental findings and adverse neonatal outcomes, defined as perinatal death, early onset sepsis (EONS), necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), major brain pathology by MRI, and retinopathy of prematurity (ROP).
Results: Of 123 cases included, 58 placentas had histologic chorioamnionitis (HCA), 47 had maternal vascular malperfusion (MVM), and 13 cases had both HCA and MVM. Five cases had no pathology. HCA was associated with perinatal death (OR 10.21, 95% CI [10.01-103.8], p=0.030) and NEC (OR 10.81, 95% CI [1.4-82.3], p=0.011). Subanalysis of cases with HCA showed increased odds of BPD in cases with a foetal inflammatory response (OR 3.57, 95% CI [1.15-11.08], p=0.028).
Conclusion: Placental histology may be useful to assess the risk of adverse neonatal outcomes following extremely preterm birth.

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PS-20-005
Autopsy findings in 4 patients with active COVID-19 infection and intrauterine foetal death
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Background & objectives: Studies on vertical transmission of SARS-CoV-2 from infected mothers were published without clear results. Nevertheless, placental infection has been confirmed with detection of SARS-CoV-2 in trophoblast by immunohistochemistry (IHC) and in situ hybridization (ISH), as well as the neonatal transmission.
Methods: We make a review of medical record, complementary tests and autopsies (fetoplacental unit) from stillbirths detected in 4 patients at their 37, 31, 27 and 20 gestation weeks. Mothers were between 24 and 38 years old who presented active symptomatic COVID-19 infection with good oxygen saturation. Two of them presented comorbidities (multiple sclerosis and obesity, diabetes and hyperthyroidism).
Results: The autopsy findings revealed adequate weight according to gestational age and the absence of structural abnormalities, except for one case of unilateral renal agenesis. All of them presented acute

hypoxia-ischemia signs. The placental study showed diffuse trophoblastic necrosis, affecting 80 to 90% of the placenta, identifying intense and granular cytoplasmic trophoblast positivity for SARS-CoV-2 by IHC and ISH. The real time-polymerase chain reaction (RT-PCR) in placental tissue was positive in all cases. In one case, the lung RT-PCR was positive. However, the presence of the virus could not be confirmed by IHC or ISH in foetal tissue. The rest of RT-PCRs where negative.
Conclusion: In all cases, acute placental insufficiency secondary to diffuse trophoblastic damage produced by the SARS-CoV-2 infection was the cause of death. Despite one foetus showed positivity by SARS-CoV-2 RT-PCR, IHC and ISH were negative. So, we cannot affirm that it is a congenital infection. More foetal autopsies studies of mothers with active COVID-19 infection are needed to elucidate possible congenital infection by SARS-COV-2.

PS-20-006
Bone marrow disease assessment in neuroblastoma: is it significant in patient management?
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Background & objectives: Neuroblastoma is the most common extracranial tumour in children. Evaluation of bone marrow disease is very important in disease management in neuroblastomas. The purpose of this study is to investigate the predictive significance of histopathological examination BM in neuroblastomas.
Methods: The study included 61 cases with archival bone marrow biopsy tissues. The cases were evaluated examining the percentage of the metastatic tissue and its differentiation. Primary tumour slides were also reviewed to perform Shimada classification based on differentiation status and mitosis karyorrhexis index. Patients' age, gender, NMYC amplification, clinical risk group and disease outcome were also noted.
Results: Of 61 cases, 17 had bone marrow involvement. Of those, eight cases (47.1%) were refractory NB showing disease relapse. Based on bone marrow examination, five cases (29.4%) were categorized as complete response, seven (41.2%) progressive disease, three (17.6%) minimal disease and two (11.8%) stabile disease. Progressive disease category was significantly related with refractory disease and NMYC amplification along with high-risk category ($p = 0.002$ and $p = 0.003$ respectively). The undifferentiated histology and presence of more than 20% of tumour tissue in the bone marrow biopsy at diagnosis were significantly associated with progressive disease category ($p = 0.01$ and $p < 0.001$, respectively).
Conclusion: Bone marrow is the most common site of metastasis in neuroblastomas. The status of metastatic disease in the bone marrow (BM) is a predictor of poor outcome. We conclude that evaluating the percentage of metastatic tumour tissue and tumour differentiation in bone marrow biopsies is of clinical importance in the management of neuroblastoma patients.

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PS-20-007
Histopathological findings in placentas from pregnant women with SARS-CoV-2 infection
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Background & objectives: For pathologists, placenta is the "black box" of pregnancy, because its examination provides significant information about maternofoetal health. Since the onset of SARS-CoV-2 pandemic, the impact of viral infection on foetal development and vertical transmission capacity has been debated.
Methods: Although several viral infections may be associated with specific placental lesions, no histopathological pathognomonic changes for SARS-CoV-2 infection have been reported to date. This study includes 25 placentas from mothers aged 16-43 years, confirmed by RT-PCR with SARS-CoV-2 infection. All specimens have been thoroughly examined using the Amsterdam consensus recommendations.
Results: Over 75% of all placentas were below the 90th percentile in terms of placental weight relative to gestational age. The most common lesions of maternal vascular malperfusion were intervilosal thrombosis and decidual arteriopathy. Distal villous hypoplasia was identified in only 12.5%. Among foetal vascular malperfusion lesions, the following were observed: increased index (6.06) of umbilical cord twisting (75%), thrombosis of vessels with muscle walls (12.5%), avascular villi (18.5%), delayed villous maturation (31.25%) and ectasia of chorionic vessels (25%). The only inflammatory changes identified were secondary to ascending intrauterine infection (acute subchorionitis).
Conclusion: No placental changes pathognomonic for SARS-CoV-2 infection were identified. Most specimens showed varying degrees of maternal vascular malperfusion, which could suggest an etiopathogenic link with altered anticoagulant and microangiopathic status induced by SARS-CoV-2 infection. No placental inflammatory changes associated with SARS-CoV-2 infection were identified. Two placentas showed maternal inflammatory response secondary to ascending intrauterine infection.

PS-20-009
Prognostic value of PD-L1 expression in neuroblastoma
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Background & objectives: Neuroblastoma is the most common solid tumour in childhood and is the most common extracranial solid tumour in children. The present study examined PD-L1 expression, detected by immunohistochemical labelling in neuroblastoma (NBL) cases.
Methods: The study group consisted of 40 NBL patients. Data included gender, age at diagnosis, tumour location, International Neuroblastoma Staging System (INSS) stage, risk group according to the Children's Oncology Group (COG) risk stratification system, histologic subtypes, bone marrow involvement, genetic alterations, clinical follow-up, and final outcome.
The primary antibody used in was: anti PD-L1 (EPR1161(2); 1:200 dilution; ab174838, Abcam).
Results: Of the 40 cases of NBL included in the study 32 (80%) cases expressed PD-L1 while 8 (20%) were found to be PD-L1 negative. Immunostaining for PD-L1 in ganglioneuroma or ganglioneuroblastoma was generally lower than it was for NBL cases. In addition, worse tumour differentiation was marginally associated with PD-L1 expression ($p < 0.05$). The relapse rate was significantly higher in PD-L1 positive patients compared to the other patients ($p < 0.001$). The percentage of PD-L1 positive cells in patients with MYCN amplification was 100%. The stage IV was slightly higher in PD-L1 patients compared with stage I, II, III patients, albeit without statistical significance ($p = 0.053$).

Conclusion: In the quest for new treatments, immunotherapy is potentially useful for chemotherapy-resistant disease. The inhibition of the programmed death ligand 1/programmed death 1 (PD-L1/PD-1) pathway has introduced a new era in cancer treatment.

PS-20-010

Body weight and crown-heel length autopsy standards in a Macedonian perinatal population: single centre experience

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Background & objectives: Foetal reference values are available for several European countries, but no reference values exist for the North Macedonian population.
We aimed to establish accurate body weight and crown-heel length standards, indigenous to our country.
Methods: We reviewed 4,073 consecutive foetal/perinatal autopsies performed between 2012 and 2019. Excluded were cases with: multiple pregnancies, unknown gestational age, congenital abnormalities, intrauterine growth restriction, hydrops, severe septicaemia/virosis, fixed/frozen specimens, newborns aged >24 hours, severe haemorrhage, and alloimmunization. BW was measured in grams and CHL in centimetres at the day of admission. Percentile curves were calculated with the Altman method.
Results: 1,129 cases met the inclusion criteria (age range: 11-42 gw, 64.07% males, 35.93% females, 1.15% undetermined sex), of which 456 (40.39%) were miscarriages, 326 (28.86%) stillborn foetuses, 243 (21.52%) neonates and 15 (1.33%) foetuses were medically terminated pregnancies. BW in grams (BWg) had the following relationship with gw: BWg = 302.923 + gw * -68.766 + gw2 *3.481 ($R2 = 0.930$, $p < 0.0001$). The relationship between CHL in cm (CHLcm) and gw was calculated as following: CHLcm = -23.89 + gw * 2.926 + gw2 * -0.0268 ($R2 = 0.926$, $p < 0.0001$). Corresponding standard deviations were modelled to derive lower and upper reference limits.
Conclusion: The current autopsy study provides bodyweight and crown-heel reference standards with standard deviations, at each gestational age, which are representative of our mixed population. The easy-to-use percentile charts could serve as a valuable tool for the practicing pathologist when performing perinatal autopsies. We believe that strict adherence to the eligibility criteria, the consistency of the autopsy procedure, and the well-designed statistical approach, support the reliability of our results.

PS-20-011

Juvenile xanthogranuloma in children

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Background & objectives: The family of Juvenile Xanthoganuloma (JXG) is a non-Langerhans cell histiocytosis occurring predominantly in neonates and children. We present the clinical and histological characteristics of JXG in children and the correlation of morphology/immunophenotype with the clinical behaviour.
Methods: A retrospective review was performed of 65 biopsy specimens from our laboratory between 2006-2020.
Results: Age ranged from 6 days to 15 years, with female predominance [35 females: 30 males], 50 patients were under 3 years. Solitary cutaneous lesions accounted for 56/65 (86,1%), 3 (4,6%) cases presented as soft tissue mass, 3 (4,6%) cases had visceral involvement and 3 neonatal cases (4,6%) had systemic JXG. Classical JXG was the most frequent 55/65 (84,6%), with variable Touton giant cells and foamy histiocytes. Spindle cell morphology was observed in 11 cases. The immunophenotype CD68/PGM-1(+), CD163 (+), Fascin(+), Factor XIIIa(+), CD1a(-), Langerin (-) was observed in all cases. The expression of Ki-67 was variable regardless of presentation and morphology. One case with systemic disease expressed ALK-1/p-80
Conclusion: JXG presents in children as a cutaneous lesion, less often as a solitary extracutaneous lesion and rarely as a systemic disease, with a favourable prognosis in localized disease. The immunophenotype is characteristic regardless of the clinical and morphologic features and contributes in the diagnosis of the systemic type of JXG which requires treatment.

PS-20-012

Expression of eNOS and CD34 in placental villi of monochorionic diamniotic twins

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Background & objectives: Endothelial NOS (eNOS) and CD34 as known markers of placental villi's endothelial cells are essential for angiogenesis and vasculogenesis. The aim of the study to evaluate eNOS, CD34 expression in placenta of monochorionic diamniotic twins with selective foetal growth restriction (sFGR).
Methods: Histological(H&E) and immunohistochemical studies to primary antibodies to eNOS, CD34(Spring Bioscience) on the paraffin-embedded slices of placental samples taken after caesarean section at 28-36 wks from 22 patients of 24-36 yrs with monochorionic diamniotic twins has been performed. The group with sFGR consisted of placenta samples from 15 puerperas and for control - placenta samples from7 ones. Cases with feto-fetal syndrome excluded.
Results: Histological and immunohistochemical study showed expression CD34 in blood vessels' endothelium of placental villi. We revealed 10x increase number of smaller diameter vessels within one villi in sFGR group(more than 10 vessels in one villi, normally 3-7 vessels), predominant branching of blood vessels($p<0,05$). In cases of sFGR eNOS expression was significantly increased in some placental areas with compensatory changes, whereas in other areas it decreased up to lost staining($p<0,05$). Moreover eNOS expression was detected in the syncytiotrophoblast as membrane cytoplasmic and granular staining. This confirms the high level of angiogenic factors in the trophoblast. In controls eNOS, CD34 expression was moderate in the villous tree and placentas were within gestational age.
Conclusion: CD34, eNOS expression indicates depletion of the compensatory mechanisms of the placenta with sFGR in cases of monochorionic diamniotic twins.

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PS-20-013

Mole and twin: a complete hydatidiform mole and coexistent surviving foetus case report

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Background & objectives: Twin pregnancy with a complete hydatidiform mole and a coexistent viable foetus is a rare entity, with associated risks both during and after pregnancy. A case with a surviving neonate is presented.

Methods: A 31-year-old woman presented at 33 weeks of gestation with a foetal growth restriction alongside a placenta with 50% normal-looking and 50% vacuolated aspect on ultrasound examination. Chorionic villi sampling at the first trimester revealed a 46XY karyotype. At 35 weeks, a spontaneous preterm infant was delivered, with 2,110g and 9/10/10 Apgar score. The placenta was sent to pathologic examination.
Results: On gross examination of the placenta, half was normal with a 36cm in length umbilical cord eccentrically inserted, and the other half was partially fragmented and composed of vesicles of various sizes (max.1,5cm). Both parts were adjacent to each other with an abrupt transition between them. The total placenta weighed 437g.
Microscopic examination revealed two totally separate populations of near normal villi with accelerated maturation, and molar villi with decidua interposed among the two. The molar placenta showed enlarged, round villi with central cisterns and absence of blood vessels, together with circumferential trophoblastic proliferation. Immunohistochemistry with p57 antibody presented <10% nuclear staining of villous cytotrophoblasts and stroma cells.
Conclusion: The presented features were compatible with a viable foetus with a normal placenta coexisting alongside a twin molar placenta. It is important to recognize the increased risk of developing severe complications in this kind of gestation such as preterm delivery, foetal loss, pre-eclampsia, haemorrhage, hyperthyroidism, development of persistent gestational trophoblastic disease or other pregnancy complications. Therefore, close surveillance during molar pregnancy and consequent follow-up is essential.

PS-20-014

The post-autoptic consultation in pregnancies with adverse outcome

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Background & objectives: Miscarriage and stillbirth are common events. Foetal autopsy has a main role in providing answers for the parents. We analysed our experience, providing clinical and emotional care through post-mortem examination and following interview offering them information for a subsequent follow-up.
Methods: This retrospective study includes all foetal post-autopsy interviews carried out at Ospedale Policlinico San Martino from 1/1/2013 to 1/3/2021. Bereaved parents asked to meet the specialized pathologist who performed post-mortem examination. All the autopsies have been reported with a standardized check-list based protocol including microscopic and macroscopic analysis and placental examination. A standardized check-list based report followed every pathologist-parent meeting.
Results: This retrospective study includes all foetal post-autopsy interviews carried out at Ospedale Policlinico San Martino from 1/1/2013 to 1/3/2021. Bereaved parents asked to meet the specialized pathologist who performed post-mortem examination. All the autopsies have been reported with a standardized check-list based protocol including microscopic and macroscopic analysis and placental examination. A standardized check-list based report followed every pathologist-parent meeting.
Conclusion: Foetal autopsy and placenta examination appear critical, providing information for prevention and clinical management. Gynaecologists and Geneticists have an active role in follow-up. The pathologist, meeting with the parents, provides a clear explanation of the causes, helping them in coping with grief and preventing medicolegal issues. Overall, the pathologist-parents interview has been positively perceived, with sporadic difficulties due to socio-cultural differences, psychiatric disorders and underlying animosity.

PS-20-016

Structural profile of vascular remodelling of the stem and terminal villi during pregnancy with congenital heart defects

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Background & objectives: The advances in heart surgery resulted in increased number of women with congenital heart defects (CHD) survived to childbearing age. The risk of developing maternal and foetal complications in such cases depends on structural and functional responses of the system 'mother-placenta-foetus'.
Methods: Twenty term placentae in cases of CHD and 15 controls from physiological pregnancy were studied morphologically. Histopathologic findings and morphometry data were correlated with immunohistochemical (IHC) studies results. The immunohistochemical staining protocol with monoclonal mouse antibodies to SMA (Dako, 1:500) for placental tissue samples had been developed. Differences between groups' data were elucidated by non-parametric Mann-Whitney. Reliability established at $p<0.05$.
Results: Microscopic examination and morphometry revealed an increased volume fraction (VF) of the stem villi' arterial vessels(ASV) lumen – 59.0 (9.5)* and a decrease in the VF of the terminal villi capillaries(CTV) lumen - 24.0 (8) * in comparison with the control group (respectively: 48.0 (14.75) and 28.0 (12), $p<0.05$). The study of SMA expression in the myofibroblasts of the walls of the vessels of the ASV and CTV showed that, in the contrast to the control group, a diffuse increase in expression was registered in CHD cases($p<0.05$).
Conclusion: Structural changes of the ACV and CTV walls indicate the development of placental malperfusion as a response to circulatory hypoxia due to hemodynamic disorders in women with CHD. The impaired vessels remodelling with inadequate placenta function results in various pregnancy complications. Vascular malperfusion leads to a decreased oxygen exchange between the mother and the foetus. Placental dysfunction results in foetal growth retardation. Clinical assessment of pregnancy in CHD cases must be performed with consideration of the oxygen stress risks due to placental malperfusion.

PS-20-017

Assessment of the vascular endothelial growth factor expression and proliferation index in the placental villi syncytiotrophoblast under circulatory hypoxia conditions

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Background & objectives: Circulatory hypoxia during pregnancy may cause placental dysfunction with adverse health consequences for a mother and her child. Violations of blood flow adaptation in pregnant women with congenital heart defects(CHD) could result in placental malperfusion, with negative effect on placental syncytiotrophoblast(PST) functions.
Methods: The associations of VEGF(RTU,Spring) and Ki-67(RTU, BOND) expressions in PST with structural remodelling of the placental villi epithelium in CHD non-operated (group I - 20 cases), in cases of CHD surgical correction(group II - 19) and 15 cases of physiological pregnancy(control group-CG) were studied. The differences between groups were identified by Mann-Whitney U-test. The validity of the data were established at $p<0.05$.
Results: Microscopic examination revealed multiple foci of the placental terminal villi' epithelium damage in non-operated CHD, which were less noticeable in the condition of surgical correction of the defect. Adaptive

proliferation of the terminal villi' epithelium with syncytial nodes' formation, the increased number and length of syncytio-capillary membranes were noted in cases of CHD surgical correction. The compensatory processes detected both in the central and peripheral parts of the placental disc. The IHC study of group I placentae revealed the increased VGEF expression in PST, accompanied with an increased proliferation index. The IGH peculiarities of group II were characterized by a shift in the expression of VGEF and Ki-67 close to the CG parameters.
Conclusion: Structural remodelling and IHC features of PST are discussed in the aspect of placental adaptation to the conditions of hypoxic stress caused by CHD and in cases of the defect's surgical corrections before pregnancy. Knowledge of the possible mechanisms of the placental response to the lack of oxygen in the fetoplacental complex can contribute to the development of obstetric adequate management schemes for the women with congenital heart defects.

PS-20-018
Value of systematic placental examination in foetal loss
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Background & objectives: The causes of foetal loss are diverse. The aim of our work was to evaluate the role of systematic placental examination in determining the causes of foetal loss and to specify the type and frequency of placental and foetal malformations.
Methods: A retrospective study concerning fetoplacental examinations including abortions (more than 12 weeks), stillbirths and children died perinatally. The cases were referred in the department of pathology of a Hospital in North of Tunisia (North Africa) from 1994 and 2018. The classification of placental anomalies was based on the recommendations of the Amsterdam Protocol of 2014.
Results: We included 507 fetoplacental examinations. The mean maternal age was 31.1 years. Maternal conditions were dominated by preeclampsia and gestational diabetes. 279 placentas were pathological and 228 were normal. Of the 279 pathological placentas, 199 were not associated with foetal abnormalities(39%) and in 80 cases(16%) foetal malformations were found. For the 228 normal placentas, the corresponding foetuses showed abnormalities in 123 cases(24%). In 105 cases there were no placental lesions or associated foetal malformations(21%). The main placental abnormalities were maternal vasculostromal lesions(27.4%) followed by foetal vasculostromal lesions(16.9%). Concerning foetuses, the sex ratio was 1.5 and the medium term was 19.4. The most frequent malformations were facial abnormalities(20.7%) followed by chromosomal aberrations(10.3%).
Conclusion: Systematic placental examination has an important role in determining the causes of foetal loss and was determinant in 39% of cases. Therefore, an efficient foetopathological examination should be as complete as possible, and consistent with current recommendations.

PS-20-019
SARS-CoV-2 infection in pregnant women and gestational losses
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Background & objectives: It has been raised whether there is vertical transmission of SARS-CoV-2 to foetuses, and which is the mechanism in cases of foetal death. The study of foetal autopsies of COVID-19 affected mothers with the study of placentas may provide answers.
Methods: We analysed a series of 46 pregnancies from two hospitals in which SARS-CoV-2 infection was evidenced during gestation, from which placenta and/or foetal autopsy were available for anatomopathological study. SARS-CoV-2 infection was investigated in placental tissues through immunohistochemistry (IHC) and positive cases were further confirmed by in situ hybridization (ISH) and PCR.
Results: Ten women were affected by COVID-19 at the time of delivery, with gestational loss occurring in three of them, two in the third trimester. In these two cases, the placentas showed massive involvement by "diffuse trophoblastic damage" (necrosis of the trophoblastic lining with stromal preservation and collapse of the intervillous space with fibrin and mixed inflammation) with positivity for SARS-CoV-2 by PCR in the placental tissue and by immunohistochemistry and in situ hybridization in the trophoblastic lining.
Two other placentas had identical but focal lesions with IHC and ISH positivity. One of these women had active disease 19 days before delivery, and the other during the second trimester.
Conclusion: From the series studied, third-trimester foetal demises were associated with extensive placental findings characteristic of SARS-CoV-2 infection with the demonstration by various techniques (PCR, IHC, and HIS) of viral involvement of the placenta. Identical lesions but of lesser extent can be found in placentas of live, healthy new-borns. We consider that the deaths occur due to placental dysfunction because of the extensive lesional involvement, rather than secondary to vertical transmission.

PS-20-020
Paediatric ovarian tumours: an 11-year experience at a single institution from Tunisia
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Background & objectives: Ovarian tumours in childhood and adolescence are rare, distinguished from those of adulthood by their histological subtype and favourable prognosis. Our aim is to investigate clinicopathologic characteristics and outcomes of ovarian tumours occurring in paediatric population originating from south Tunisia.
Methods: This is a retrospective study conducted in paediatric patients under 21 years old, managed surgically by ovarian masses and diagnosed at the department of pathology of Habib Bourguiba university hospital of Sfax in south Tunisia, between 2010 and 2021. The analysed data were symptoms, treatment, outcomes and pathology.
Results: We identified 140 patients with ovarian masses of which 94.2% were benign and 5.7% were malignant. The mean age at diagnosis was 17.6 years [3-21years]. Abdominal mass/pain was the most common presenting symptom (80%). Five percent of cases were incidentally discovered during appendectomy. All patients had fertility-preserving surgery, either cystectomy (7,1%) or unilateral salpingo-oophorectomy (92,8%). Tumours were bilateral in 3% of cases. Among benign tumours, the majority were serous cystadenoma (38,5%). Mature teratoma accounted for 26,4% of cases. There was one case of juvenil-granulosa tumour and 2 fibro-thecomas. Malignant tumours comprised 5 immature teratomas and 3 dysgerminomas. At follow up, there was no reports of recurrence or contralateral ovarian tumour.
Conclusion: Paediatric ovary tumours are very rare with a reported incidence rate of 2.2/100,000 girls. They have an excellent prognosis even in advanced stages when managed with fertility preserving procedures. They may arise as the first manifestation of a cancer predisposition syndrome. Correct diagnosis of the syndrome may offer the possibility of surveillance for other members of the patient's family. Close follow-up is necessary, given the risk of recurrence.

PS-21 | Pathology in Favour of Developing Countries Posters

PS-21-001
Syphilis: an old enemy masquerading as a new "friend"

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Background & objectives: Syphilis is a STI and a spirochetal disease that has plagued mankind for centuries with recent data showing increasing rates of infection worldwide due to HIV. It has four stages with diagnosis made mostly by serological assays.
Methods: Seven cases of syphilis diagnosed over a two-year period (2018-2019) were retrieved from our departmental archives. Patient data were extracted from their case files and paraffin blocks were cut and stained with routine H&E. Wartin-starry stain was done on all cases. Data was analysed using spss version 24.
Results: The age range of presentation of Syphilis was 25-65 years, with a mean age of 55±13.5 and a male female ratio of 2.5:1. All patients presented with past history of urethral or vaginal discharge. Two patients presented with foot and vaginal ulcers which were biopsied. The remaining five patients presented with a tumour in various part of the body with the scrotum and legs been the commonest site. Biopsy of these sites showed perivascular aggregates of plasma cells with intense fibrosis. Warthin -starry stain was positive in all seven cases. In all cases the physician was not thinking of syphilis.
Conclusion: Syphilis can present as a tumour or ulcer in our setting. To the unsuspecting physician, it is a case of a tumour that is excised and patient is cured but, to the pathologist it is a case of an enemy masquerading as a tumour that needs to be adequately manage to prevent morbidity and mortality. We advocate high index of suspicion of syphilis for any sexually active patient with pass history of genital discharge presenting with a tumour or ulcer.

PS-21-002
Clinicopathological study of de novo metastatic prostate cancer in Yaoundé (Cameroon)

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Background & objectives: The presence of metastasis at diagnosis in a patient, de novo metastatic prostate cancer (mPCa), is a sign of poor prognosis and characterized by low survival rates. The objective was its study in the capital of Cameroon, Yaoundé.
Methods: We reviewed the histopathology reports from the 722 patients diagnosed of prostate cancer at the Centre Pasteur du Cameroon in Yaoundé from 01/06/2020 to 31/08/2020. We included in our descriptive study all patients who presented with at least one confirmed metastasis on imaging followed by prostate biopsy at diagnosis. We housed demographic, clinical and pathological data in an Excel spreadsheet.
Results: Thirteen patients presented with at least one metastasis at diagnosis (1.8%). The average age at diagnosis was 67. Patients lived only in Yaoundé area. The mostly reported initial symptoms were lower limb paraplegia and bone pain (69%). The average total PSA was 182.6 ng/ml. The mostly assigned Grade Group was 5 (54%). Some pathological findings detected were: cribrifom pattern (54%), perineural invasion (38%), chronic inflammatory infiltrates (38%), and high grade PIN (15%). Lymph node involvement was detected in 69% of cases. The most common sites of distant metastasis were spinal vertebrae and pelvic bones (54%) followed by brain, lung, pleura and liver.
Conclusion: The frequency of de novo mPCa reported in our study was probably affected by the intrinsic limitations of a medically underserved area with inadequate pathology laboratory infrastructure. Further work encompassing a larger target population and sample size in all regions of Cameroon is needed. In low-income African countries, it is necessary to improve current plans on early diagnosis of prostate cancer due to limited access by the general population to drugs that increase advanced prostate cancer survival.

PS-21-003
Hepatic space-occupying lesions masquerading as hepatobiliary tumours: a clinicopathologic study

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Background & objectives: The need for liver biopsy for hepatic space-occupying lesions has been sharply reduced due to advancements in non-invasive techniques. We conducted a clinicopathologic study to evaluate liver biopsy's diagnostic value compared with non-invasive techniques in assessing hepatic space-occupying lesions.
Methods: A 6-year retrospective analysis was conducted at a tertiary hospital in Thailand. All cases in which the provisional clinical (i.e., pre-biopsy) diagnosis was primary liver carcinoma were retrieved. The histopathology of all recruited cases was reviewed. The pathological diagnosis was rendered primarily based on routine histopathology using immunostaining as an adjunct.
Results: A total of 302 clinically diagnosed primary liver carcinoma was retrieved. After a thorough histopathological examination, most of these cases (97.7%, N=295) were correctly diagnosed by radiological studies. Only seven non-hepatobiliary tumours, accounting for 2.3% of our series, were initially misclassified as hepatobiliary neoplasms, including hepatocellular carcinoma and intrahepatic cholangiocarcinoma. Epstein-Barr virus-associated smooth muscle tumour, endometriosis, and leiomyosarcoma could clinically mimic intrahepatic cholangiocarcinoma. In contrast, gastrointestinal stromal tumour, neuroendocrine neoplasms (including well-differentiated neuroendocrine tumour and poorly differentiated neuroendocrine carcinoma), and angiosarcoma could mimic hepatocellular carcinoma.
Conclusion: Pre-biopsy (i.e., radiological) diagnosis is very accurate in terms of diagnosing hepatic space-occupying lesions. However, pathological evaluation still plays a role in a minority of cases. Pathologists should be familiar with a wide variety of histomorphology of uncommon primary liver tumours and metastases with appropriate use of immunohistochemistry to diagnose these rare hepatic space-occupying lesions.

PS-22 | Pulmonary Pathology Posters

PS-22-001
Validation of VENTANA (SP263) PD-L1 immunohistochemistry (IHC) assay in formalin-fixed, paraffin embedded (FFPE) cytology samples

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Background & objectives: Assessment of PD-L1 expression to determine suitability for treatment with immunotherapy is important in non-small cell lung carcinoma (NSCLC). Here we describe the validation of fine needle aspirate (FNA) cytology samples for reliable reporting of PD-L1 expression in NSCLC.
Methods: Fine needle aspirate (FNA) samples from NSCLC patients were obtained as FFPE blocks. 4-5μm sections were stained using the VENTANA PD-L1 (SP263) Assay. Scoring was performed at a cut-off of ≥ 1% tumour cells (TC) with membrane positivity for PD-L1 at any

intensity above background. Intermediate and inter/intra-reader precision and cut slide stability were evaluated.
Results: Prevalence of TC ≥ 1% in the commercially obtained cohort was 50.3% (82/163). Intermediate (inter-day) precision (overall agreement) at the TC ≥ 1% cut-off was 100.0% (95%CI: 94.0-100.0%). Intra-reader precision was 98.3% (95%CI: 95.8-100.0%) and inter-reader precision was 96.7% (95%CI: 91.7-100.0%). Average positive and negative agreement were >95% across all reader precision studies. The cut slide stability for unstained slides was confirmed up to two months. Additional time points could not be tested due to sample yield limitations.
Conclusion: The VENTANA PD-L1 (SP263) Assay is robust and reliable at a TC ≥1% cut-off when used on FFPE FNA samples from NSCLC patients. In cases where a cytology sample is the only sample available, a situation common in early-stage disease, use of such samples for PD-L1 testing may remove the requirement for invasive tissue biopsies, thereby increasing the opportunity for a PD-L1 test result for NSCLC patients.

PS-22-002
BAP-1 immunohistochemical expression in pleural and peritoneal mesothelioma
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Background & objectives: Somatic BAP-1 (BRCA1-Associated Protein 1) mutations are reported in mesothelioma. In this study, we aimed to investigate the contribution of loss of BAP-1 expression of mesothelioma and the relationship between BAP-1 expression loss and survival.
Methods: BAP-1 expression was examined immunohistochemically in 41 mesothelioma cases (36 pleural, 5 peritoneal). The BAP-1 slides were evaluated semi-quantitatively as “focal loss”, “total loss” and “no loss”.
Results: The ages of the cases were in the range of 36-80 (median 68). Of the 41 cases, 27 were epithelioid (65.9%), 9 were biphasic (22%), and 5 (12.2%) were sarcomatoid type mesothelioma. Survival data of 39 cases were available. 78% of the cases had died. Overall survival ranged from 1 month to 48 months. BAP-1 loss was evaluated as total loss in 53.7% and focal loss in 12.2% of the cases. BAP-1 loss was not observed in any of the sarcomatoid type mesothelioma cases. A statistically significant relationship was found between BAP-1 loss and histopathological type (p=0.004). Overall survival was increased in mesothelioma cases showing loss of BAP-1 (p=0,025).
Conclusion: In the literature, most of the studies show that loss of BAP-1 expression is associated with epitheloid subtype and longer survival. In our study, we did not observe BAP-1 loss in any of 5 sarcomatoid mesothelioma. Although our study supports the literature, since the number of our cases is low, this situation should be supported by more studies.

PS-22-003
Immunohistochemical profile of control cell cycle and proliferation proteins of atypical lung epithelium with diffuse alveolar damage in comparison with lepidic-predominant adenocarcinoma of the lung
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Background & objectives: Morphology of atypical lung epithelium (ALE) caused by diffuse alveolar damage (DAD) is similar to lepidic-predominant adenocarcinoma (LPA) of the lung therefore it is hard to distinguish them in some cases. We aim to compare expression proteins in ALE and LPA.
Methods: Twenty-four autopsy cases of patients who died from acute respiratory damage syndrome induced by COVID-19 and four cases of LPA. We made slides with the following antibodies: p53, Ki67, p16 for each of the cases, and p63 for four cases. We used H-score for estimating and U-test for statistical analysis.
Results: We found statistically significant differences only in p16 H-score subgroup (group ALE< group LPA, p-value=0,0057). Also, we noticed differences in p63 H-score subgroup (ALE - 66 and 27; LPA - 0 and 0), but the sample is not enough for statistical analysis.
Conclusion: We found that in LPA cases level of expression p16 is significantly higher than in ALE cases with DAD caused by COVID-19, also there were no significant differences in subgroups p53 and Ki67. We suggest, based on a small sample, that expression p63 is significantly higher in AE, but it is required further research.

PS-22-004
Changes in the respiratory system indicators and the leading mechanisms of pathological disorders of the airway patency by workers of the tungsten-molybdenum mine
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Background & objectives: An urgent problem of modern occupational medicine is the study of the role of exogenous and endogenous factors, the assessment of changes in the indicators of ventilation function and the leading mechanisms of pathology of the bronchopulmonary system in miners.
Methods: There were investigated 30 healthy workers with an average work experience (5-15 years) and 80 miners with occupational lung diseases by spirography method: First (I) group 30 people with chronic dust bronchitis-37.5%; II group - 25 persons with chronic obstructive dust bronchitis -31.25%; III group - 25 people with chronic obstructive bronchitis complicated by emphysema of the lungs -31.25%.
Results: Spectrographic analysis revealed a decrease to 70.03% (P<0.001) and 67.10% (P<0.001) in groups I and II compared to the norm - 92.57%. In group III miners, the decrease to 60.71% (P<0.001) was pronounced.
In group 2, the capnographic index significantly increased by 12.43% (P<0.05) and in group III by 9.44% (P<0.01) than in healthy workers with 5-10 years of experience.
The patency of the proximal bronchi in group II significantly decreased by 70.37% (P<0.01) and in group 3 to a pronounced degree to 59.03% (P<0.001), which indicates destructive changes in the histomorphological properties of lung tissue. The patency of the distal bronchi depends on the residual lung capacity in all groups.
Conclusion: The emphysema index showed a significant increase in group III of 1.13 kPa (P<0.001), expressed in group II of 0.87 kPa (P<0.05), in group I they tended to significantly increase.
Pathological changes are caused by mechanisms: 1) predominance of bronchospasm, 2) tracheobronchial dyskinesia, 3) obstruction of the bronchial tree with viscous mucus and sputum, 4) "valve mechanism", which depend on the histomorphology of the tissue, genetic predisposition and high resistance of the disease by workers and progress with increasing work experience.

PS-22-005
Non-small cell lung cancer (NSCLC) PD-L1 testing landscape challenges in the context of upcoming in vitro diagnostics regulation (IVDR) implementation
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Background & objectives: Impending IVDR implementation potentially disrupts current PD-L1 testing practice for all indications. IVDR compliance will require laboratories use only approved therapy specific CE IVD tests. Alternatively, criteria will exist for health institution laboratories to justify Laboratory Developed Test (LDT) use.

Methods: Our DXRX data repository consisting of real-world data from 116 pathology laboratories performing PD-L1 testing for NSCLC across France, Germany, Italy, Spain, and the UK was analysed from January-June 2020 to understand laboratory accreditation status, institution type, and PD-L1 testing practices, including LDT vs kit preference, to assess the potential impact of IVDR enforcement on NSCLC PD-L1 testing.
Results: PD-L1 testing practice varies extensively. Commercial kit use occurs primarily in the UK (100%) and Spain (87%). Most utilized kits are Dako 22C3 pharmDx (29%) or VENTANA PD-L1 (SP263) Assay (13%). LDTs (standalone antibodies or kits used off-label) are more commonly used in France (96%), Germany (88%) and Italy (66%). At least 4 different clones are employed as LDTs across European labs, with most diverse selection observed within Germany. Ventana, Dako, Leica, and Zytomed platforms are installed, with Ventana having the largest footprint (71%) across all markets. The extent of LDT use identifies that IVDR enforcement will potentially impact up to 62% of PD-L1 testing labs across Europe.
Conclusion: Laboratories using LDTs will need to comply with accreditation and LDT/commercial kit equivalence requirements. IVDR adherence in the NSCLC PD-L1 context will be challenging for many European labs justifying continued LDT use versus transitioning to multiple approved kits and/or platforms. Availability of limited sample, specific IHC platform and multiple PD-L1 drug-CDx pairs will further challenge compliance. Inability of laboratories to comply with IVDR may reduce the number of accessible PD-L1 test options and potentially introduce treatment bias in patient management.

PS-22-006
Histopathological features of novel coronavirus (COVID-19) pneumonia in patients with lung cancer: review of cases of an oncology institute
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Background & objectives: COVID-19 is an infection caused by the recently discovered coronavirus SARS-CoV-2. Pulmonary changes are significant, the majority of reported cases showing diffuse alveolar damage. We pretend to describe histopathological findings caused by COVID-19 in patients surgically treated for lung cancer.
Methods: We're analysing pulmonary histopathological features of all patients with lung carcinoma that had COVID-19 disease and were treated with surgery in our Oncology Institute since the beginning of the pandemic. Because all specimens harbour a neoplasm, besides tissue sampling for histology to document tumour, we're sampling pulmonary parenchyma, some with macroscopically visible lesions, photographing and documenting all pathological findings.
Results: The majority of our patients have lung adenocarcinoma. Surgery is the mainstay of therapy, with or without neoadjuvant radiotherapy and/or chemotherapy. Depending on the length of the disease and previous treatment, the morphological features seen in lung specimens vary. Pathological examinations reveal that, apart from the tumour and its inherent changes in the adjacent parenchyma, the lungs of these patients have interstitial proliferation of fibroblasts, lymphocytic infiltration, intra-alveolar macrophages, organizing pneumonia, type II pneumocyte hyperplasia and multinucleated enlarged pneumocytes. Some still have areas with fibrin deposition and hyaline membranes. At the moment, the major changes seen in our lung specimens represent a subacute phase with organizing pneumonia pattern.
Conclusion: COVID-19 is still affecting many countries globally and most pathological information collected and described at this time is from autopsies of patients that died with acute disease. Histopathological data regarding COVID-19 survivors with full recovery, reparative aspects or persistent disease is still very limited. Our access to these patient's lung specimens is a crucial opportunity to recall and share important information that can help to further understand the evolution of this disease.

PS-22-007
Peripheral squamous cell carcinoma in situ of the terminal respiratory unit: an unusual presentation of a preinvasive neoplasia
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Background & objectives: Preinvasive precursor lesions for bronchial-pulmonary carcinomas keep being searched for early diagnosis. Peripheral squamous metaplasia / basal cell hyperplasia with dysplasia and carcinoma in situ have not yet been described as the majority arise in central airways.
Methods: A 65-year-old man, smoker, with previously diagnosed hepatic cirrhosis that evolved to hepatocellular carcinoma, and submitted to surgery in 2017, presented in routine follow up a pulmonary nodule with 33x22x24mm in the right lower lobe. After biopsy was performed, diagnosis of adenocarcinoma of the lung was established and the patient was submitted to lobectomy and lymphadenectomy.
Results: Gross examination showed a white to grayish, firm mass with 4,5x4x1,6cm, well delimitated. Several sections for the carcinoma and pulmonary parenchyma were observed.
Acinar adenocarcinoma with lepidic, papillary and micropapillary patterns was reported. The neoplastic cells were positive for CK7, TTF1 and PD-L1 (70%) and presented a low proliferation index (5%). Occasional mucinous neoplastic cells were characterized (PAS-D).
In surrounding tissue, a terminal respiratory unit (TRU) exhibited a lesion we called squamous cell carcinoma in situ composed of cells with eosinophilic cytoplasm and pleomorphic nuclei with prominent nucleoli and occasional mitotic figures, expressing CK5.6 and were negative for CK7 and CD56. TTF1 with low intensity was expressed in some cells.
Conclusion: The final report was of adenocarcinoma (acinar predominant with micropapillary, papillary and lepidic patterns) with mucinous cells and peripheral in situ squamous cell carcinoma of the TRU. Neuroendocrine cells hyperplasia was also present.
Peripheral localization of a squamous cell carcinoma in situ is recognized after bronchiolization of bronchus epithelium, especially when related to smoking.
Several samplings of lobectomy support the identification of preinvasive lesions as described in this case.

PS-22-008
Endobronchial lipomas, a rare entity: clinicopathological study of 12 cases
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Background & objectives: Lipomas are benign tumours that can arise in nearly any location. In the bronchial tree, lipomatous tumours have been reported rarely. The diagnosis is additionally complicated by the common presence of adipose tissue within pulmonary hamartomas.
Methods: Cases were obtained by searching the surgical pathology archives of the 2 hospitals, originally diagnosed as lipoma involving the bronchus for the period 1990 to 2020. The cases were reviewed by the authors, yielding a study group of 12 cases. Clinical information was obtained from the existing medical record.
Results: The patients ranged in age from 60 to 81 years. All patients were male. All but three patients were smokers. Sites of involvement in the bronchial tree included: right main bronchus (1), left main bronchus (1), right lower lobe bronchus (1), right upper lobe bronchus (2), left lower lobe bronchus (2), and left upper lobe bronchus (5). All lesions were described as "polypoid" at the time of bronchoscopy, and the clinical impression was that of a benign neoplasm. All lesions showed similar morphology: mature adipose tissue predominated. Examination of all sections did not reveal any areas of cellular atypia or mitoses. Typical features of pulmonary hamartoma were not identified.

Conclusion: Bronchial lipomas, such as the current serie, are extremely rare. They are often found incidentally. Endobronchial lipomas tend to cause symptoms, particularly those related to obstruction. In our series these tumours are more common in men and in the left lung. Most of the tumours in our series were small and discovered incidentally. Endobronchial lipomas should be distinguished from fat-rich pulmonary hamartomas. All endobronchial lipomatous tumours in the present series behaved in a benign manner.

PS-22-009

The rat lungs reaction to the silicon compound solved in water of different hardness

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Background & objectives: It is known that inhalation of amorphous silica particles leads to the lung fibrosis. Is it possible to find similar changes in lungs when the silicon intake occurs with the drinking water of the different hardness?
Methods: We studied the lung of white outbred male rats. Control groups (n=5 in each group) received ad libitum drinking bottled water, distilled water and tap water. Experimental groups received the same water supplemented with sodium metasilicate (10 mg/l). After 9 months rats were sacrificed. The lungs were isolated, fixed in 10% formalin, embedded in paraffin, cut and stained with hematoxylin-eosin.
Results: The specific gravity of the lungs relative to body weight of rat was 1,44% (333 g) and 0,85% (487,5 g) for experimental and control group with bottled water respectively. In histological slides of lungs, we noticed that under the influence of the silicon numerous areas of necrosis appeared. Also, we found the number of alveoli decreased (1,7 times), alveoli merged together, the diameter of the alveoli increases 1,4 times, the interalveolar septa in rats receiving silicon 1,6 times thinner than those in the rats of the control group. Similar visible and microscopic changes were also observed in the lungs of rats that received silicon compound with tap and distilled water.
Conclusion: Our results indicate that the silicon acts on the lungs of laboratory rats in the same and does not depend on the hardness of the water in which it is dissolved. The daily use of water in rats with the addition of silicon negatively affects the state of the lungs, leading ultimately to silicosis, regardless of the original composition of the water.

PS-22-010

PD-L1 expression in NSCLC - our institution experience

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Background & objectives: Treatment with immune checkpoint inhibitors is limited to patients with advanced stage non-small cell lung cancer (NSCLC) and high tumour expression of programmed death ligand 1 (PD-L1). The objective this study was to examine PD-L1 expression in patients with NSCLC.
Methods: We retrospectively evaluated 22C3-PD-L1 expressions of 204 patients from Institute for Lung Diseases of Vojvodina in Sremska Kamenica that were diagnosed with NSCLC. The percentage of viable tumour cells showing partial or complete membrane staining at any intensity was tumour proportion score (TPS). PD-L1 status was reported as: negative (TPS<1), low expression (TPS 1-49%), and high expression (TPS≥50%).
Results: In this study, 123 men and 81 women were included with an average age of 64 years (from 31 to 86). The most patients were in III/IV stage NSCLC (179; 88%) and had good performance status (199; 96%), positive smoking history (176; 86%) and had adenocarcinoma histology (119; 58%). TPS was negative in 85/204 (42%) patients, in 65/204 (32%) showed low expression and in 54/204 (26%) demonstrated high expression.
Conclusion: The rate of 22C3-PD-L1 expression of NSCLC detected in this study was similar to the frequencies of the published data in world literature.

PS-22-011

Comparison of transthoracic fine needle aspiration cytology and surgical biopsy in patients with peripheral pulmonary lesions

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Background & objectives: Transthoracic fine needle aspiration (TTFNA) has become a widely used technique for peripheral lung lesions evaluation. The objectives of our study were to examine the adequacy of samples and sensitivity of TTFNA in the diagnosis of peripheral pulmonary lesions.
Methods: Retrospective study included 248 patients who underwent TTFNA of peripheral pulmonary lesions and consequential surgical procedure in 5-year period. The material was processed at the Department of Pathology and Molecular Diagnostics. The following were analysed: sex, age, adequacy of cytological samples (CS) for diagnosis and molecular testing, tumour localization and dimensions, as well as cytological and pathohistological characteristics of lesions.
Results: The adequacy of the CS was 93.15%. The proportion of adequate-diagnostic samples was higher in patients with lesion >4cm and this difference shows statistical significance. CS of lung adenocarcinoma have a high adequacy for EGFR analyses of 92.75% and it doesn't depend on the size and location of the lesion. The most commonly diagnosed lung tumour was adenocarcinoma (45.51%), squamous cell carcinoma (31,43%) and NSCLC-NOS (16,77%). Patients with NSCLS-NOS in CS, after pathohistological analyses were diagnosed most commonly with adenocarcinoma (53.85%), followed with squamous cell carcinoma (26,92%) and large cell carcinoma (11,51%). The sensitivity of TTFNA for peripheral lesions was 71% - for malignant (75.24%) and for benign (28.57%).
Conclusion: TTFNA is an effective and highly sensitive method in determining the aetiology of peripheral pulmonary lesions.

PS-22-012

Feasibility of next-generation sequencing in RNA obtained from fibroblastic foci of a bleomycin-induced pulmonary fibrosis rat model

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Background & objectives: Bleomycin-induced pulmonary fibrosis murine models are used to dissect out lung fibrogenesis mechanisms. The main goal of the study was to extract adequate RNA from lung tissue microdissected fibroblastic foci (FF),the active lesion in usual interstitial pneumonia pattern, for RNA-sequencing.
Methods: Bleomycin-induced pulmonary fibrosis rat models (Sprague Dawley) were used to isolate FF by laser microdissection and to extract RNA using the RNeasy® FFPE kit, modified in our Laboratory. The final RNA concentration was assessed by the Qubit RNA Assay Kit and the RNA quality by a 2100 Bioanalyzer Agilent 6000 Pico Kit (expressed as percentage of RNA fragments >200 nucleotides-DV200).
Results: Six bleomycin-induced pulmonary fibrosis rat models were developed, and two of them were treated with Nintedanib. After morphological evaluation of lung tissue samples, clear-cut signs of fibrotic remodelling were detected in all animals, but treated rats showed a very small number of FF. FF from two rats, one treated and one untreated, were isolated (area: 0.03 and 0.11mm2) and, despite the small tissue amount, adequate RNA was extracted: its average concentration was 750pg/μL with a DV200 mean value of 52% (low-medium quality). These results are in line with those obtained from tissue samples of

patients with idiopathic pulmonary fibrosis (mean area: 0.40mm2, average RNA concentration: 2992.8 pg/µl, mean DV200: 47%).
Conclusion: These data showed that this protocol, optimized in our laboratory, led to the extraction of adequate RNA for RNA-sequencing from small formalin-fixed paraffin-embedded tissues. The study of gene expression signatures in specific cells/areas of archival tissue, also obtained from experimental animal models, represents an important issue for a better understanding of disease pathogenesis and for the identification of crucial biomarkers. RNA-sequencing results will be presented during the forthcoming congress, particularly focusing on gene expression in clinical vs experimental samples.

PS-22-013
Multicentre evaluation of the Idylla™ GeneFusion cartridge in lung cancer
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Background & objectives: Targeted therapy in NSCLC requires the assessment of multiple oncogenic driver mutations, including fusion genes. This retrospective study evaluated the Idylla™ Genefusion cartridges, which detect alterations in the ALK, ROS1, RET and NTRK1/2/3 genes, and MET exon14 skipping mutation (METex14).
Methods: This multicentre study (17 centres) included 312 FFPE tissue samples from NSCLC patients : 117 ALK; 43 ROS1; 21 RET; 3 NTRK1 and 1 NTRK3 rearrangements; 31 METex14, and 96 wild-type samples, previously obtained by routine reference methods (NGS/FISH/rt-PCR). One to 3 sections of 5 to 10 µm FFPE tissue were used with ≥ 10% of tumour content.
Results: Valid results for all biomarkers were obtained with Idylla™ in 275 cases. The overall concordance between Idylla™ and reference methods was 93%, the global sensitivity and specificity were respectively 93.4% and 93.5%. The positive concordance was 97.2%, 91.9%, 100%, 100%, 100% for ALK, ROS1, RET, METex14, and NTRK, respectively and the negative concordance was 96.9%, 97.9%, 98.8%, 98.6%, 99.4% for ALK, ROS1, RET, METex14 and NTRK, respectively. The discordances were divided into 6 samples with alteration identified by Idylla™ and not detected by the reference methods ; and 13 samples with no detected alteration by Idylla™ but identified by the reference methods, including 7 FISH without NGS validation.
Conclusion: Idylla™ GeneFusion is an automated, reliable, ease-of-use, simple (<2 minutes hands-on time) test, and has the shortest turnaround time compared to existing diagnostic tests (3 hours turnaround time), enabling the detection of clinically relevant alterations in ALK, ROS1, RET and NTRK1/2/3 rearrangements, and MET exon 14 skipping mutation, without necessitating molecular expertise or infrastructure.

PS-22-014
Pulmonary congenital cystic adenomatoid malformation: particular cases diagnosed in adults
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Background & objectives: Pulmonary congenital cystic adenomatoid malformation accounts for 25% of congenital lesions. It is usually diagnosed in neonatal period but can be diagnosed during adulthood. Our aim was to describe the clinical, microscopic features of 7 cases diagnosed in our department.
Methods: between 2000 and 2011, 7 cases of pulmonary congenital cystic adenomatoid malformations were diagnosed. The information concerning the age, sex, symptoms, radiological findings, therapeutic modalities and microscopic findings were collected.
Results: Our study contained 6 men and 1 woman with a mean age of 16.2 years. The most frequent symptoms consisted in bronchitis in 6 cases, with chest pain in 2 cases. Radiologic findings consisted in a heterogeneous cystic opacity in all cases. CT-scan revealed cystic lesions in 6 cases and bronchial dilatation lesions in 1 case. Surgical resection was performed in all cases consisting in lobectomy in 6 cases and pneumonectomy in 1 case. Microscopic exam concluded to a pulmonary congenital cystic adenomatoid malformation in all cases. No patient presented complications within a follow-up period of 28.8 months.
Conclusion: Inspite of the rarity of pulmonary congenital cystic adenomatoid malformations in adults, the diagnosis should be suspected when facing a symptomatology of recurrent bronchitis associated with multilocular cystic masses. The prognosis of the lesions depends on the microscopic subtype and the size of the lesions. The treatment is based on surgical excision.

PS-22-015
KRAS G12C mutated lung adenocarcinomas: a morphological and molecular cartography
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Background & objectives: KRAS mutations are present in 30% of lung adenocarcinomas (LUADs). KRAS G12C LUADs have become a major subject of interest after promising clinical trials of Sotorasib. We present a cartography of a LUADs series harbouring the KRAS G12C mutation.
Methods: All LUADs with a KRAS G12C mutation diagnosed between 2016 and 2020 using a Next Generation Sequencing 26 gene panel for lung cancer were included in our study. Each case was individually assessed by two experienced pathologists for morphological characteristics including histological type, nuclear atypia, necrosis, and tumour-infiltrating lymphocytes (TILs) count. Immunohistochemical analysis was performed for TTF1 and PD-L1.
Results: 200 KRAS G12C mutated LUAD were retrieved. The mean age was 62 years; 36.5% female and 63.5% male. The principal histologic subtypes were adenocarcinoma not otherwise specified 40% and acinar 30% of cases. The number of TILs was high or moderate in more than 50% of cases. Nuclear atypia was present in 68.5% and necrosis in 30% of cases. The immunohistochemical profile showed TTF1 positivity in 78% and PD-L1 positivity in 42% of cases. The molecular profile showed a strong association between KRAS G12C and STK11 mutations in 25% of cases. The co-mutated KRAS G12C-STK11 cases were associated with a higher number of TILs and a lower PD-L1 positivity.
Conclusion: KRAS G12C mutated LUADs represent a particular subtype characterized by a high inflammatory infiltrate, a relatively low PD-L1 positivity and a complex molecular profile with intricate interaction with various genes including STK11. A more in-depth characterization of the tumour histology, surrounding microenvironment and molecular profile of this specific subtype of LUAD could be useful to better select the patients that could benefit from novel targeted therapies to achieve the best treatment response.

PS-22-016
Detection of mutant KRAS in blood and liquid based cytology (LBC) specimens in patients with Non-Small Cell Lung Cancer (NSCLC)
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Background & objectives: Diagnosis of lung cancer entails invasive procedures such as endobronchial ultrasound and needle biopsy posing significant risks. Could the molecular detection of oncological markers be diagnostic when performed using minimal material from liquid based cytology (LBC) or peripheral blood specimens?

Methods: As part of the KEBI-Cyto study, we aim to recruit 100 adults with a new diagnosis of NSCLC over a 24 month period. Application of the Biocartis Idylla Cartridges to both LBC and peripheral blood for the detection of mutant KRAS will be compared against standard processing of FFPE clot cytology specimens to determine the reliability of the novel method.
Results: To date we have recruited 21 patients diagnosed with cancer by endobronchial ultrasound FNA. 11 samples have a confirmed diagnosis of lung adenocarcinoma, 4 EUS samples of SCC and 2 NSCLC. Detection of mutant KRAS was found in 4 cases: 3 adenocarcinoma cases and 1 NSCLC; 3 G12C mutations and 1 G12V mutation. All 3 G12C mutations were detected in peripheral blood. 1 case where mutant KRAS was not detected in peripheral blood was staged at T1cN1M0. Of the 17 samples where mutant KRAS was not detected, Wild type KRAS was detected by both tissue and plasma testing. Therefore confirming 100% specificity and an actionable basis for G12C treatment.
Conclusion: Our preliminary results show promise for the detection of mutant KRAS in NSCLC LBC and peripheral blood samples. Such application provides a means of rapid, non-invasive diagnostic turnover at local centres. Furthermore, given the reported higher prevalence of the KRAS mutation to the mutually exclusive molecular mutations (EGFR, ALK and ROS-1) we propose testing for the KRAS mutation first. This could therefore rationalise molecular testing and furthermore streamline molecular diagnostic resources.

Funding: Biocartis Idylla TM provided funding of the cartridges used in the study to enable the study to go ahead. No other conflicts of interest known.

PS-22-017
SMARCA4-deficient undifferentiated thoracic tumour: a case report and a review of literature on a rare novel entity
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Background & objectives: SMARCA4-deficient undifferentiated thoracic tumour is a recently described entity with particular clinicopathologic (male predominance, smoking history, mediastinum, lung and/or pleura involvement) and molecular (SMARCA4 mutations/expression loss) features. The prognosis is poor with a median survival time of 6-7 months.
Methods: Here we report a case of a 68-year-old male with a 50 pack-year smoking history who recently quit. He underwent a thoracic CT scan due to respiratory symptoms (cough and dyspnea for minimal efforts) with detection of a right lower lung mass with 36mm. A transthoracic biopsy was performed.
Results: Histological examination showed lung parenchyma extensively occupied by a solid pattern neoplasia composed by epithelioid and rhabdoid cells with amphophilic cytoplasm, some with rhabdoid inclusions, and round vesicular nucleus with prominent nucleoli. Immunostains show focal equivocal positivity for CAM5.2 and pan-keratin. However, the tumour cells are also clearly negative for SMARCA4, indicating loss of the product of this gene in SWI/SNF complex, and in addition, there is strong nuclear positivity for SOX2 and SALL4.
Conclusion: The SMARCA4-deficient undifferentiated thoracic tumour is a challenging diagnosis, especially in the context of a lung/mediastinal biopsy where the product is usually scarce. Awareness of this entity and its morphology are essential for a correct diagnosis. It is important to disclose this neoplasia because as it becomes more well-known and additional cases begin to be identified, a more complete and accurate picture of its presentation, prognosis, and how these tumours should be staged and treated will become more apparent.

PS-22-018
T Lymphoblastic lymphoma: histopathological evaluation of 49 cases
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Background & objectives: T Lymphoblastic lymphoma is a rare form of aggressive non-Hodgkin's lymphoma. It is a neoplasm of lymphoblasts committed to T-cell lineage. The aim of this study is to describe the clinicopathological characteristics of T lymphoblastic lymphomas.
Methods: We report a retrospective study of 49 cases of T Lymphoblastic lymphoma diagnosed at our department of pathology between 2001 and 2020. The diagnosis was made on lymph node biopsies in 11 cases, pleural biopsies in 15 cases and mediastinal biopsies in 23 cases. Immunohistochemical studies using CD3, CD20, Tdt, CD99 and CD1a antibodies were realized in all cases.
Results: Of the 49 patients, 31 were men and 18 were women aged between 6 to 87 years with a mean of 29. Histopathologic examination showed a dense and diffuse lymphoid proliferation composed of small to medium size tumour cell with scant cytoplasm, slightly distorted round nuclei with fine chromatin and indistinct or small nucleoli. Mitotic figures were numerous. Immunohistochemical studies showed that the tumour cells expressed CD3, CD99 and CD1a in all cases and Tdt in only 44 cases. CD20 was negative in all cases.
Conclusion: T lymphoblastic lymphoma is a rare disease which represents about 2% of all non-Hodgkin lymphomas occurring in late childhood adolescent and young adult men. Mediastinal mass, pleural and pericardial effusions are the major clinical presentations of T lymphoblastic lymphomas. The main differential diagnosis involves type B1 thymoma with prominent immature T-cells. Generally, a poor prognosis has been related to T-phenotype relative to B-cell lineage.

PS-22-019
Potential role of Tenascin C (TNC) in human lung adenocarcinoma progression
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Background & objectives: Tenascin C (TNC) is an extracellular matrix protein and a potential biomarker affecting progression of different tumour types, such as pancreatic and lung cancer. In this study, we investigated the functional role of TNC in adenocarcinomas of the lung.
Methods: TNC expression was evaluated by IHC of 130 patients including lung adenocarcinomas (LUAD), normal tissues and metastases. Based on The Cancer Genome Atlas data set, we examined the correlation between TNC mRNA expression and EGFR aberration. LUAD cells (with/without EGFR mutation) were tested for their invasion capabilities during exposure to human lung fibroblast (HLF) conditioned medium after siTNC knockdown.
Results: Immunohistochemical staining of TNC in LUAD showed a peritumoral stromal expression, which was significantly increased ($P<0.0001$) expression in primary tumour samples compared to normal lung tissue. Further, we found a significant correlation between TNC mRNA expression and EGFR aberration, especially an increased TNC mRNA expression in cases with higher EGFR copy number as well as EGFR protein level ($P<0.0001$; $R=0.276$). In line with these results, the EGFR-mutated H1975 LUAD cell line demonstrated a significant decrease in cell invasion when cultured with TNC-depleted HLF-medium and displayed a smaller lamellipodia perimeter and smaller surface area after treatment with TNC-depleted HLF medium.
Conclusion: Increased TNC protein level is observed in the peritumoral stroma of lung adenocarcinoma samples and correlates with EGFR aberrations in silico. Inhibition of TNC in lung fibroblasts leads to reduced invasiveness of LUAD cells harbouring EGFR-activating mutations. This study provides the evidence that TNC expression might be a biological relevant factor in LUAD progression in an EGFR-dependent manner and that it regulates tumour cell invasion by rearrangement of the actin cytoskeleton, especially affecting lamellipodia formation.

PS-22-020

Systemic extra-nodal Rosai-Dorfman disease with increased serum IgG4 level and absence of KRAS and MAP2K1 mutations: a case report

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Background & objectives: Rosai-Dorfman disease and IgG4-related disease(IgG4-RD) are both uncommon entities which have been reported showing overlapping histopathological features. Herein, we reported a case of systemic extra-nodal Rosai-Dorfman disease with increased serum IgG4 level, and histolopathologically mimicking IgG4-RD.
Methods: Rosai-Dorfman disease and IgG4-related disease(IgG4-RD) are both uncommon entities which have been reported showing overlapping histopathological features. Herein, we reported a case of systemic extra-nodal Rosai-Dorfman disease with increased serum IgG4 level, and histolopathologically mimicking IgG4-RD.
Results: An excision biopsy of the left chest wall lesion was carried out and it featured a histiocytic neoplasm composed of large histiocytes with conspicuous emperipolesis. These histiocytes are positive for S100, CD68 and CD163, negative for CD1a. The surrounding stroma displayed fibrosis and an increased IgG4 positive plasma cell rich (IgG4/IgG ratio >40%) lymphoplasmacytic infiltration.
Next generation sequencing was performed on the chest wall lesion. No mutations, particularly KRAS and MAP2K1 or gene fusions were identified. The patient was treated with steriods after the resection. The follow-up at three months interval showed decreased size of the left posterior parietal lesion and no other new lesion.
Conclusion: The Rosai-Dorfman disease has been known to demonstrate overlapping features of IgG4-RD on histopathological ground. The unusual presence of increased serum IgG4 level in current case may mislead the clinical judgment. However, a careful histology examination in conjunction with the awareness of the overlapping features of these two diseases will help us to arrive on a correct diagnosis.

PS-22-021

Clinical-radiopathological correlation in post-mortem pulmonar biopsies of patients with COVID 19

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Background & objectives: Numerous studies have confirmed the presence of diffuse alveolar damage (DAD) as the main cause of respiratory failure in patients with COVID 19.
We have studied 57 post-mortem biopsies with others relevant findings.
Methods: Percutaneous core needle biopsies post-mortem were performed to patients with a confirmed diagnosis of SARS-CoV-2 infection. Five groups of anatomo-pathological findings were constituted (DAD in exudative phase, DAD in proliferative phase, mixed DAD, lung tissue with nonspecific alterations and lung tissue without alterations). Each group was correlated with clinical and radiological variables.
Results: 57 biopsies were performed. The mean age was 81 years (range 52-97), 68% men. DAD in exudative phase 10.2%, DAD in proliferative phase 33.9%, mixed DAD 25.4%, non specific alterations in 15.3% and normal lung tissue in the remaining 15.3%. Among the patients with proliferative and mixed DAD, 7 cases with acute organized fibrinoid pneumonia (AFOP) were included. Signs of bronchopneumonia were observed in 23. The evolution time was approximately 20 days. The presence of bronchopneumonia led to a faster outcome towards death, reducing the evolution time by 12 days. The predominant symptom was dyspnea. 70.5% of the patients with DAD had radiological alterations at the time of admission.
Conclusion: In addition to DAD in the exudative and / or proliferative phase, the frequent finding of lymphoid interstitial infiltrate corroborates the severe inflammatory response caused by the virus in the lungs. Highlight the significant number of AFOP cases in our series. From the radiological point of view (chest X-ray and / or pulmonary CT) there is a high level of concordance for the diagnosis of bronchopneumonia and DAD in general, but without differentiating between the exudative and proliferative phase.

PS-22-022

Morphometry the lungs atelectatic areas in radiation-induced injury

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Background & objectives: In the malignant tumours' treatment, such as breast cancer, lungs or oesophagus, radiation therapy plays a substantial role. However, this method can damage healthy lung tissue and can lead to pulmonary collapse or fibrosis up to 30% of cases.
Methods: Six groups and a control one of male white non-linear rats were took in this study. A single dose of 12Gy of γ-radiation was given on the cardiac lobe of the right lung. Lung tissue samples were removed on the 7,14 and 50-day after exposure. For histology examination the lung tissue was fixed, sectioned, stained with H&E and then digitalized.
Results: For morphometry and statistical analysis, we used ImageJ and R. Areas of pulmonary collapse were detected in 27% of cases. On the 7-th day, the area of atelectasis were detected subpleural. The morphometry showed the decrease of thickness of alveolar septa(5.29±0.74μm vs 6.69 ±1,0μm in control); the mean alveolar volume (520± 233 μm2 vs control 839.58 ±156.63 μm2). Moreover, the ratio of stromal and air region was higher than control up to 23%. However, 14-th day of experiment, we found the enlargement of alveolar septa, progressive increasing stromal/air ratio, and intrapulmonary atelectasis. Additionally, the muscle shortening(%) of the small bronchi had tendency for increasing up to 43%vs15 ±5,3% in the control group.
Conclusion: On the 50-th day of experiment, the previous atelectasis areas had tendency to develop in the "honey-comb" lung or fibrosis.
Radiation exposure can induce fast lung damage that may manifest with subpleural atelectasis on the 7-th day. The reduction of alveolar wall thickness may correlate with the death of alveolocytes. Intrapulmonary atelectasis requires a prolonged period of time and correlates with bronchoconstriction.

PS-22-023

MMP9 and TGFβ expression in non small cell lung cancer

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Background & objectives: An important role in the pathogenesis of non-small cell lung cancer (NSCLC) is applied by growth factors and their receptors, as well as matrix metalloproteinases (MMPs), which are associated with tumour progression. To study the features of MMP9 and TGFβ expression in patients with NSCLC.
Methods: A surgical material was analysed from patients with NSCLC (n=32) and a control group (n=32). Morphometric and statistical analysis of the MMP9 and TGFβ expression was performed using AperioImageScope v12.4.0.5043, Statistica10, MedCalc19.6 software, $p<0.05$.
Results: MMP9 expression in tumour cells, regardless of the histological type of lung cancer, was significantly higher than in the alveolar and bronchial epithelium of the control group (U=442/p<0,000), and also had even higher values of positivity and intensity in the foci of lymph node metastases (U=1935/p=0,003 and U=127/p<0,000 respectively).
The slightly different trend was observed in relation to the expression of TGFβ: it was the highest in the control group, decreased both in positivity and intensity in the primary tumours (U=451/p<0,000) and increased in lymph node metastases (U=85/p<0,000).

It was found following parameters were associated with the cancer-specific survival of patients with NSCLC: the epithelial expression of MMP9>87.5% and TGFβ>1.91%.
Conclusion: The significantly higher expression and activity of MMP-9 in tumour tissue and lymph nodes metastases and lower expression TGFβ in tumour tissue and higher in lymph nodes metastases than in surrounding tissue supports the important role of these markers in the growth and progression of lung cancer, and the possibility of their using as a suggested therapeutic targets.

Funding: 2.129 "To develop an algorithm for determining subclinical recurrence of non-small cell lung cancer based on the morphological characteristics of the tumour and molecular genetic markers"

PS-23 | Soft Tissue and Bone Pathology Posters

PS-23-001
Intravascular fasciitis of an upper-arm blood vessel
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Background & objectives: Intravascular fasciitis was first described by Patchefsky and Enzinger in 1981 as an unusual variant of nodular fasciitis, which exhibited an intimate association with vascular walls. The lesion is commonly located in the head, neck, and extremities.
Methods: A 50-year-old Caucasian male presented with a subcutaneous mass on his right upper-arm. He reported that the lesion had increased in size over the past weeks and denied any history of pain. Clinical examination revealed a 2.7 cm x 1.8 cm firm, smooth-surfaced, movable nodule. An excisional biopsy of the soft tissue mass was performed.
Results: Grossly, the surgical specimen consisted of a soft, tan, well-demarcated mass. Microscopic examination of the Hematoxylin and Eosin (H&E) stained sections revealed a spindle cell proliferation arranged in a swirling and intersecting pattern entirely localized within the lumen of a dilated blood vessel. The nuclei of the spindle cells were relatively uniform. Mitotic activity was noted but no atypical mitotic figures were identified. Multinucleated giant cells were scattered among the spindle cells, along with extravasated red blood cells and lymphocytes. Immunohistochemistry revealed reactivity of the spindle cells for SMA, with a Ki67 proliferation rate of less than 2%. Staining for CD34 demonstrated immunoreactivity of the vascular wall, outlining the proliferation.
Conclusion: Through this rare case report we would like to raise awareness towards this non-neoplastic lesion, as it could be misdiagnosed as sarcoma or an intravascular neoplasm which may lead to a more aggressive treatment. The diagnosis of this lesion may be facilitated by special stains for elastic fibres or immunohistochemical stains for vascular markers. Treatment consists of complete surgical excision, although cases of recurrences have been reported in the scientific literature.

PS-23-002
A case report of newly described entity: histiocyte-rich rhabdomyoblastic tumour
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Background & objectives: Skeletal muscle tumours are classified into benign (rabdomyoma) and malign (rabdomyosarcoma subtypes) according to WHO book. But recently, a rabdomyoblastic tumour with certain morphological features, as circumscription, accompanying histiocyte and lymphocytes, very low mitosis, favourable prognosis and without myoD1 mutation is defined.
Methods: A 39-year-old male presented with a painless mass in the thorax wall without any traumatic history. Ultrasonography showed a solid lesion in the pectoral muscle with a suspicion of lymph node. Tru-cut biopsy and after reporting tru-cut biopsy excision was performed.
Results: Sections showed cellular spindle cell proliferation, some were pleomorphic, some had eosinophilic cytoplasm. No mitosis was seen. Tumour cells were positive for desmin, SMA; patchy positive for myoD1, focally for myogenin; negative for S-100, CD34, caldesmon. Ki-67 was 5%. We concluded, this lesion can be a pseudosarcomatous proliferative myositis or an atypical rabdomyoblastic tumour with uncertain malignant potential. Patient received wide excision. Macroscopically, well circumscribed, 2x1,8x2 cm, nodular lesion is detected. Morphological and immunohistochemical findings were similar with tru-cut biopsy, in addition, foamy histiocyte proliferation and peripheral lymphoid tissue were easily seen. We made the diagnosis of histiocyte-rich rhabdomyoblastic tumour. After 4 months of follow-up, no tumour recurrence was observed.
Conclusion: Histiocyte-rich rhabdomyoblastic tumour(HR-RMT) is an unusual neoplasm showing skeletal muscle differentiation, involved in trunk, lower limb, neck and seen in young-to-middle age adults with intermediate malignancy. This tumour is clinically, morphologically and molecularly distinct from other tumours of skeletal muscle and angiomatoid fibrous histocytoma. Also, very recently, it is showed that inflamatuar leiomyosarcoma and HR-RMT have similiar morphologic, immunohistochemical and genetic features and proposed reclassification as inflammatory rhabdomyoblastic tumour. Additionally, well characterised cases are necessary to fully understand this tumour.

PS-23-003
Epstein-Barr Virus associated smooth muscle tumour of bilateral adrenal glands: report of two cases belonging to two siblings
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Background & objectives: EBV associated smooth muscle tumour (EBV-SMT) is a smooth muscle tumour related to EBV infection. EBV-SMTs share similar features with conventional leiomyomas. In addition, two common findings are reported: presence of small cells with irregular nuclear contours and intratumoral T lymphocytes.
Methods: Four years old male patient with severe asthma and allergic symptoms presented with recurrent abdominal pain. On physical examination cafe au lait spot and multiple inguinal lymphadenopathies were seen. Detailed patient history revealed that parents were third cousins. Imaging studies showed bilateral adrenal mass (5,2 cm and 1,1 cm) and biopsy was taken with adrenocortical carcinoma as preliminary diagnosis.
Results: Morphologically tumour consisted of spindle cell mesenchymal neoplasm with mild pleomorphism, no mitoses or necrosis. Immunohistochemically SMA, desmin, caldesmon expression were seen with low Ki67 proliferation index. EBER-ISH was positive; case was signed out as EBV-SMT. Four months later 9 year old brother of the patient presented with similar symptoms. Imaging studies showed bilateral adrenal mass and biopsy was taken. Morphogical and immunohistochemical findings were similar, concordant with EBV-SMT.
Conclusion: EBV-SMT is a rare neoplasm seen within a wide age range. They are seen in the setting of immune suppression from a variety of causes, including HIV infection, congenital immunodeficiency and post-transplant immunosuppression. It has been shown that childhood tumours are usually associated with primary immunodeficiency syndroms, mostly being multicentric (71%). Prognosis depends on patient's immune system rather than morphology. We report two unique cases of bilateral adrenal gland EBV-SMT's presented in two brothers with no prior diagnosed immunodeficiency syndrome.

PS-23-004

Clinicopathologic features of a series of pleomorphic liposarcomas from a tertiary cancer referral centre in India

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Background & objectives: To study various clinicopathological features and outcomes of retrospectively diagnosed pleomorphic liposarcomas(PLPS).
Methods: Fifty cases diagnosed as PLPS, including those diagnosed as pleomorphic sarcomas with mention of "lipoblast" (January 2014-December 2019), at our Institute, were evaluated(BR with SG), as per established diagnostic criteria.
Results: Eleven(22%) cases were excluded (mostly dedifferentiated liposarcomas(DDLPSs). Thirty-nine(78%) cases were included. Age-range was 19-83 years(median=50). M:F ratio was 1.8:1. All tumours were deep-seated, including 14(35.8%) in lower extremity. Tumour size ranged from 4-25.1cm(average=12.8). Microscopically, all tumours displayed variable numbers of lipoblasts, including pleomorphic forms. Most tumours(21/39, 53.8%) displayed lipoblastic differentiation, followed by pleomorphic sarcomatous(n=15), myxofibrosarcoma-like(n=5) and epithelioid(n=8) type. Other patterns were hibernoma-like, hemangiopericytoma-like and rhabdoid-like. Immunohistochemically, tumour cells were positive for S100P(17/24,71%), CD34(5/13), AE1/AE3(2/11) and SMA(5/13). Therapeutically(n=32),most patients(11,34%) underwent surgical resection with adjuvant radiotherapy. Eleven patients(34.4%) developed recurrences and 16(50%) developed metastases. Median disease-free survival(DFS) was 10.5 months. Estimated 5-year DFS was 20.2% and estimated 5-year overall survival rate was 66.9%.
Conclusion: This constitutes the first study from our country describing a wide clinicopathological spectrum of PLPS. Classical histopathology remains its diagnostic gold standard. DDLPS and other pleomorphic sarcomas are close differential diagnoses. Surgical excision was treatment-mainstay with adjuvant radiotherapy, in large-sized tumours. Certain clinicopathological features, such as larger T-size (exceeding 8 cm) and epithelioid morphology were associated with recurrences and metastasis.

PS-23-005

Concurrent cutaneous squamous cell carcinoma and giant atypical fibrous histiocytoma – is there a link?

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Background & objectives: Fibrous histiocytoma (FH) is usually a benign, small lesion, treated with surgical excision. We present a case report of an extraordinary example of a giant, relapsing fibrohistiocytic tumour with the development of cutaneous squamous cell carcinoma (cSqCC) in its vicinity.
Methods: The 63-year-old male with a 15-year history of a back tumour, irradiated (50Gy) and diagnosed as FH on excision biopsy, reported 5 years later with a relapse. The tumour was re-excised. Macroscopic evaluation revealed a well demarcated lesion measuring 10.5x17x2.1cm centred in the subcutis. There was epidermal ulceration (8cm in diameter) with distinct infiltration underneath spreading directly into the tumour.
Results: Histologically, the recurrence was composed of mildly-atypical spindle cells forming short intersecting fascicles and histiocyte-like cells admixed with numerous foamy cells. The lesion's stroma was collagenous with stag-horn vasculature. A well-formed storiform pattern was focally present. Mitoses were rare (3/50 HPF). Necrosis was absent. The neoplastic cells showed diffused, strong staining for CD31 and CD68, and were negative for CKAE1/AE3, ERG, CD34 and SOX100. There was no COL1A1-PDGFB rearrangement in FISH analysis, excluding dermatofibrosarcoma protuberans. Evaluation of the ulcerated lesion revealed an infiltration of well-differentiated keratinizing cSqCC intimately intermixed with the fibrohistiocytic neoplasm. Mark epidermal hyperplasia next to the cSqCC origin was clearly visible.
Conclusion: The coexistence of a rare example of a giant fibrous histiocytoma and cSqCC in its immediate vicinity, has been reported poorly so far. The development of tumours following radiotherapy is commonly observed. However, short interval between radiotherapy and carcinoma occurrence (ca. 5 years) is quite unusual for the therapy-related tumourigenesis. It raises a question about a possible induction of cSqCC by a long-standing fibrous histiocytoma and is another reason to recommend an excision of fibrohistiocytic tumours, instead of their irradiation.

PS-23-006

Differential immunohistochemical expression of SLUG and ALDH1 in malignant peripheral nerve sheath tumour (MPNST) and monophasic synovial sarcoma (MSS)

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Background & objectives: ALDH1 is a mesenchymal stem cell marker indicating nerve sheath differentiation in neoplasia. SLUG is an epithelial-mesenchymal transition (EMT) transcription factor, involved in MSS pathogenesis. We investigated the diagnostic potential of ALDH1 and SLUG in the problematic MPNST-MSS differential.
Methods: Slides of 4-mm tissue microarrays from MPNST (n=22) and MSS (n=21) were stained for anti-SLUG (Novus, 1:150) and anti-ALDH1 (BD, 1:1000). Any cytoplasmic-nuclear staining for ALDH1 was evaluated as positive, whereas total loss of nuclear SLUG expression was negative.
Results: For the diagnosis of MPNST over MSS, sensitivity and specificity of ALDH1 were %59,1 and %90,5, respectively, while the loss of SLUG expression had a sensitivity of %52,4 and a specificity of %85. When these two markers are combined, the specificity of SLUG-/ALDH1+ phenotype for MPNST raised to %100 at the expense of sensitivity, which dropped to %35.
Conclusion: S100, SOX10, and loss of H3K27me2/3 are used in routine practice for the diagnosis of MPNST with limited sensitivity and specificity. When used in differential diagnosis with MSS, ALDH1 and SLUG have also limited sensitivity like conventional markers; however, the SLUG-/ALDH1+ combination has a high specificity for MPNST.

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PS-23-007

Solitary fibrous tumour of the orbital cavity: a case series with histopathologic and clinicopathologic evaluation

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Background & objectives: Solitary fibrous tumour is a fibroblastic tumour which is rarely encountered in the orbit. Our aim in this study is to retrospectively describe the clinical and histopathological characteristics, outcomes of 4 patients with solitary fibrous tumour (SFT) of the orbit.
Methods: A retrospective, noncomparative review of a series of patients treated at a single institution with histopathologic diagnosis of SFT. Demographic, clinical, and imaging data were collected. Paraffin-embedded tissue sections were evaluated for the histopathological characteristics.
Results: Four patients were identified with mean age of 36,2. Computed tomography revealed well-circumscribed, contrast-enhancing lesions

with cystic and solid features for 3 of the cases. Two patients had local recurrence. No metastatic disease or tumour-related death were observed. Tumours were located in the nasolacrimal gland and temporoorbital bone. Mean tumour size was 2,8 cm. Tumour borders, cellularity, pleomorphism, necrosis, hemorrhagia, and mitosis count were evaluated on tissue sections. Of the cases: 2 had infiltrative borders, 2 had increased cellularity, 2 showed moderate pleomorphism, 1 had necrosis, and 4 had hemorrhagia. As the immunohistochemical stain evaluation, all cases were positive with CD34, vimentin, and STAT6.
Conclusion: Solitary fibrous tumours are rare to encounter in the orbital cavity. These tumours should be differentiated from other spindle cell, mesenchymal neoplasms of the orbit since SFT has an unpredictable tumour behaviour. Therefore, histopathological and clinical features are useful for the diagnosis and follow-up of the patients.

PS-23-008
Expression of amphiregulin in enchondromas and central chondrosarcomas
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Background & objectives: Enchondroma and chondrosarcoma are cartilaginous matrix-producing tumours with distinct biological behaviour. There are histological similarity between enchondroma and low-grade chondrosarcoma that can make their distinction a challenge. This work evaluates the role of Amphiregulin protein in enchondromas and central chondrosarcomas.
Methods: This was a retrospective study of 31 enchondromas and 67 central chondrosarcomas, diagnosed in the Department of Pathology (State University of Campinas) from 1994 to 2019. Clinical data (age, sex, location, type of bone affected and follow-up information) were retrieved from medical files. This work analyses the immunoexpression of Amphiregulin in cartilaginous tumours.
Results: Amphiregulin was positive in 15 of the 31 enchondromas (48.40%) and in 24 of the 67 chondrosarcomas (35.82%). There was no difference in the expression of Amphiregulin between enchondromas and low-grade chondrosarcomas. Amphiregulin was positive in 39 lesions (16 in short bones; 13 in long bones and 10 in flat bones), with a higher percentage of positive cells ($p = 0.0030$) and intensity of immunohistochemical expression ($p = 0.0055$) in short bone lesions. Among the 25 enchondromas localized in short bones, 60.00% expressed Amphiregulin; whereas all of the 06 cases localized in long bones were negative for this marker ($p = 0.0177$).
Conclusion: Amphiregulin was not found to be useful in distinguishing enchondroma from low-grade chondrosarcoma. This is the first study to document the expression of this immunohistochemical marker in enchondromas. Its particular expression in enchondromas localized in short bones demonstrates a phenotypic distinction from those in long bones. Therefore, this phenotypic difference may contribute to a better understanding of the pathogenesis of these lesions.

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PS-23-009
NTRK gene fusion detection over more than 100 paediatric undifferentiated round cell sarcomas: diagnostic opportunities and pitfalls
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Background & objectives: The aim of our study was to detect NTRK fusions in a cohort of paediatric undifferentiated round cell sarcomas (URCS), after a systematic review of the diagnosis, according to the new WHO Classification of Soft Tissue Tumours and Bone.
Methods: 105 patients (age range, 1-21 years), with diagnosis of a round cell sarcoma involving the bone or soft tissue were retrospectively evaluated. Pan-Trk immunohistochemistry testing was performed on formalin-fixed paraffin-embedded tissues. Tumour RNA was extracted and subjected to next-generation-sequencing (NGS) library preparation, using a 10-gene fusion panel, sequenced on an Illumina MiSeq. NGS-positive cases were confirmed by real-time PCR.
Results: After the morphological, immunophenotypical and molecular review, the cohort was predominately composed of Ewing sarcoma (96), additionally EWSR1-non-ETS round cell sarcoma (3), sarcoma with BCOR genetic alteration (1) and undifferentiated round cell sarcomas (5). On immunohistochemical screening, 12/105 (11.4%) cases were positive using the pan-Trk antibody, including 9 Ewing sarcomas, 2 undifferentiated round cell sarcomas and 1 sarcoma with BCOR genetic alteration, showing three different staining patterns, with the cytoplasmic distribution being most common. Upon RNA extraction and quantification, 10 of the 12 cases were suitable for sequencing. Molecular analysis using NGS and confirmed by the real-rime PCR detected two undifferentiated round cell sarcomas cases positive for ETV6-NTRK3 fusion.
Conclusion: URCS do not belong to the group of tumours with a high prevalence of NTRK gene fusions, despite an IHC positive rate of 11% in our study. This result is consistent with previous works performed on other cancer types sharing similar histologic features with Ewing sarcoma and it confirms the fundamental role of a molecular analysis following the IHC screening. Further investigations are also needed to better explore the possible coexistence of NTRK and other gene rearrangements in URCS.

PS-23-010
Extra-skeletal osteosarcomas: a clinicopathologic study of 9 cases
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Background & objectives: Extra-skeletal osteosarcomas are very rare soft tissue tumours. It accounts for 1% of soft tissue sarcomas. In this study, we aimed to share our practice about this unique entity with evaluation of clinical and histopathological features of extra-skeletal osteosarcomas.
Methods: A follow-up investigation of 9 cases of extra-skeletal osteosarcomas diagnosed at the Department of Pathology, Ankara University School of Medicine, Turkey, in the period from 2005-2021 was undertaken. The clinicopathological features of the patients including age, gender, tumour localization, tumour size, clinical presentation and histopathological findings were recorded.
Results: Among our cases, 4 of them were female and 5 were male with a mean age of 56.4 (49-68 years). Only 2 of 9 cases were localized in the soft tissue of the upper extremity. 7 cases were located in the lower extremities. Mean size of tumours was measured as 10.6cm (4-30cm). Macroscopically all of the tumours had irregular borders. 7 of 9 cases showed solid pattern whereas cystic component was observed only in 2 cases. Histopathologically, the tumour consisted of a spindle or round-shaped cells with pleomorphism in all cases. Mitosis, diffuse-focal necrosis and osteoid formation were common. During the follow-up period 7 cases (77%) had developed lung metastasis.
Conclusion: Extra-skeletal osteosarcomas are rare, high-grade malignancies that usually metastasize to the lungs and bones. Accurate diagnosis is difficult due to the rarity of the tumour and the lack of specific clinical features.

PS-23-011
Pleomorphic myxoid liposarcoma in a child with Li-Fraumeni syndrome
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Background & objectives: Pleomorphic myxoid liposarcoma (PML) is an exceptionally rare entity recently recognized by the WHO classification. It occurs almost exclusively in children and might be associated with Li Fraumeni syndrome (LFS). We report a case and review the literature.
Methods: A 5-year-old girl with previous history of choroid plexus carcinoma diagnosed at 3 months of age, presented with a dorsal swelling. Ultrasonography displayed a 46mm-sized expansive, hypoechoic and hypervascular soft-tissue mass involving the right scapular muscles. After multidisciplinary discussion, a wide surgical excision of the lesion was performed.
Results: Grossly, the mass was well-demarcated with a solid, tan-red cut surface surrounded by adipose tissue. Histology revealed a myxoid tumour, with hypo and hypercellular areas, exhibiting a prominent branching capillary network, lipoblasts and mostly bland oval-to-spindle-shaped cells with scattered pleomorphic cells. Mitotic figures were seen (5mitosis/10HPF) and no necrosis was found. S100 protein highlighted lipoblasts. No FUS/EWSR1-DDIT3 gene fusions or MDM 2 amplification was detected by FISH studies. A diagnosis of PML (high grade sarcoma) was rendered. The occurrence of a second primary cancer led to identification of a pathogenic germline mutation in TP53, consistent with LFS. Subsequent staging work-up found no evidence of recurrent or metastatic disease.
Conclusion: PML is a rare distinct subtype of liposarcoma (only 26 cases reported to date) showing mixed histological features of conventional myxoid liposarcoma and pleomorphic liposarcoma with no specific cytogenetic signatures. Besides poorly studied, it is probably an underrecognized entity, therefore its prevalence and association with LFS might be underestimated. To our knowledge, this is the fifth and the youngest documented case of PML associated with LFS, a hereditable cancer disorder with impact on oncologic treatment decisions and postoperative surveillance.

PS-23-012

Fine needle aspiration for bone tumours at a university-affiliated tertiary hospital in East Java, Indonesia

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Background & objectives: Fine needle aspiration (FNA) for bone tumours is not a widely-used procedure in Indonesia, mostly performed at large centres. We aim to review FNA for bone tumours at our centre to inform local practice.
Methods: A retrospective study of FNA for bone tumours at the Department of Anatomic Pathology of Saiful Anwar General Hospital Malang, East Java was conducted. FNA reports for bone tumour cases diagnosed within a 4-year period (January 2015 - December 2018) were obtained and reviewed. The cytology findings were compared with the available histopathological results.
Results: A total of 187 FNA reports for bone tumours were retrieved, 93 were males (49.73%) and 94 were females (50.27%), with a mean age of 34.10 ± 26.87 years old and a median age of 31 years old. Inadequate specimens were found in 6 cases (3.21%). The most common site for FNA was in the lower extremity (n=135; 72.19%). Neoplastic cases were more prevalent than non-neoplastic cases (90.91% vs 5.88%). Malignancies predominated the neoplastic cases (n=141; 82.94%). Further histopathological examinations were performed in 37 cases (20.44%); among these cases, the accuracy of FNA in determining the benignity/malignancy and the specific histological type were 97.30% (n=36) and 91.89% (n=34), respectively.
Conclusion: Wider utilization of FNA for the diagnosis of bone tumours (especially in smaller centres and underserved areas) is encouraged due to its ease of use, cost-effectiveness, and diagnostic accuracy. Clinico-Pathological Conference (CPC) in our centre plays a key role in further improving the diagnostic accuracy of FNA for bone tumours, as it correlates the clinical, radiological, cytological, and histopathological findings. CPC is particularly beneficial in resource-limited settings, where complete immunohistochemical markers or other advanced diagnostic modalities are unavailable.

PS-23-013

Dedifferentiated solitary fibrous tumour with heterologous elements: two cases of a rare entity

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Background & objectives: Solitary fibrous tumour (SFT) is a fibroblastic neoplasm featuring a typical staghorn vascular pattern and NAB2-STAT6 gene rearrangement. Dedifferentiation has been described as a rare phenomenon in SFT, comprising an abrupt transition between classic SFT morphology and a high-grade sarcoma.
Methods: We describe two cases of dedifferentiated SFT (DSFT) with heterologous elements, drawing attention to the additional diagnostic challenge it imposes, with a review of the literature.
Results: Case 1 refers to a 67-year-old man presenting with a 30 cm pelvic mass and case 2 refers to a 54-year-old woman with an 8 cm cervical posterior mass. Microscopically, the tumours were mainly comprised of typical areas of SFT, showing diffuse immunoexpression of CD34 and STAT6, juxtaposed to areas of a high-grade sarcoma showing osteosarcomatous differentiation and SATB2 positivity, with loss of CD34 and STAT6. In both cases, a diagnosis of DSFT with osteosarcomatous differentiation was rendered. Patient 1 is alive and disease-free 1-year after surgery, with no adjuvant therapy. Patient 2 had adjuvant radio and chemotherapy, with disease progression and lung metastasis at 6-months of follow-up.
Conclusion: DSFT has only recently been described and its rare occurrence limits our awareness of this entity. As in other mesenchymal tumours, the presence of a conventional area of SFT is the key for the diagnosis and the presence of a high-grade sarcoma with or without heterologous elements is now recognised as part of an expanded histomorphological range of SFT features. Although dedifferentiation poses higher risk of recurrence and/or metastasis, literature is still scarce about clinical outcomes.

PS-23-014

Myositis ossificans: 3 case reports of this benign and challenging entity.

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Background & objectives: Myositis ossificans (MO) is a benign mesenchymal disorder characterized by the formation of heterotopic bone in soft tissues. MO progresses through parallel radiographic, clinical, and histopathologic stages or zonal patterns. We aim to describe clinical and pathological findings of MO.
Methods: It was a retrospective study of 3 cases. There were 2 men and one woman with a mean age of 19.3 years ranging from 7 to 30 years with no history of trauma. Symptoms consisted in pain, joint stiffness and swelling involving the thigh in 2 cases and the buttock in one case. All cases were diagnosed by surgical biopsy.
Results: Microscopically, all specimen showed a zonal architecture composed of a central, intermediate and mature zone. Central zone was composed of variably sized capillary network with proliferating fibroblastic tissue with mild cellular pleomorphism and mitotic activity. Intermediate zone showed areas of immature woven bone mixed with fibroblastic tissue surrounded by peripheral areas of bone forming osteoblastic elements and

cartilage. Stroma was myxoid in one case with collagenous vascular and oedematous areas infiltrated by sparse chronic inflammatory cells. No reverse zoning pattern was observed which ruled out the main differential diagnosis of an extra osseous osteosarcoma. All patients underwent surgical resection with no recurrence after 6 months follow-up.
Conclusion: MO is a benign entity occurring in young male adults, usually after trauma. This condition, when not related to trauma, is challenging for the pathologist as it can mimic a malignant neoplasm or an inflammatory disease. MO is also a dynamic phenomenon as the clinical, imaging and microscopic findings keep of changing as the stages advance. Accurate diagnosis of these tumours is imperative to ensure optimal therapy.

PS-23-015
Epithelioid haemangioendothelioma: report of a case with aggressive clinical behaviour
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Background & objectives: Epithelioid hemangioendothelioma (EHE) is a rare malignant vascular tumour, with a highly variable clinical course and overlapping features with angiosarcoma and haemangioma. Prognosis varies with anatomical site and genetic abnormalities. Diagnosis and therapeutic selection can be challenging.
Methods: 57-year-old woman presenting with cough and fatigue. CT and PET scans revealed a large pulmonary mass on the upper right lobe, with mediastinal invasion, pleural effusion, and nodular lesions on the contralateral upper lobe.
Lung and mediastinal biopsies confirmed the presence of a malignant vascular tumour, raising the differential diagnosis between EHE and angiosarcoma.
Patient underwent palliative chemotherapy with doxorubicin.
Results: At 9-months of follow-up, clinical examination detected increased breast volume. PET-scan reported stability of the lung mass and de novo metabolic activity in breast and anterior chest wall.
Breast biopsy showed extensive parenchymal infiltration by malignant neoplasm, composed of epithelioid cells, with abundant basophilic cytoplasm, often with intracellular lumina. Neoplastic cells were arranged in trabeculae, small aggregates or forming vascular spaces, within a myxoid-hyaline stroma. Mitotic figures were present, and necrosis was absent.
Immunohistochemistry revealed positivity for CD31, ERG1, FLI1 and D2-40 and negativity for CD34, cytokeratins, ER, PR and HER-2. FISH analysis detected a WWTR1 gene rearrangement, allowing the definitive diagnosis of EHE.
Patient initiated paclitaxel therapy.
Conclusion: At 12-months of follow-up, PET-scan confirmed disease progression with lymph node, lung, pleura, bone, breast and muscle metastasis, prompting treatment with panzopanib. The patient passed away at 14-months of follow-up.
Despite being historically considered a low-grade vascular tumour, EHE can display an aggressive behaviour similar to angiosarcoma. A conclusive differential diagnosis between these two entities can be made by genetic analysis. Further studies may allow for targeted therapies in the future.

PS-24 | Thymic and Mediastinal Pathology

PS-24-002
Mature cystic teratoma of the thymus in Northern Tunisia
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Background & objectives: Mature cystic teratomas of the thymus (MCTT) are a rare phenomenon. They account only 8% of all tumours in the mediastinum. The aim was to describe the clinicopathological characteristics and discuss the differential diagnosis of this disease.
Methods: We performed a retrospective study of 11 cases of MCTT diagnosed at our department, between 2004 and 2020.
Results: Our series included 6 male and 5 female patients. Mean age was 33,81 years old. All patients underwent a surgical resection. On gross examination, mean size of the masses was 11,7 cm. The outer surface was smooth and tan-white, and the cut inner surface contained multiple cystic structures filled with a tanbrown greasy substance and a few strands of hair. Microscopy showed variable mature elements comprising of cysts lined by ciliated pseudo stratified epithelium and secretory epithelium. Other mature elements seen were intestinal mucosa, sebaceous glands, smooth muscle, adipose tissue, hair follicles, cartilage and pancreatic tissue. The cyst wall was fibrous with hyalinised areas. There was no evidence of immature, neuroepithelial elements.
Conclusion: Mature teratomas of the mediastinum are rare tumours but should be considered in the differential diagnoses for mediastinal anterior lesion, include: thymoma, lymphoma, carcinoma, thyroid disease and aortic aneurysm. Complete surgical resection is recommended in all mature teratomas with favourable survival rates.

PS-24-003
Posterior mediastinal paragangliomas: report of 6 cases
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Background & objectives: Mediastinal paragangliomas are rare neuroendocrine neoplasms that originate from chromaffin cells, representing less than 0.3% of mediastinal tumours and less than 2% of all paragangliomas. The aim was to describe histopathological and immunohistochemical features of mediastinal paragangliomas with literature review.
Methods: We report a retrospective study of 6 cases of mediastinal paraganglioma diagnosed at our department between 2004 and 2020.
Results: There were one male and five female. Mean age was 45 years old. All patients underwent a surgical resection. On gross examination, mean size of the masses was 7, 9 cm. They were firm well circumscribed tumours with yellow-brownish cut surface. Microscopically, they were composed of chief cells arranged in nests that are surrounded by an inconspicuous single layer of spindle-shaped cells called sustentacular cells. Immunohistochemically, the chief cells were positive for chromogranin and synaptophysin and sustentacular cells were positive for PS100. The postoperative course was uneventful in all patients. No patient required additional treatment postoperatively, and neither recurrence nor distant metastases were noted during follow up.
Conclusion: The diagnosis of mediastinal paraganglioma is based on histology, which is unreliable in predicting malignancy, making lifelong follow up after surgical resection mandatory.

PS-24-004
Mediastinal granulomatous lymphadenitis may not be in initial clinical diagnosis but should be in pathologist's differential diagnosis
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Background & objectives: Mediastinal lymph node(MLN) sampling is a widely preferred diagnostic method for staging of lung malignancies and diagnosis of lymphoproliferative or granulomatous diseases. Preliminary-certain diagnoses and evaluation of clinical diagnosis after sampling and their relationships constitute the aim of our study.
Methods: We documented MLN biopsies examined in our department between 2012 and 2021. We excluded specimens which was including

tissues and/organs other than MLN simultaneously. We analysed the demographic data, biopsy diagnoses, former and follow-up clinical history of patients from the hospital information system.
Results: Total 331 patients with MLN samples were eveluated, 253(76,4%) of 331 negative for malignancy, 100(39,5%) of 253 with granuloma were detected, 11 of 100 had also caseating necrotizing, 49 of 100 had known clinical initial diagnoses. Clinicians were suspicious for at least one granulomatous disease in 29(59%) of patients with granuloma histopathologically proved. The rest 20(41%) of 49 underwent cytological sampling or mediastinoscopy for mediastinal staging for lung carcinoma. Only 23 of 100 had history of a certain disease;17 malignancy, 4 autoimmune disease and 2 tuberculosis. The clinical history of sarcoid patients were 3 autoimmune diseases,2 lymphomas and 2 carcinomas. There were 10 carcinomas,2 tuberculosis and 1 autoimmune diseases in clinical history of patients diagnosed as tuberculosis.
Conclusion: The overall incidence of granulomatous inflammation of MLN samples is 30,2% in our seria. Clinicians may be suspicious for granulomatous diseases, but 41% of our cases were diagnosed as granulomatous lymphadenitis without any initial clinical diagnosis or suspicion. When we compare the cases of sarcoidosis and tuberculosis, a history of autoimmune disease or lymphoma may be a hint of sarcoidosis in terms of differential diagnosis.

PS-24-005
Distribution and clinical correlation of malignant infiltrations of mediastinal lymph nodes (MLNs)
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Background & objectives: MLNs are the most common metastatic targets of lung cancer and other malignant tumours. Mediastinoscopy or EBUS guided cytological sampling of MLNs is helpful for clinicians to make better diagnosis and treatment decisions. We aimed to determine malignancy distribution in MLNs.
Methods: We documented MLN biopsies examined in our department between 2012 and 2021. We excluded specimens which was including tissues and/organs other than MLN simultaneously. We analysed the demographic data, biopsy diagnoses, former and follow-up clinical history of patients from the hospital information system.
Results: The percentage of malignant infiltration of MLNs in 331 patients was 23,5%(n=78). Distribution of malignancies found in MLNs was 45(57,6%) non-small cell lung carcinoma(NSCLC),11(14%)small cell and large neuroendocrine carcinoma,11 (14%) lymphoid malignancy and 11(14%) primary tumours other than lung.45(57,6%) of 78 had information of clinical suspicion for any disease.43 of 45 underwent mediastinal sampling for either staging and/or diagnosis of malignancy. Diagnoses of two patients with previously known malignancy were unexpected, one patient with history of lymphoma diagnosed as NSCLC and, other with history of colonic adenocarcinoma diagnosed as lymphoma. The rest two patients with preliminary diagnosis were evaluated for tuberculosis and/or lymphoma by clinicians. Both of these two patients were diagnosed as NSCLC.
Conclusion: The incidence of malignant infiltration of MLNs is 23,5% in our seria. Pulmonary carcinoma (71,7%) is the most common primary malignancy for our metastatic MLNs. Lymphoma involvement is seen 14% of our patients. Four of 45 cases, there are unexpected diagnoses, either new intercurrent malignancies as NSCLC and lymphoma or unforeseen carcinomas as NSCLC while waiting for diagnosis of tuberculosis clinically.

PS-24-006
Evaluation of PROX-1 expression in thymic epithelial tumours
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Background & objectives: Thymic epithelial tumours (TETs) are primary anterior mediastinal neoplasms. PROX-1 is a member of the homeobox transcription factor family with lymphangiogenic and angiogenic properties, and a central role in carcinogenesis. The clinical significance of PROX-1 expression was determined in TETs.
Methods: Tissue microarrays were constructed out of 95 TETs (11 type A, 21 type AB, 17 type B1, 18 type B2, 13 type B3, 2 micronodular thymomas, 13 thymic carcinomas) and immunohistochemically stained for PROX-1. Cases were classified as H-score-high or H-score-low using the H-score average as the cut-off. Pearson's chi-square test was applied for statistical analysis.
Results: There was epithelial nuclear expression of PROX-1 in 17/95 cases. The H-score ranged between 0 and 120. The lymphocytic component was negative for PROX-1. Higher expression of PROX-1 was more common in B3 thymomas (30.7%) and thymic carcinomas (46.1%), less common in type B1 (11.7%) and type A (9%) thymomas, and rare in other subtypes (0-4.7%) [p=0.006]. The average H-score was 22 (range: 0-120) in thymic carcinomas and 13 (range: 0-90) in B3 thymomas. No correlation with gender, Masaoka stage, margin status, myasthenia gravis or other autoimmune manifestations was seen.
Conclusion: PROX-1 is expressed in TETs and its expression levels correlate with the more aggressive tumour subtypes B3 thymoma and thymic carcinoma.

PS-24-007
Neuroblastic mediastinal tumours: a retrospective study about 23 cases
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Background & objectives: Neuroblastic tumours of the mediastinum are rare and heterogeneous. Our aim was to describe the clinical and microscopic features of these tumours.
Methods: We describe a retrospective study about mediastinal neuroblastic tumours diagnosed over a 25-year-period
Results: 23 neuroblastic tumours were diagnosed during the period of study. They consisted in 20 ganglioneuromas, 2 neuroblastomas and 1 ganglioneuroblastoma. The mean age of the patients was 29 years. They consisted in 5 men and 18 women. The most frequent symptoms consisted in chest pain. The diagnoses were made on biopsic samples in 2 cases and surgical specimen in 21 cases. Histoprognostic classification of neuroblastomas concluded to a poor prognostic group. The treatment was surgical in 21 cases. The survival of the 2 neuroblastomas was 3 months. 2 patients with neuroblastomas died after 6 months.
Conclusion: Mediastinal neuroblastic tumours are rare. The diagnosis necessitates a narrow collaboration between clinicians, radiologists and surgeons. They may cause a therapeutic challenge especially in immature tumours.

PS-25 | Uropathology Posters

PS-25-001
Analysis of SATB2 expression in nephrogenic adenoma
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Background & objectives: SATB2 positivity, usually found in intestinal adenocarcinomas, has been reported in some renal cell carcinomas. Nephrogenic adenoma (NA) is a renal tubular cell metaplasia with heterogeneous architecture, that may simulate malignancy. We have investigated the expression of SATB2 in NAs.

Methods: Formalin-fixed paraffin sections of 42 NAs cases were immunostained for SATB2, using an enzyme-conjugated multimer complex (OptiView, Ventana) with a rabbit monoclonal antibody (clone EP281, prediluted, Cell Marque). The intensity of the staining was evaluated as negative (-); or weak (+), moderate (++) or strong (+++) positivity; and the extent as focal (<50% of the cells) or diffuse (≥50%).
Results: The main location of the NAs was the bladder, except 6 in prostatic urethra, and 1 in renal pelvis. The most frequent sample was transurethral resection of the bladder. All of the cases presented mixed papillary and tubulocystic architectures, outstanding 11 cases with flat areas, 1 associated with intestinal metaplasia, and 4 with signet-ring cell like areas. SATB2 staining was positive in 22 cases (52 %), being focal in 13 cases (2 weak/ 6 moderate/ 5 strong) and diffuse in 9 (4 moderate/ 5 strong). Differences in the staining pattern according to architecture were seen, with microcystic areas prone to show strong and diffuse staining versus papillary or flat ones.
Conclusion: SATB2 is commonly expressed in NA, occurring in more than 50% of our cases, with diffuse staining in 41% and focal in 59% of them. This immunoreactivity should be kept in mind in order to avoid misdiagnosis, specially when dealing with variants of NA such as microcystic or signet-ring cell like patterns. These histological features and the possible SATB2 positivity can difficult the differential diagnosis with adenocarcinomas, specifically signet ring variants of the digestive tract.

PS-25-003
Can grading of tumour infiltrating lymphocytes be used as a prognostic marker in penile carcinoma?
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Background & objectives: Increased Tumour Infiltrating Lymphocytes (TIL) numbers is associated with improved survival in Human Papilloma Virus (HPV)-positive oropharyngeal carcinomas. Our objective was to determine if TIL grade is associated with HPV-status and whether grading TILs stratifies survival rates in penile carcinoma.
Methods: We identified a retrospective cohort of 126 patients with penile carcinoma over a 10 year period. Chi squared tests were performed to look for correlations between TIL grade, TNM8 staging and HPV-status, or HPV-status and pathological grade and stage. The prognostic significance of TIL grade for overall survival was investigated using Kaplan-Meier Survival curves.
Results: HPV-status was not associated with pT stage, nodal status, histological grade or TIL grade in our dataset. TIL grade showed no association with pT stage (p=0.22) or nodal status (p=0.776). Deaths by TIL Grade group were as follows: 17/42 (40.5%) in TIL Grade1, 21/51 (41.2%) in TIL Grade2 and 5/27 (18.5%) in TIL Grade3, however the Kaplan-Meier Survival Analysis did not show a significant difference between the survival curves when all three groups were compared (p=0.118, Log rank test). Interestingly, the difference in overall survival between the TIL2 and TIL3 Kaplan-Meier curves was close to statistical significance (p=0.053; Log rank test).
Conclusion: TIL grading showed no statistically significant association with traditional pathologic prognostic measures and did not stratify patients from our dataset by overall survival. Future research could explore TIL subtypes as some evidence suggests that this may be of relevance and could enhance our understanding of potential immunotherapeutic targets for penile carcinoma.

PS-25-004
Renal oncocytosis: institutional retrospective review of clinical and pathological features in eight cases
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Background & objectives: Renal oncocytosis is an extremely rare disease. It is characterized by the presence of one/several renal masses (oncocytomas) along with oncocytic changes in the renal parenchyma. We report the clinical-pathologic features found in our hospital related to this disease.
Methods: We reviewed the computerized health records and the slides of paraffin-embedded tissue preparations of eight patients with histological diagnosis of renal oncocytosis in our hospital between January 2010 and December 2020. Pulmonary and/or cutaneous history, type of surgery, renal tumour pathology and testing for genetic abnormalities are described.
Results: Eight patients were males and the median age at diagnosis was 68 years (55-79). One patient underwent prior radical nephrectomy for chromophobe carcinoma and along with another patient had a history of non-specific pulmonary nodules. They underwent genetic evaluation dismissing Birt-Hogg-Dubé syndrome. The remaining patients had no history of cutaneous/lung lesions. Renal masses were identified by imaging, except for one patient with bilateral tumours detected incidentally at autopsy. Among the 7 patients with unilateral tumours, 5 had partial nephrectomies. Each kidney contained a dominant mass and multiple tumours varying in size (5-0.8 cms). They had histologic features of oncocytoma associated with oncocytosis. Two patients died during follow-up.
Conclusion: Patients with renal oncocytosis usually present with multiple and bilateral renal nodules. The diagnosis of renal oncocytosis requires a thorough histological examination. The use of immunohistochemical techniques is useful to verify the diagnosis. In case of confirmation of the diagnostic suspicion, it is advisable to carry out a genetic study to rule out a hereditary origin of the disease.

PS-25-006
High-grade oncocytic renal tumour (HOT) - a case report of a novel entity
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Background & objectives: Continuous development regarding renal tumours results in the emergence of new entities with distinctive morphological, immunohistochemical, molecular, epidemiological and clinical features. HOT has been recently described in this context. We herein report a case of this new entity.
Methods: A 51-year-old male, with no relevant medical history and no genitourinary symptoms, was observed in the outpatient clinic of our institution due to a 20mm tumour found in the inferior pole of the left kidney during a routine ultrasound. On contrast-enhanced computed tomography scan the tumour was classified as Bosniak III category. A partial nephrectomy was performed.
Results: The cut surface revealed a solid, well circumscribed, non-encapsulated tumour, with expansive borders and 23mm in greatest dimension. On histological examination the tumour was composed of a proliferation of small nests and tubules. Tumour cells had eosinophilic to pale cytoplasm, frequent intracytoplasmic vacuoles and enlarged round nuclei with conspicuous nucleoli (high-grade features). Central oedema and thick walled vessels were notable features. There was no vascular invasion, necrosis or sarcomatoid differentiation. Immunohistochemical panel showed diffuse positivity for CK8/18, PAX8, CD10, CD117 and cathepsin K. CK7 was positive only in scattered cells. The TFE3 stain was negative and SDHB expression was preserved. These findings were consistent with the diagnosis of HOT.
Conclusion: HOT has similarities with other types of oncocytic tumours, like chromophobe RCC, oncocytoma or "hybrid" oncocytic tumours, but morphological and immunohistochemical characteristics are inconsistent with these diagnosis, and therefore it is important to recognise it as a

distinct entity. Despite the high-grade cytology and limited follow-up time on reported cases, behaviour seems indolent. Hence it is important for pathologists to recognise and promote awareness of this emerging entity in order to improve diagnostic accuracy and ultimately optimize clinical management.

PS-25-007

Matrix metalloproteinases correlates with aggresive behaviour of prostate adenocarcinoma but not with Gleason score

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Background & objectives: MMP2 and MMP9 are gelastinases implicated in progression and metastases of different tumours. MMP2 has proteolytic actions and activate another major gelatinase called MMP9 involved in degradation of extracellular matrix, tumour angiogenesis and invasion.
Methods: We analysed 21 cases of prostatic adenocarcinoma with perineural invasion (PnI) and 27 cases without PnI. In areas of maximal angiogenesis, CD34 positive microvessels were counted and divided in 2 groups. MMP2 and MMP9 expressions were evaluated according to percentage scale (0<10%, 10-50%, >50%). MMP2, MMP9 and microvessel density were correlated with Gleason score and PnI.
Results: MMP-2 and MMP-9 immunoexpression in tumour cells was cytoplasmic, finely granular, and varied in intensity and percentage. MMP-2 was significantly more strongly expressed in tumours with PnI. Regarding Gleason score, no significant differences between low Gleason score (<7) and high-grade cancer (Gleason score >7) was found in expression of MMP2 and MMP9. MVD was higher in prostatic adenocarcinoma with PnI.
Conclusion: Matrix metalloproteinases MMP2 correlates with perineural invasion and microvessel density, suggesting a link with aggressive behaviour in prostate adenocarcinoma. We observed no association with Gleason score of any MMP2 or MMP9. These findings highlight the need to modulate the follow-up of patients with prostate adenocarcinoma considering all the factors that influences the evolution.

PS-25-008

Expression of matrix metalloproteinases and their inhibitors in de novo and recurrences of urothelial carcinoma

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Background & objectives: Bladder carcinoma is the most common cancer of the urinary tract. Tumour invasion and progression are a multifactorial process promoted by microenvironmental changes that include overexpression of matrix metalloproteinases (MMPs), activity controlled by tissue inhibitors of metalloproteinase (TIMPs).
Methods: We examined the tissue expression of MMP2, TIMP2 and MMP9 in 43 tumour samples from 18 patients with bladder carcinoma with recidives. The cytoplasmic, finely granular expression pattern was considered for analysis. The percentage of stained cells was noted as: 0 (no detectable immunostain), 1 (<10% nuclei), 2 (11%-50% nuclei), and 3 (>50% nuclei). The intensity was scored 1-3 (mild/moderate/strong).
Results: We used a combined score, multiplying the percentage score of tumour cells expressing the marker and the intensity with which the tumour cells expressed it. Higher expression levels of MMP-2 and TIMP2 were observed in recurrences compared with primary tumours, both in low-grade and high-grade tumours, with or without invasion. MMP9 was weakly expressed in tumours recurrences without any statistical significance.
Conclusion: Higher expression of both MMP2 and TIMP2 in tumour recurrences suggest a balance between MMPs and their inhibitors activity. Enhancing MMPs inhibitors activity could represent a promising target in a better control and avoiding an unfavourable prognosis.

PS-25-009

Expression and clinical relevance of HLA-G in human renal cell carcinoma

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Background & objectives: The human leukocyte antigen G (HLA-G) expression has been implicated in the immune suppression favouring tumours development. We aimed to characterize the immunohistochemical expression of HLA-G in renal cell carcinoma (RCC) and investigate its correlation with clinico-pathological parameters.
Methods: Seventy-two cases of primary carcinoma of the kidney, collected over 18 years, were retrieved. The IHC staining was performed with mouse monoclonal antibody against HLA-G. Labelled tumour cells percentage was determined. A percentage ≤ 25% defined HLA-Glow and a percentage >25% determined high HLA-G expression.
Results: RCC tumoral tissue significantly expressed HLA-G compared to healthy renal tissue ($p < 0.0001$). This expression was significantly higher in multifocal tumours ($p = 0.0007$), in clear cell carcinomas, in grade 3 and 4 papillary carcinomas ($p < 0.0001$), in the presence of a sarcomatoid component ($p = 0.0085$), in cases with infiltration of perirenal fat ($p = 0.0033$), as well as for advanced stages (pT3 and pT4 stage) ($p = 0.049$) and regional metastatic lymph nodes extension (pN1) ($p = 0.0005$). Besides pT stage, these factors were significantly correlated with high HLA-G.
Conclusion: HLA-G was, preferentially, detected in RCC and rarely in adjacent normal tissue, suggesting its specific association with tumour growth. Additionally, HLA-G expression was clearly associated with poor prognostic factors for renal cancer suggesting its involvement in the tumour escape.

PS-25-010

Clinico-pathological details of small cell neuroendocrine carcinoma of the urinary bladder for improving patient selection to clinical trials

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Background & objectives: Small cell carcinoma (SCC) of the urinary bladder is a rare, aggressive, poorly differentiated neuroendocrine neoplasm accounting for 0,3-0,7% of bladder tumours. Few protocols encounter small cell neuroendocrine carcinoma with detailed clinico-pathological features among clinical trials.
Methods: We reviewed the parameters displayed at morphology among a series of SCC arising from urothelium. Clinical and histopathological features of 45 SCC of the bladder were recruited from 2012 to 2021. 35 patients were males and 10 females, ranging in age from 63 to 90. Cystoscopic examination with TURBT was performed. Gross haematuria was the most common symptom.
Results: Tumours showed nests of small round malignant cells with pyknotic round to oval nuclei and evenly dispersed and foci of necrosis were also observed. The mitotic rate was high. 30 cases were pure small cell carcinoma, whereas 5 were associated with high grade infiltrative urothelial carcinoma; 7 case was associated with carcinoma in situ and 3 with areas of squamous differentiation. Tumour cells were positive for CKAE1/AE3, p53, Ki-67, and focally for CK7, CK20, TTF-1, CD117 and p63. All cases were immunoreactive for neuroendocrine markers as CD56 and NSE were strongly and synaptophysin and chromogranin A focally positive.
Conclusion: SCC of the bladder occurs more often in elderly males and prognosis is poor; tumour cells are strongly positive for CKAE1/AE3,

p53 and focally for CK7, CK20, TTF-1, c-Kit, p63 and are immunoreactive for neuroendocrine markers; recognition of this rare entity should enable better detailed tumour clustering when designing clinical trials using drugs targeting patient affected by small cell neuroendocrine phenotype of urothelial carcinoma.

PS-25-011

The unknown role of CD31 in the seminal tract

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Background & objectives: It has recently been described that the transmembrane glycoprotein PECAM-1 or CD31 is expressed in vas deferens epithelium. We have investigated the expression of CD31 and its possible ligand, CD38, in the different segments of the seminal tract.
Methods: 110 sections from surgical specimens of the male genitourinary tract from prepubertal and post pubertal patients, were immunostained (Optiview, Ventana) with prediluted monoclonal antibodies (Cell Marque), for CD31 (clone JC70) and CD38 (clone SP149). Epithelial staining was evaluated assessing its intensity (weak, moderate or strong) and extension (focal when <50% of positive cells, diffuse if ≥50%).
Results: CD31 is expressed in the cell cytoplasm of the vas deferens epithelium from post pubertal cases only in its scrotal part (vasectomy specimens), with weak-to-moderate and diffuse staining. CD31 has no expression in the pelvic part and ampulla of vas deferens. Neither does it in the epithelium of seminal vesicles or prostate. The results for CD38 are complementary: it is negative in the scrotal vas deferens epithelium and positive in the more distal portions studied, as well as in the seminal vesicles. Epithelium of prostate glands is positive only for CD38, being focal but strong. No expression for CD31 nor CD38 was observed in testicular parenchyma, rete testis or epididymis.
Conclusion: CD31 is expressed in the epithelium of the scrotal portion of vas deferens being negative in other segments of the seminal tract. A reversal pattern is observed for CD38, a reported ligand for CD31. CD31 positivity was observed in post pubertal vas deferens but not in prepubertal samples. These features suggest a hypothetical physiological role for CD31 expression (in cell maturation or sperm capacitation) in vas deferens, which could be more than a simple conduit for spermatozoa and deserves further investigation.

PS-25-012

Sarcomatoid carcinoma of the prostate: a case report and review of literature

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Background & objectives: Sarcomatoid carcinoma of the prostate is a rare neoplasm with an aggressive clinical course. Histologically, it is a biphasic tumour composed of a malignant epithelial component and a distinct mesenchymal malignant component. Its pathogenesis remains unclear.
Methods: Herein, we report the clinicopathological features of a case of sarcomatoid carcinoma of the prostate along with a brief review of the literature.
Results: A 75-year-old men with perianal pain and rectal fullness was found to have a large, heterogeneous prostatic mass. A differential diagnosis between sarcoma and sarcomatoid carcinoma was suggested by transrectal biopsy examination, and a pelvic exenteration was performed. Grossly, the gland was occupied by a 6 cm multinodular, fleshy, necrotic tumour, infiltrating the bladder neck, anterior wall of the rectum and both seminal vesicles. Microscopically, a high-grade pleomorphic sarcoma with osteosarcomatous differentiation was observed, with a minor component of Gleason score 8(4+4) acinar adenocarcinoma. A diagnosis of sarcomatoid carcinoma was rendered. The patient died after surgery due to post-operative infection.
Conclusion: Sarcomatoid carcinoma is an aggressive neoplasm associated with poor patient outcome, despite clinical intervention. According to literature, about half of the patients have a prior history of an acinar adenocarcinoma of the prostate and have received therapy for it. The presence of heterologous elements in the sarcomatous components may pose challenging diagnostic difficulties, especially if the epithelial component is not apparent in transrectal biopsies.

PS-25-013

Renal neoplasias in nephrectomies of patients with autosomal dominant polycystic kidney disease

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Background & objectives: Autosomal Dominant Polycystic Kidney Disease (ADPKD) is common (1/400 to 1/1000 individuals). It is unknown if it carries an increased risk of kidney neoplasms.
Methods: Retrospective study of nephrectomies due to ADPKD in our centre (1988-2020). Age and sex data were recorded; laterality, weight and size of the kidneys; presence or absence of tumour lesion, macroscopic and in CT-scans; tumours characteristics (type, grade and stage); time on dialysis and follow-up. Estimation of the cumulative incidence of renal neoplasias in our cohort.
Results: We collected 93 patients with ADPKD (120 nephrectomies). Macroscopically we identified 14 solid lesions in 10 nephrectomies and 6/10 were detected previously by imaging. Microscopic study revealed 4 chromophobe carcinomas, 3 clear cell carcinomas, 2 oncocytomas, 1 papillary carcinoma type 1, 1 papillary clear cell carcinoma and 1 mucinous tubular and spindle cell carcinoma (MTSCC); in addition to 2 angiomyolipomas. All lesions were pT1 (UICC 8th ed) and grade 2 or 3 (WHO 2016). One patient had 6 synchronous lesions with bilateral involvement. Patient with MTSCC died 7 months after diagnosis due to metastatic spread of his neoplasm. The rest are disease-free with a mean follow-up time of 52 months.
Conclusion: In our series, 7.5% of the nephrectomised ADPKD patients had a renal carcinoma. MTSCC had not been previously described in these kidneys. The risk attributable to ADPKD remains to be defined and the role of dialysis in the incidence of tumours in these patients has to be clarified. CT scans are capable of detecting a part of the tumours in this context (60% in our series). However, an exhaustive macroscopic study is essential for the correct diagnosis of these lesions.

PS-25-014

Role of arginine methylation in prostate cancer: Correlation with pathological parameters and markers of epithelial-to-mesenchymal transition

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Background & objectives: Protein Arginine Methyltransferases (PRMTS) catalyse arginine methylation, a post-translational histone modification and have been implicated in various cancer-associated pathways i.e. epithelial-to-mesenchymal transition (EMT) and cell-cycle regulation. However, their role in prostate cancer (PCa) has not been clarified yet.
Methods: PRMT2, PRMT7 and JMJD6 (a demethylase) nuclear, membranous and cytoplasmic expression was immunohistochemically assessed in tissue samples from 107 PCa patients (PGG1: 25 cases PGG2: 11 cases, PGG3: 21 cases, PGG4: 13 cases, PGG5: 37 cases, pT2:30, pT3a: 10, pT3b: 67). Fourteen cases had received neoadjuvant androgen ablation therapy. Findings were correlated with the expression of EMT and cell-cycle mediators.

Results: PRMT2 and PRMT7 membranous expression and PRMT7 cytoplasmic expression were inversely correlated, whereas and JMJD6 expression (in all cell compartments) was positively correlated with disease stage ($p<0.001$, $p=0.01$, $p=0.03$ and $p<0.01$ respectively). PRMT2 and PRMT7 membranous expression was higher in PGG1 cases compared to PGG5 ($p<0.001$ and $p=0.001$, respectively). In contrast, membranous JMJD6 expression was higher in PGG4 compared to PGG1 ($p=0.026$) and nuclear JMJD6 expression was higher in PPG5 compared to PGG1 ($p=0.006$). PRMT7 and JMJD6 nuclear expression was higher in treated compared to hormone naïve cases ($p=0.001$, $p=0.01$, respectively). Both PRMTs and JMJD6 expression strongly correlated with ZEB1, TWIST, E-cadherin and cyclinD1 expression ($p<0.001$, $r>0.3$).
Conclusion: Our findings indicate that membranous PRMT2 and PRMT7 are inversely associated, whereas JMJD6 is positively correlated with disease progression. In addition, our findings indicate a potential intracellular trafficking of these enzymes, driven by the antiandrogen therapy. Finally, a potential interplay with EMT mediators (ZEB1, TWIST, E-cadherin) and the cell cycle regulator CyclinD1 is indicated that needs further study in order to elucidate the underlying mechanisms and indicate whether PRMTs may represent potential therapeutic targets.

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PS-25-015
significance of mixed grade papillary urothelial carcinoma comparison with low and high-grade papillary urothelial carcinoma
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Background & objectives: A small part of papillary carcinoma is mixed-grade (MG) that is composed of a predominantly low-grade cancer with a little high-grade (25% or less) component. We aimed to assess the clinicopathological features of mixed-grade urothelial carcinoma (MGUC).
Methods: The study included 40 patients with LGUC, 52 patients with MGUC, and 40 patients with HGUC among all bladder transurethral resection (TUR) specimens diagnosed with urothelial carcinoma between 2010 and 2021.
Results: The mean age of all patients was 65,9 years and the mean follow-up was 34 months. The rate of lamina propria and muscularis propria invasion of MGUC was lower than that of the HGUC($p=0,000$) but the rate of lamina propria invasion was higher than LGUC at the presentation. Additionally, the rate of in situ carcinoma of MGUC was lower than that of the HGUC($p=0,000$) but was higher than LGUC. Recurrence of patients with MGUC occurred in 15 cases (29 %): 2 as MGUC and 13 as HGUC. The rate of recurrence of patients with MGUC higher than LGUC but it was not statistically significant.
Conclusion: A small part of papillary carcinoma is mixed-grade (MG) that is composed of a predominantly low-grade cancer with a little high-grade (25% or less) component. MGUC presented histopathologic prognostic features in between LGUC and HGUC. MGUC grade progression was significantly higher than LGUC ($p=0,002$). Patients with LGUC did not show stage progression. MGUC had a lower incidence of stage progression (7%) compared to HGUC patients (20%). Larger prospective studies are needed to better characterize the biological behaviour of MGUC.

PS-25-016
Detection of human polyomavirus JCPyV DNA in urothelial carcinomas of urinary bladder
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Background & objectives: JCPyV is a human neurotropic polyomavirus that is associated with encephalitis and nephropathy. JCPyV has been detected in the urine and tissue of urothelial cell carcinomas (UCC). The pathogenesis of the presence of JCPyV-DNA in UCC is not yet proved.
Methods: We evaluated the relationship of the presence of Decoy urine cytology specimens (UCS) with the detection of JCPyV-DNA in UCC. A large single-institution database was searched for UCS positive for Decoy cells, suggesting polyomavirus infection. The available urine sediments and formalin-fixed paraffin-embedded (FFPE) tissue samples of UCC were tested for the presence of JCPyV-LTAg by PCR and confirmed by sequencing.
Results: Typical Decoy cells were reported in 30 patients out of the database with 22.867 UCS in the period 2004-2019. Of these, fourteen patients were diagnosed with UCC of the urinary bladder (14/30; 46.6%) before presenting with Decoy cells in the urine. JCPyV-DNA was identified in five UCS and three FFPE samples of UCC.
Conclusion: These findings correlated with the hypothesis that JCPyV infection can be linked to urothelial carcinoma. Thus, further research is needed to clarify the relationship between JCPyV and UCC.

PS-25-017
AHNAK2 ELISA-based urinary test for bladder cancer detection and monitoring: a pilot study
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Background & objectives: Non-invasive bladder cancer (BC) detection markers are urgently needed. Recent studies demonstrated that AHNAK nucleoprotein2, (AHNAK2) differentiates between cystitis and BC.
We aimed to perform an ELISA urine test to compare AHNAK2 levels in BC patients with the control's levels.
Methods: Voided urine specimens were collected from 27 patients with histologically proven BC and 28 healthy controls.
AHNAK2 concentrations were measured using a quantitative sandwich ELISA test, according to the manufacturer's protocol.
Associations between groups and the diagnostic performance of the assay were evaluated with the Student t-test, Spearman's Rank correlation, Mann-Whitney U Test, and Receiver Operating Curve (ROC) curve analysis.
Results: Mean AHNAK2 urine levels were higher in BC patients (80.7pg/ml; Median 13.87), compared to the controls (5.19pg/ml; Median 2.25) ($p<0.05$). In the BC group, we found a statistically significant difference in AHNAK2 urine values between non-invasive and invasive BC patients ($p<0.01$). We noted a moderate positive correlation between AHNAK2 urine levels and pT status ($r=0.69$; $p<0.05$), but no correlations were found with gender, age, and histologic grade. With a cut-off value of 11.84pg/ml (Mean+SD of the control group), the sensitivity and specificity of the assay were 51.85% and 85.71%, respectively. Alternatively, in a proposed cut–off value of 5.19pg/ml, the sensitivity increased to 62.96%, but the specificity declined to 67.86%.
Conclusion: The measurement of AHNAK2 urine concentrations could represent an inexpensive, adjunct tool in the diagnostic evaluation of patients suspected of having BC. Future research should refine and validate these findings, which might ultimately reduce the number of unnecessary cystoscopies.

PS-25-018
Immunohistochemical study of microsatellite instability in tumours of the urogenital zone
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Background & objectives: Microsatellite instability (MSI) is a predictive marker for immunotherapy. Objective: To study MSI in bladder

cancer (BC) and cervical carcinomas (CC) by immunohistochemical (IHC) method and to assess its relationship with prognostic factors of the disease and PD-L1 tumour status.
Methods: The MSI phenotype of the IHC method was studied on 50 patients with bladder cancer and 43 patients with cervical cancer. The following antibodies VENTANA anti-MSH2 (G219-1129), VENTANA anti-MSH6 (SP93), VENTANA anti-PMS2 (A16-4), VENTANA anti-MLH1 (M1) with detection system - OptiView DAB IHC Detection Kit with OptiView Amplification Kit were used.
Results: MSI was found in 52.0% of bladder cancer samples. A correlation was found between an absence and/or a decrease in the expression of MMR proteins and the degree of differentiation of bladder cancer and stage T. A tendency to a decrease in the expression of the studied proteins in the zone of invasive tumour growth was found.
In cervical cancer, MSI was a rare event and was detected in 4.7%. Intratumoral heterogeneity of IHC staining of MMR proteins was noted in 27.9% of cervical cancer specimens. The absence and/or heterogeneity of expression was most common in the MLH1 / PMS2.
Conclusion: MSI was statistically significant more often in bladder cancer (52.0%) than in cervical cancer (4.7%) (p-value = 1.427e-07). A tendency towards a decrease in the expression of the studied MMR proteins in the zone of invasive tumour growth was found. An association was found between the absence and/or a decrease in MMR proteins' expression and the degree of differentiation of tumours and stage T. Intratumoral heterogeneity of MMR proteins was noted.

PS-25-019
Oncocytic renal neoplasms: a ten-year retrospective review of cases in light of emerging entities
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Background & objectives: Oncocytic renal neoplasms are a heterogeneous tumour group. Given the emerging entities Low grade Oncocytic tumour and Eosinophilic vacuolated tumour, we proposed to review cases of Oncocytoma and Hybrid Oncocytic/Chromophobe tumour reported over a 10-year period within our unit.
Methods: We identified all cases reported as Oncocytoma or Hybrid Oncocytic/ Chromophobe tumour (HOCT) diagnosed in our department between 2010-2020 to determine retrospectively whether there would be any reclassification of these tumours based on current information. We also wanted to determine the outcome of this group of patients over the course of the study period.
Results: 84 tumours, previously designated as oncocytoma or HOCT were reviewed by two pathologists with an interest in renal neoplasms. Four tumours were reclassified as Low grade Oncocytic tumours (LOTs), and a further two were reclassified as Eosinophilic vacuolated tumours (EVT). A small number of tumours would have been better classified as Oncocytic neoplasms of Low malignant potential NOS.
Patients with LOT had a mean age of 68.5 years and all were female. Mean tumour size was 43 mm. Patients with EVT had a mean age of 49.5 years and were also both female. The two tumours measured 43 and 123 mm (mean 83 mm).
Conclusion: Our results show 7% of historical oncocytoma and HOCT diagnoses required a reclassification in light of the new entity descriptions of LOT and EVT. Our data supports the original finding that these are indolent tumours with no evidence of progression or metastatic disease in these patients.

PS-25-020
Assessment of programmed death ligand-1 (PD-L1) immunohistochemical expression using 22C3 clone in urothelial carcinoma variants
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Background & objectives: Variants of urothelial carcinoma (UC) are increasingly reported in invasive (UC) and are relevant for treatment and prognosis. The aim of our study was to determine the PD-L1 immunohistochemical (IHC) expression of 22C3 clone (Dako) in different variants of UC.
Methods: Our study included 33 cases of radical cystectomy performed for muscle-invasive UC in the Urology Department from Târgu-Mureş County Hospital (România) and Centre Hospitalier Lyon Sud (France). PD-L1 IHC expression was assessed using 22C3 clone (DAKO). The Combined Positive Score (CPS) was applied with a positive cut-off value set at 10.
Results: The majority of patients were men (n=27, 81.8%) with only 6 (18.2%) women. The mean age of the patients was 67.35±9.98 years. Eleven (33.3%) cases displayed lymph node involvement, while distant metastases were documented in 7 cases (21.2%). Among all the 33 cases of UC variants, PD-L1 CPS score was positive in 16 (48.48%) cases: 5(15.15%) squamous UCs, 4(12.12%) poorly differentiated UCs, 3(9.09%) sarcomatoid UCs, 2(6.06%) micropapillary UCs and 2(6.06%) mixed UCs, respectively. Concerning the tumour stage, the majority of PD-L1 positive cases were pT3 (n=8 cases, 50.0%), followed by pT4 (n=5, 31.2%) and pT2 (n=3, 18.8%).
Conclusion: Positive PD-L1 expression appears to be frequent among UC variants. Our data may provide rationale and further support to include UC variants in clinical trials, in order to identify patients who may benefit of anti-PD-L1 targeted chemotherapy.

PS-25-021
Mucinous tubular and spindle cell carcinoma of kidney: a study of four cases and review of the literature
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Background & objectives: Mucinous tubular and spindle cell carcinomas (MTSCC) are low-grade renal epithelial neoplasms, account for less than 1% of all renal neoplasms. The aim of this work is to analyse the clinical and the pathological features of this entity.
Methods: Retrospective study involving 4 cases of MTSCC of the kidney, diagnosed in our department of pathology between 2006 and 2021.
Results: Average age was 67.25 years (extreme: 62-79). All patients were female. Diagnosis was made on an enlarged nephrectomy in 3 cases and partial nephrectomy in 1 case. Mean tumour size was 11,6 cm (extreme: 6-24 cm). Tumours were upper polar in 2 cases, lower polar in 1 case and occupying the entire kidney in 1 case. They were solitary, unilateral, well-demarcated and yellowish-white in colour. Histologically, all cases showed a compact tumour proliferation, consists of anastomosing tubes, without papillary structures in a myxoid stroma; associated with fasciculated spindle cell sectors. Nuclear atypia, mitosis and necrosis were rare. In Immunohistochemistry, cells were positive for CK7, EMA, vimentin; and negative for CD10.
Conclusion: MTSCC of the kidney is an extremely rare neoplasm. It occurs in middle-aged adults, with a female predilection. It has a favourable prognosis. Although uncommon, this entity should not be confused with other aggressive tumours of the kidney such as papillary carcinoma, carcinoma of the collecting tubes, sarcomatoid carcinoma and primary or metastatic sarcomas.

PS-25-022
cfDNA methylation of NANOG as a potential screening biomarker in patients with testicular seminoma
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Background & objectives: Seminoma is the most common testicular germ cell tumour (TGCT) representing 50% of all TGCTs. Seminoma screening and diagnostic biomarker is yet to be identified. NANOG epimutations could be the answer to this challenge.
Methods: Twenty- four tissue samples of patients with seminoma were routinely stained for HE and immunohistochemistry. Nuclear NANOG expression in seminoma, germ cell neoplasia in situ and unaffected seminiferous tubules was scored according to intensity and percentage of positive cells. cfDNA methylation level was analysed in pre and post-orchiectomy semen samples by pyrosequencing. Results were considered statistically significant when $p<0.05$.
Results: Positive strong nuclear immunohistochemical expression of NANOG in more than 75% of tumour cells was demonstrated in all examined samples of seminoma and germ cell neoplasia in situ, while no expression was present in unaffected seminiferous tubules with retained spermatogenesis. Regarding the analysis of semen samples, statistically significant cfDNA hypomethylation of NANOG promotor was detected in all preoperative when compared to postoperative samples.
Conclusion: NANOG is expressed in pluripotent germline stem cells in TGCT. Our study has confirmed NANOG expression in seminoma tissue and germ cell neoplasia in situ. To the best of our knowledge, this is the first study detecting cfDNA hypomethylation of NANOG promotor in seminal plasma samples with statistically significant difference between pre and postoperative samples. Therefore, according to presented data, cfDNA methylation of NANOG could present a screening and diagnostic biomarker for detection of seminoma.

PS-25-023
Many faces of nephrogenic adenoma: a clinicopathological mimic of malignancy
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Background & objectives: Nephrogenic adenoma(NA) is an uncommon benign lesion of the urinary tract with polymorphous histology masquerading as a malignant tumour.
Methods: The pathology database of our institute was searched for ' nephrogenic adenoma' using our search engine over a period of 10 years. (2010-2019). The clinical details and follow up were recorded from the electronic medical records.
Results: Thirty-seven patients were retrieved for histological and immunohistochemical(IHC) review. The median age of diagnosis was 63years(14-81years) with a male: female ratio of 3:1. Lesions were localized to urinary bladder (92.3%) urethra (5.1%) and ureter (2.5%). Cystoscopy (30 cases) showed flat erythematous (60%) or papillary (40%) lesions mimicking urothelial carcinoma. Histology showed tubular, papillary and microcystic growth pattern with minimal cytological atypia. The lesional cells were flat, cuboidal to low columnar with eosinophilic cytoplasm. Hobnail, signet ring-like and clear cell changes were identified in a subset of cases. Immunohistochemistry (IHC) was performed in 27 cases. PAX-8(n=22) and CK7(n=21) expression were seen in 100% of the cases AMACR was positive in 89.4% cases (n=17/19).
Conclusion: Nephrogenic Adenoma is a benign lesion of the urothelial tract which is often misdiagnosed clinically and histologically as a malignancy. Meticulous histological evaluation along with a careful selection of IHC panel is critical for correct diagnosis.

PS-25-024
Clinical and pathohistological risk factors of relapse in non-muscle-invasive bladder cancer
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Background & objectives: Aim of our research was to evaluate the influence of clinical and pathohistological features of urothelial non-muscle-invasive bladder cancer (NMIBC) on the risk of recurrence. A retrospective study included 100 patients (69 males, 31 females, 32-94 y.o.) with NMIBC.
Methods: Each study participant underwent TUR with intravesical chemotherapy. After 6-month follow-up period the subjects were divided into two groups with presence or absence of relapse. Parameters like gender, age, clinical manifestations, tumour size, tumour localization, number of malignant foci, pathohistological degree of tumour differentiation (PATO) – high-, moderate, poorly differentiated (G1, G2, G3, respectively) were compared within each group.
Results: The study found that the PATO G1 had on average a smaller tumour size than PATO G2 and G3 ($p=0.002$). It was shown that the average age of patients with G2 and G3 tumours is higher than in the subgroup of patients with G1 tumours ($p=0.022$, $p=0.03$, respectively). It was noted that multiple lesions of the bladder led to relapse almost twice as often as single tumours ($p=0.001$). With an increase in size of tumour and with a decrease in the degree of differentiation, the chances of relapse significantly increased ($p<0.05$).
Conclusion: The data of the study shows that the clinical and pathohistological parameters (PATO, focality of tumour, size of lesion) are interrelated with the recurrent course of bladder cancer.

PS-25-025
Mesenchymal prostate tumours, the surprise you do not expect. A single centre thirty-year experience
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Background & objectives: Mesenchymal tumours of the prostate represent less than 0,1% of primary malignant prostatic tumours. They have variable histological features; therefore, they pose a diagnostic challenge. The objective is to make a 30-year review of these cases in our centre.
Methods: We reviewed our files searching for all primary malignant prostatic lesions diagnosed from January 1, 1990 to March 1, 2021. All samples were classified according to WHO 2016 classification. Our collected variables were age at diagnosis, outcome, sample type, architectural pattern, histologic diagnosis and grade.
Results: After reviewing 55.672 core biopsies from 20.736 patients and 4.630 surgical specimens from 4.447 patients, we obtained a cohort of 10 patients. Five were rhabdomyosarcomas, diagnosed in 2 transurethral resections (TUR), 2 cores biopsies and 1 pelvic resection specimen, all embryonic type with a mean age of 7 years. In adults, the mean age was 67,4 years; one was a leiomyosarcoma diagnosed in a TUR; two were prostatic stromal tumour of uncertain malignant potential on cores biopsies and two high grade prostatic stromal sarcomas. We have available clinical data of outcome from 6 cases, two died from these tumours (rhabdomyosarcoma and leiomyosarcoma), two from other causes and two are alive.
Conclusion: Prostatic mesenchymal tumours represent 0.02% of all prostate samples and specimens in our centre. Consistent with the literature, all cases of rhabdomyosarcoma were diagnosed in the paediatric age and the others in adults. Neuroectodermic differentiation in these tumours is an unusual histologic finding. Overall, prostatic tumours of uncertain malignant potential and prostatic stromal sarcomas have a better prognosis than rhabdomyosarcoma and leiomyosarcoma.

PS-25-026
En bloc resection of bladder tumours: histopathologic features of a prospective study
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Background & objectives: En bloc resection of bladder tumour (ERBT) focuses on resecting the tumour in one piece including detrusor muscle and tumour free mucosa. Our objective is to precisely assess the morphological features of the ERBT specimens.
Methods: Patients with primary suspected non-muscle invasive bladder cancer (NMIBC) < 3 cm in size were prospectively included. Tumours were totally embedded for whole mount section. Sections were analysed to determine the adequacy of the resection in terms of artefacts, spatial orientation of the tumour, presence of detrusor muscle and state of the resection margin.
Results: Sixteen patients (19 tumours) were included. Mean tumour diameter was 1.56 cm (0.4-2,8). Seven and 12 tumours were High- and Low- grade urothelial carcinoma respectively. Five were pT1 and 14 pTa. No prominent cautery damage or crush artefact effected the diagnosis and staging of the tumour. The spatial arrangement of tissue with orientation of tumour, lamina propria and detrusor muscle were detected in 14 tumours.
Detrusor muscle was lacking in 2 out of 5 pT1 tumours. In 7 tumours both mucosal margins were free of tumour or CIS. In 1 case of HGpT1, CIS was found in the mucosal margin. EBRT lead to clinical stage in 85% of primary NMIBC.
Conclusion: Preliminary data shows the feasibility of morphological analysis of EBRT specimens. ERBT provides a well oriented specimen that allows exact determination of tumour stage and surgical margins. The rates of detrusor presence and mucosa-free margins are not superior to the conventional endoscopic resection technique, justifying the lack of difference in recurrence rates between EBRT and conventional resection reported in the literature. Notwithstanding, EBRT provides the solid ground to identify clinically relevant recurrence causes.

PS-25-027
Testicular pathology and the effects of national lockdown in a district general hospital
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Background & objectives: Low incidence of testicular cancer means orchiectomies are infrequently reported by district general pathologists. National lockdown threatened to exacerbate this with reductions and delays in cancer diagnoses. This audit compared reporting of orchiectomy specimens before and after lockdown was imposed.
Methods: A search of the local pathology database was conducted. The pathology reports of testicular orchiectomies performed April 2019 – April 2021 were retrieved. Chi square statistical analysis was performed to compare pathology reporting in the year leading up to and the year following the National lockdown announcement. Concordance with tertiary centre reporting was assessed using Kappa.
Results: Forty-one orchiectomies were performed in the year leading up to national lockdown with 68.3% for benign indications. In the following year 43 orchiectomies were performed and 53.5% were for the treatment of testicular neoplasms. The proportional change in workload was significant (p=0.04). Average reporting time overall was 12 days. Prior to lockdown only 41.5% of testicular orchiectomy reports were authorised within 10 days versus 76.7% of reports in the year after (p=0.001). Of 33 testicular neoplasms referred to a tertiary centre reporting errors were identified in 4 cases (12.1%). Overall concordance showed "substantial agreement" (Kappa=0.70). There was no difference in reporting concordance before and after lockdown.
Conclusion: The covid pandemic and lockdown raised concerns regarding NHS ability to achieve standardized targets. We reviewed testicular orchiectomies performed within a single institution. Volume of work has remained consistent. Proportionally more orchiectomies were performed for the treatment of neoplasms in the year following lockdown with fewer benign orchiectomies. Turnaround times improved with no impact on reporting quality. Further assessment is needed to understand the true impact of national lockdown on the ability of pathology departments to deliver standardized care.

PS-25-028
Prostatic calculi cause collagen type I overexpression in prostate cancer tissue
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Background & objectives: Prostatic calculi (PCa) causes morphological and immunohistochemical transformation of connective tissue of prostate cancer (PC) which has an important role in disease progression. Objective: To study the effect of prostate calculi on connective tissue composition of prostate cancer tissue.
Methods: For this study we used 60 PC samples (30 PC samples with PCa and 30 samples without biomineralization). Initially all samples were stained with hematoxylin-eosin. Immunohistochemistry was performed with antibodies against Collagen type I and Collagen type II. Data sets were analysed by Shapiro-Wilk test, Mann-Whitney's U-test and Student's t-test.
Results: The presence of PCa in tumour tissue was combined with epithelial desquamation, inflammation and mechanical tissue damage. We found that tissue with PCa had a higher area of Collagen I expression ($p < 0.05$) and was localized predominantly in the foci of biomineralization. During this study, we detected no significant difference in Collagen type II expression between groups ($p > 0.05$). This supports the idea that PCa causes high Collagen I expression and by so doing supports the development of PC osteoblastic immunophenotype.
Conclusion: PC causes cell damage and remodelling of tumour connective tissue. It creates a specific environment for osteoblastic immunophenotype development of PC cells. It worsens disease prognosis and supports bone metastases development.

PS-25-029
Decreased FAS expression predicts poor survival in muscle-invasive bladder cancer
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Background & objectives: FAS (CD95) is a death receptor critically involved in the induction of apoptosis. The aim of this study was to analyse the expression pattern of FAS in muscle-invasive urothelial bladder cancer and to assess its prognostic significance.
Methods: The study comprised 150 muscle-invasive urothelial bladder cancer (pathologic stage T2). Tumour samples were incorporated in tissue microarrays and analysed by immunohistochemistry to the expression of FAS receptor. FAS expression status was correlated with pathological parameters and follow-up data.
Results: Decrease or loss of FAS was found in 53,3% of the tumours. High FAS expression correlated with the finding of carcinoma in situ in the surroundings of invasive tumours (p=0.038). Tumours with squamous differentiation showed significant loss of FAS (p=0,002), while tumours with glandular differentiation and variant morphology demonstrated high FAS expression (p=0,042, and p=0,020, respectively). Patients with muscle-invasive tumours with high FAS expression had significantly longer survival (p=0,003). Decreased FAS expression was strongly associated with cancer-specific death (p=0,001).
Conclusion: The expression of FAS may play an important role in the prediction of muscle-invasive bladder cancer prognosis. Decrease or loss of FAS expression in tumour tissue indicates aggressive disease and poor survival. Loss of FAS expression in muscle-invasive tumours should impel radical cystectomy with neoadjuvant chemotherapy or trimodal therapy as a mandatory treatment modality.

PS-25-030

Adenomatoid tumour of the testis: a study of five cases

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Background & objectives: Testicular adenomatoid tumours are rare benign tumours of male genital tract. They appear mostly in the third to fifth decades. They are easily misdiagnosed as malignant tumours. The aim of this study is to analyse their epidemiological and histopathological characteristics.
Methods: In our retrospective study, we reviewed 5 cases of adenomatoid tumour of the testis, that were diagnosed at the Pathology Department of Habib Bourguiba Hospital over a 17-year period (2004-2020). An analysis of the histological data and a review of the clinical records were carried out in all cases.
Results: The average age of our patients was 32 years (range between 13 and 51). All tumours were solitary and unilateral. They occurred as an intratesticular masses (n = 2) or extra testicular masses: in the epididymis (n = 3). They ranged in size from 0.5 to 1 cm (mean 0.8 cm). All patients underwent surgical treatment. Microscopic findings revealed a proliferation of variably sized tubules and pseudo-vascular spaces lined by eosinophilic cuboidal or flattened cells, with focal intracytoplasmic vacuolization. Nuclear atypia and mitotic figure were absent. Admixed smooth muscles were also present. Immunohistochemistry showed positivity for calretinin, pancytokeratin, vimentin, focally for EMA and negativity for CD34, inhibin and BerEP4.
Conclusion: Testicular adenomatoid tumour is a rare testicular benign tumour. They usually present as extra testicular masses than an intratesticular masses. By imaging, they are easily misdiagnosed as malignant tumours with removal of organs. Histologically, adenomatoid tumours are characterized by adenoid, solid and cystic pattern. When the cystic pattern predominates, the tumour can simulate lymphangioma. The mesothelial cell origin can be proved on the basis of an immunohistochemistry stain using markers typical of mesothelial origin, including calretinin, WT1 and HBME1.

PS-MD-01 | Molecular Pathology Diagnostics Symposium Posters

PS-MD-01-001

miRNA biomarker candidates in pancreatic cyst fluids

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Background & objectives: The accurate diagnosis of pancreatic cystic lesions (PCL) is vital for adequate patient management. Molecular analyses have gained importance in PCL diagnostics. Therefore, we aimed at identifying miRNAs that could serve as molecular biomarkers for risk stratification of PCL.
Methods: Total RNA was isolated from pancreatic FFPE tissue (n=29) and cyst fluids (n=40). RNA from FFPE tissue was used for library preparation using the 'VAHTS small RNA library prep kit for Illumina' and subsequently sequenced on the MiSeq system. miRNA levels of miR-21-5p, miR-221-3p, miR-200a-5p and miR-217a-5p were then investigated using TaqManTM Advanced miRNA-Assays in pancreatic cyst fluids.
Results: miRNA sequencing revealed a differential expression in IPMNs and PDAC compared to normal pancreatic tissue in following four miRNAs: miR-21-5p, miR-221-3p, miR-200a-5p and miR-216a-5p. Based on the sequencing results, relative expression of these miRNAs was then investigated in pancreatic cyst fluids: miR-21-5p and miR-200a-5p were more expressed in cyst fluids from mucinous cysts and PDAC compared to pseudocysts and serous cysts. miR-221-3p expression was only elevated in PDAC and miR-216a-5p did not show any differential expression in cyst fluids.
Conclusion: Overall, three of four miRNAs that were detected as differentially expressed in FFPE specimens show potential to distinguish pancreatic mucinous cysts from non-mucinous cysts and may aid accurate diagnosis of PCL and improve adequate patient management.

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PS-MD-01-002

A comparative study between neoplastic nuclei percentage and allelic fraction in lung carcinomas analysed by NGS

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Background & objectives: Accurate definition of malignant cell fraction is pivotal to determine the quantity of tumourDNA/RNA acceptable for molecular testing. Our aim was to verify the correlation between neoplastic nuclei percentage(NNP) and allelic fraction(AF) detected by NGS in a series of lung cancer.
Methods: We revised the data resulting from NGS analysis of 349 lung carcinomas, studied in our Institute from January-May2020. We selected and analysed 320 cases, that presented at least one mutation, aiming to verify a correlation between morphological assessment of NNP, made by a pathologist/technician, and the allelic fraction detected. All cases with lower NNP(5-10%) were reviewed by another pathologist.
Results: The genes more frequently mutated were: KRAS (40%), EGFR (33%), BRAF (6%), HER2 (5%) and MET (2,5%). In 248 cases (77,5%) we observed an expected relation between NNP and AF of the mutated gene by NGS, in other words a relation approximately from 2:1. In 72 cases (22,5%) there was no correlation, with a low NNP compared to the AF. These cases were re-evaluated by another pathologist in order to exclude an inter-observer disagreement in the estimation of NNP. Nevertheless, the absence of correlation was confirmed.
Conclusion: In most of the cases(77,5%) there was a good agreement between the estimation of NNP and the AF. However, in 22,5%cases there was possible underestimation of the NNP, which has been demonstrated in other studies. Tumour heterogeneity, differences between the real number of neoplastic nuclei observed and those dissected for NGS, due to different section levels of cutting and a rare possibility for a double/triple hit in some of the genes, can explain the discrepancies found in about(1/4)of the cases.

PS-MD-01-003

Diagnostic usefulness of the detection of molecular alterations in pleural sarcomatoid mesothelioma: 3 case series with study of the homozygous deletion of 9p21 and immunohistochemistry for BAP1

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Background & objectives: Genomic studies in mesotheliomas reveal BAP1 alteration specially in epithelioid subtypes, while in sarcomatoid mesothelioma (SM) homozygous deletion of 9p21 has greater frequency. It is being proposed to incorporate into the diagnostic algorithm of mesotheliomas the detection of molecular alterations.
Methods: We share our experience with 3 cases of SM and carry out a bibliographic review on its utility. In all cases, two mesothelial and two epithelial markers were performed in addition to BAP1 (clone C-4, Santa Cruz). The P16/CDKN2A deletion was analysed by FISH using the Zytolight® CDKN2A/CEN 9 probe, in complete sections.
Results: All were men (3), 2 ex-smokers, aged 59-84 years. One was a construction worker. They presented a pleural mass (1), pleuro-pulmonary nodule (1) or pleural nodules (1) together with hemothorax (1) or pleural

effusion (2). All 3 were diagnosed with videothoracoscopic biopsies. The loss of nuclear expression of BAP1 was observed in one case (1/3) and it was homogeneous, always identifying an internal control (lymphocytes, endothelial cells or fibroblasts). All three cases showed homozygous deletion of P16/CDNK2A. We did not perform immunohistochemistry of p16 since the published literature rules out its usefulness and, however, describe a strong correlation between loss of MTAP and the 9p21 deletion.
Conclusion: Since 2018 we have performed P16/CDKN2A FISH and BAP1 immunohistochemistry in the differential diagnosis of mesotheliomas. Although there are few cases, our series shows correlation with the data described in the literature, being the homozygous deletion of P16/CDKN2A a frequent alteration in SM. In contrast, nuclear loss of BAP1 is rare. The use of CDKN2A/CEN 9 FISH is a sensitive tool for the diagnosis of SM, being useful in cases with diagnostic doubts.

PS-CP-01 | Computational Pathology Symposium Posters

PS-CP-01-001
Potential of an AI-based digital biomarker to predict neoadjuvant chemotherapy response from preoperative biopsies of Luminal-B breast cancer
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Background & objectives: Invasive breast cancer (IBC) is increasingly treated with neoadjuvant chemotherapy. Yet, only 15-20% of Luminal-B patients achieve pathological complete response (pCR). We developed an AI-based biomarker to predict pCR of Luminal-B IBC from preoperative biopsies stained with H&E.
Methods: First, we trained a deep learning model on a multi-centric dataset of n=277 manually annotated breast cancer H&E-stained histopathology images to segment tumour, lymphocytes and other tissue. Second, we applied the segmentation model to an independent set of n=297 Luminal-B pre-treatment biopsies. For each case, we computed our biomarker: the proportion of tumour within 80μm distance from lymphocyte regions.
Results: From the Luminal-B cohort, 32/297 cases (11%) were labelled as "pCR" when no remaining cancer cells were reported for the post-operative surgical resection. The biomarker showed significant ($p<<0.01$) correlation with pCR with a point biserial correlation coefficient of 0.27. Setting a cut-off value based on the optimal operating point of the ROC curve (AUC=0.69), we reached a sensitivity of 0.53 and a specificity of 0.74.
Conclusion: The developed deep-learning based biomarker quantifies the proportion of inflammatory tumour regions. It shows promising results for predicting pCR for Luminal-B breast cancer from pre-treatment biopsies stained with H&E.

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PS-CP-01-002
Quantifying morphological features of neoplastic lymphocytes using deep neural networks on whole-slide images is useful in differentiating monomorphic epitheliotropic intestinal T-cell lymphoma from primary intestinal peripheral T-cell lymphoma, NOS
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Background & objectives: Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL) is primary intestinal T-cell lymphoma (PITL) comprising monomorphic medium-sized round nuclei expressing CD8, CD56, and cytotoxic markers, while those with pleomorphic nuclei are peripheral T-cell lymphoma (PTCL), NOS. The morphological distinction could be subjective.
Methods: We used whole-slide images of 40 PITLs from Taiwan. An instance segmentation model was trained and applied to segment lymphocytes under high-power fields. Morphological features were extracted and statistically analysed to serve as an objective quantification index. Finally, a classifier for MEITL or PTCL-NOS was trained by using extracted features with an xgboost algorithm and with a 3-fold cross validation.
Results: Our lymphocytes detector achieved an average precision of 0.906 on segmenting target cells and identified 892.18 ± 254.80 cells in each high-power field. The general linear model was employed to analyse morphological features and showed a significant difference ($p<0.001$) on several features when comparing these two types of PITL. Furthermore, cell pleomorphism could be quantified by using combinations of morphological features, which showed a clear boundary between the two groups when visualized on a scatter plot. The classification performance of machine learning models achieved an AUC (area under the ROC curve) of 0.915 by using morphological features, an AUC of 0.975 when immunophenotypical findings, namely CD8 and CD56, were incorporated.
Conclusion: Our method measured cellular morphology in a quantitative, objective, and consistent manner. We identified several indexes useful for differentiating MEITL from PTCL-NOS. For morphologically borderline cases using our method, the pathologists may incorporate immunophenotypical findings for assisting the final diagnosis. In addition to PITL, our method can also serves as an objective quantification tools for measuring pleomorphism in other diseases such as low vs. high grade follicular lymphoma, or mantle cell lymphoma of the classic vs. pleomorphic variants.

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PS-CP-01-003
Digital image analysis algorithms of HER2 score in breast biopsy tumours
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Background & objectives: Human Epidermal Growth Factor Receptor 2 (HER2) is analysed through immunohistochemistry (IHC). Roche launched an innovative image analysis algorithm to evaluate HER2. We aimed to compare ocular estimated scores with the score calculated with the algorithm.
Methods: Thirty-five breast biopsies of invasive breast cancers with IHC for HER2 from one year (2020). Slides were scanned using the VENTANA DP 200 and then analysed with the HER2 algorithm of uPath Software.
Results: The pathologists originally reported 45.7% negative (20% of 0+ and 25.7% of 1+) IHC score, 42.9% equivocal (2+) IHC score and 11.4% positive (3+) IHC score, while uPath software detected 14.3% negative (2.9% of 0+ and 11.4% of 1+) IHC score, 40% equivocal (2+) IHC score and 45.7% positive (3+). This study demonstrated the agreement of pathologists and Software in 42.9% of the cases. 31.4% of negative scores estimated by pathologists turn into equivocal (22.9%) and positive (8.5%) scores after digital imaging analysis. Finally, 25.7% of equivocal scores previously analysed by pathologists turn into positive.
Conclusion: IHC is subject to interobserver variation and lack of reproducibility. uPath is an important tool to support the pathologist's decision in determining HER2 status in breast carcinoma, providing an alternative, practical and reproducible method to manual scoring.

PS-CP-01-004

Morphometric features to predict outcome after ductal carcinoma in situ of the breast

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Background & objectives: Ductal carcinoma *in situ* (DCIS) is a potential precursor of invasive breast cancer (IBC). However, large proportion of untreated DCIS do not progress to IBC. There is an important need to distinguish harmless from aggressive DCIS to better decide treatment.
Methods: We retrieved clinical data from a case-control study of patients diagnosed with primary DCIS treated with breast-conserving surgery alone. Hematoxylin-Eosin (HE) slides of DCIS lesions were scanned and uploaded to HALO software (IndicaLabs) for DCIS classification based on artificial intelligence (AI) algorithms. We hypothesize that morphometric features observed in HE sections of DCIS might predict progression to ipsilateral IBC (iIBC).
Results: We first manually annotated DCIS regions in 20 HE sections uploaded in HALO. Annotations were used by advanced deep learning neural network to create a train-by-example tissue classifier. The AI-segmentation was tested in another 40 independent DCIS HE sections and evaluated by an expert pathologist. Finally, this classifier was applied on 559 DCIS lesions, i.e. 225 with a subsequent iIBC event (cases) and 334 without subsequent iIBC (controls). It allows us to determine if the diameter, density, and distribution of DCIS ducts found in tissue sections of primary diagnosed DCIS are associated with the risk of subsequent iIBC.
Conclusion: HALO provided the number of DCIS of each sample, coordinates and maximum diameter of each duct, with high accuracy. We have successfully built an AI tissue classifier to evaluate DCIS diameter, density, and distribution in HE sections. Currently, the association between these morphometric features and risk of subsequent iIBC is being evaluated by applying multivariate regression models, including clinical and other pathological variables. These morphometric features are promising variables to distinguish harmless from potentially hazardous DCIS.

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PS-CP-01-005

Pathologist-driven experience drives design of AI-based digital diagnostics

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Background & objectives: Digital pathology and artificial intelligence (AI) for routine clinical diagnosis is a novel, growing area. User experience (UX) research is critical to ensure pathologists can effectively and efficiently use digital viewing software and integrated AI solutions in daily clinical practice.
Methods: To understand how to deliver the most value from using a highly accurate AI-based digital diagnostic for breast cancer, various user research methods were employed including contextual inquiry and concept testing with Breast pathology specialists. Additional investigative methods included qualitative interviews and quantitative surveys with both US-based and European-based general and sub-specialized pathologists.
Results: 75% of pathologists surveyed (36/48) were interested/very interested in using AI in digital workflows. The desired level of explainability of AI results depended on the pathologist's level of confidence in identifying diagnostic features and their use setting (clinical v. non-clinical). Additionally, observing pathologists review AI results as a heatmap (visualization technique to display magnitude of findings) revealed an opportunity for improved usability; Pathologists consistently hid the heatmap to evaluate the underlying tissue identified by the AI. Consequently, a new visualization technique that avoids obscuring tissue identified by the AI was developed, resulting in greater satisfaction. Beyond slide-level visualization, AI-enabled case prioritization was perceived as high value for efficiency gains.
Conclusion: Majority of surveyed pathologists believe the incorporation of AI into digital pathology workflows has the potential to save time and reduce workload. These gains in efficiency and quality can only be achieved with thoughtful design powered by user-driven research and insights that focus on enhancing the Pathologist-AI interaction. By leveraging these research methodologies, Paige has designed novel visualization and interaction types for its digital diagnostics that have resulted in improved understanding, satisfaction, and navigational efficiencies.

E-Posters

E-PS-01 | Autopsy Pathology E-Posters

E-PS-01-001

Pericardic thymolipoma – case report

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Background & objectives: Thymolipoma is a relatively rare tumour, representing about 2-9% of thymic neoplasms, being characterized by a slow rate of growth. The aim of our study is to report a case of incidental thymolipoma, necroptically diagnosed in a 56 years-old man.
Methods: Necroptic examination has been associated to collection of tissue specimens for microscopy. Routine hematoxylin-eosin staining, along with immunohistochemistry using a panel of markers (CD3, Tdt, vimentin, p63, and cytokeratin AE1/AE3) have been performed.
Results: The histopathological examination revealed a small tumour within pericardium, of 21/19/18mm, composed of mature adipose tissue, without atypia, associated with foci of benign thymic tissue, and groups of epithelial cells. Thymocytes showed a strong Tdt immunopositivity. The groups of epithelial cells were strongly positive for cytokeratin AE1/AE3 and p63, negative for vimentin, and had a variable expression of Bcl-2.
Conclusion: Thymolipoma is usually diagnosed in the second or third decade of life but considering the slow growth and late symptoms, due to compression, it may represent an incidental finding in autopsy. It may be related to systemic diseases, such as Grave's disease, aplastic anaemia, and other autoimmune disorders. Despite their rare occurrence, thymolipomas should be considered in the differential diagnosis of mediastinal lipoma or liposarcoma, thymic hyperplasia, teratoma, and regressed thymoma. The microscopic examination and immunohistochemistry may certify the diagnosis.

E-PS-01-002

Case report of lipomatosis cordis causing myocardial infarction

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Background & objectives: Lipomatosis cordis, also known as myocardial steatosis, is the abnormal retention of lipids within the myocardium and specifically, the ventricular or interventricular septal myocardium.
Methods: A 74-year-old woman with cardiac infarction having elevated levels of adiposing tissue within the cardiac muscle especially observed within atria and ventricles. A further observation in the coronary arteries,

showed atherosclerotic lesions inside the vascular lumen. Several ventricular slices had adipose infiltrations.
Results: Following a standard protocol of paraffin-ebaded tissue, hematoxylin and eosin staining, microscopical findings implicated locally elevated interstitial oedema, interstitial fibrosis-mainly perivascular. Also, intramuscularly was in few sites observed connective tissue. Additionally, there were dispersed adipose infiltrates, in the presence of inflammatory cells, steatosis of the lumen by about 30-40%, while in a few places steatosis was in about 50-60%. Finally, there were findings of aortic segment with fractured wall sites and evidence of present atherosclerotic lesions.
Conclusion: To sum up, myocardial steatosis has clinical and pathological significance for cardiac histology, electrophysiology and therefore the whole circulation process. Ectopic fat accumulation may cause lipotoxicity in cardiac muscle, which can lead to dysfunction and induction of structural remodelling. Correlated factors to this pathologic situation are aging, female sex, insulin resistance, diabetes mellitus, obesity, CAD, aortic stenosis and pulmonary hypertension.

E-PS-01-003
Necrotizing pneumonia caused by pseudomonas aeruginosa in a patient with acquired haemophilia: an autopsy case report
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Background & objectives: Pseudomonas aeruginosa is a Gram-negative bacterium is a frequent cause of severe hospital-acquired respiratory infections, especially in immunocompromised patients. Acquired haemophilia is a rare autoimmune disorder in which immunosuppression with steroids and monoclonal antibody rituximab is usually effective.
Methods: A 69-year-old woman was admitted in our hospital's emergency department for management of general discomfort and fatigue, adding fever in the last days. She had been treated with steroids and rituximab due to recently diagnosed acquired haemophilia. Several hours after admission, the patient's respiratory condition deteriorated progressively and entered a state of shock. She died 3 days after admission.
Results: Autopsy of the whole body including the brain was performed. Notable findings were several nodular lesions with white borders in both lungs and one yellowish nodular lesion in liver. Microscopically those areas correspond to extensive necrotizing abscess formation with haemorrhage and infarction. Vasculitis and perivascular inflammatory changes caused by gram-negative bacilli invading medium-sized pulmonary vessel walls were identified and thrombosis was observed. A sample of an hepatic abscess was sent to microbiology department, confirming the result of "mixed flora with pseudomonas aeruginosa".
Conclusion: There are few reports on necrotizing pneumonia caused by P. aeruginosa. Several authors described in their series similar nodular necrotic lesions that occasionally coalesce to form cavities depending on the time following the initial onset of symptoms. It is important to highlight that it was possible to detect p. aeruginosa in culture in this case. P. aeruginosa should be considered as a rare but fatal causative pathogen of necrotizing pneumonia that may complicate the clinical course specially in immunocompromised patients.

E-PS-01-004
Unusual presentation of diffuse B-cell lymphoma as a large isolated epiglottic mass
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Background & objectives: Primary extranodal head and neck lymphomas are the second most frequent, accounting for 2.5% of all lymphoma cases. Presentation in the larynx or hypopharynx is rare (1% of all laryngeal tumours) and primary epiglottic B-cell lymphoma is even less common.
Methods: We present the case of the sudden death of a 76-year-old female. The autopsy performed revealed a large infiltrative mass involving the epiglottis, the base of the tongue and the hypopharynx. The tumour was sampled and fixed in formalin, processed, embedded in paraffin and examined on H&E and ancillary immunohistochemical stains.
Results: At grossing the tumour had ill-defined margins, forming a large mass in the epiglottis, infiltrating the base of the tongue and the hypopharynx, whitish-grey colour and firm to hard consistency. Microscopic examination showed a diffuse proliferation of medium-large, discohesive cells, with marked cytologic and nuclear pleomorphism, large nuclei, with prominent nucleoli, brisk mitotic activity and extensive necrosis, surrounded by a fibrotic stroma, invading the full thickness of the epiglottis, with ulceration of the epithelium and lymphovascular invasion. The tumour was AE1/AE3, CD3 and CD5 negative, with few scattered small reactive lymphocytes, and CD20 showed strong and diffuse positivity.
Conclusion: Extranodal non-Hodgkin, diffuse B-cell lymphomas limited to the larynx are rare, accounting for less than 1% of all laryngeal neoplasms. Despite being a part of the supraglottis, the epiglottis is rarely reported as the primary site of laryngeal lymphoma and it is even more uncommon to have a primary presentation of sudden death by tumour obstruction of the airways.

E-PS-01-005
Autopsy findings in SARS-CoV-2 "molecular healing"
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Background & objectives: Data on histopathological changes in autopsied patients who eradicated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are very limited.
Methods: Autopsy of a patient who died after 51 days of COVID-19 was performed.
During his long-time hospitalization nasopharyngeal swab turned negative.
Results: Microscopic examination showed pathological changes in several organs: acute or organising diffuse alveolar damage with fibrosis in the lungs, brain ischemic injury, superimposed bacterial meningitis, sparse microthrombi and focal myocarditis with focal myocardiosclerosis. SARS-CoV-2 RNA was not detected in lung specimen.
Conclusion: The possibility of systemic long-term effects of COVID-19 are highlighted.

E-PS-01-006
Unsuspected milliary TB in an autopsy – an ancient foe that still surprises!
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Background & objectives: Tuberculosis (TB) is caused by Mycobacterium tuberculosis (MT) complex infection. Usually affects the lungs, but it can affect any organ. Milliary TB is a disseminated form. In the recent decades, in Portugal, the incidence of TB has steadily decreased.
Methods: A 79-year old man was admitted to our hospital two weeks after the onset of asthenia and anorexia. An X-ray was done and a milliary pattern was found. MT infection was not confirmed either by PCR and IGRA. The patient was hospitalized, dying after 26 days. Autopsy was performed. At this point two MT cultures were pending.
Results: Autopsy main gross finding was a pulmonary milliary pattern with multiple small nodules 1-2mm in the lungs, compatible with milliary

TB. On histological examination, necrotizing granulomas were observed in almost every organ: lung, liver, adrenal glands, spleen, mediastinal lymph nodes and the bone marrow. The presence of alcohol acid resistant bacillus was confirmed by the Ziehl-Neelsen stain. After the necropsy study, the cultures in urine and lung confirmed MT infection.
Conclusion: Although considered a rare disease in some countries, awareness and suspicion for MT should be present, even with negative results, thus every autopsy must be performed according to biosafety protocols.

E-PS-01-007
A case of fatal retroperitoneal hematoma after delivery in a young woman with neurofibromatosis
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Background & objectives: Retroperitoneal hematoma is a rare complication after delivery. One unusual predisposing condition, associated with increased risk for vascular abnormalities is neurofibromatosis. Hemodynamic and endocrine changes associated with pregnancy have been suggested to be contributing factors by worsening pre-existing aneurysms.
Methods: Patient with known neurofibromatosis had multiple tan coloured skin nodules, scoliosis and a small adrenal gland tumour. Massive hematoma in the left retroperitoneal space was discovered with an estimated volume of 2.5 L. No abnormalities were found during the detailed gross examination of the aorta and renal arteries. A possible rupture of mesenteric vascular malformation was considered.
Results: Histology revealed the skin nodules to be neurofibromas and the adrenal tumour – pheochromocytoma, the latter being frequent incidental finding in neurofibromatosis.
Conclusion: Although a rare syndrome, we should increase our awareness of the possible complication in patients with neurofibromatosis, because many of them present as nonspecific signs, which can lead to a fatal delay in the treatment.

E-PS-01-008
Features of lung damage in case of combined COVID-19 infection and HIV: a clinical case
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Background & objectives: As HIV progresses, it infects an increasing number of CD4 + T-lymphocytes, over time their number reaches critical values. The aim of this study is to describe a case of COVID-19 infection in a patient with HIV infection.
Methods: A histopathological study of tissue samples of the lungs, spleen and brain of a 42-year-old HIV-positive patient who died from viral-bacterial pneumonia with damage to both lungs was carried out.
Results: Histological examination revealed areas of epithelial desquamation, alveolar epithelium and macrophages with viral inclusions in enlarged nuclei, interalveolar septa thickened due to oedema, mononuclear infiltration. In the alveoli and alveolar passages, hyaline membranes and fibrin were revealed along the contour. Areas of necrosis of the alveolar epithelium with exposure of the basement membrane, signs of pronounced oedema with a haemorrhagic component were determined. In the lumen of the alveoli there were haemolyzed erythrocytes, in the pulmonary parenchyma - focal haemorrhages, signs of proliferation of capillary endothelial cells. Cytomegalovirus infection with brain damage, in which large cytomegalocells with intranuclear and cytoplasmic inclusions were found, served as a sign of HIV infection.
Conclusion: The immediate cause of death was a new coronavirus infection COVID-19 with Klebsiella pneumoniae, which caused bilateral viral-bacterial pneumonia, complicated by acute respiratory failure. The presence of a background pathology of HIV infection aggravated the condition of the patient, and undoubtedly influenced the death outcome.

E-PS-01-009
Morphological and immunohistochemical characteristics of the lungs with a combination of coronavirus infection and sarcoidosis in a patient
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Background & objectives: The coronavirus type 2 SARS-CoV-2 continues to spread, affecting the health and lives of millions of people around the world. In persons with concomitant diseases, it progresses to pneumonia, acute respiratory distress syndrome, and multiple organ failure.
Methods: We present 2 clinical cases of COVID-19 infection associated with pulmonary sarcoidosis and coronary artery disease in patients aged 44 and 63 years. Both patients were not connected to Intermittent forced ventilation apparatus. A histopathological and immunohistochemical study of tissue samples of the lungs and heart was carried out.
Results: Histological examination of lung samples shows: totally desquamated epithelium, haemorrhagic exudate, and a few multinucleated cells were determined in the lumen of all alveoli. During histological examination, epithelioid-cellular granulomas ranging in size 2-8 mm, consisting of epithelioid, giant cells and lymphocytes, were located in the lungs. Granulomas with a proliferative component, with signs of coagulation necrosis and with areas of haemorrhage were determined. Revealed giant cells with cytoplasmic inclusions - asteroid bodies and Schaumann's little bodies. In the immunohistochemical study, lymphocytes were detected in the central sections of the granulomas CD-4, and CD-8 lymphocytes were found in the peripheral zone. In bifurcated lymph nodes 17-24 mm, granulomas were detected.
Conclusion: Pulmonary sarcoidosis and coronary heart disease have aggravated the course of bilateral viral pneumonia when infected with the new coronavirus infection Covid-19. Comorbidities in Covid-19 patients reduce the chances of recovery.

E-PS-01-010
Rare clinical case: coronavirus infection and dissecting aortic aneurysm
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Background & objectives: Analysis of patient mortality data from COVID-19 showed that the most common comorbidity is arterial hypertension. There have been reports of a significantly higher risk of adverse outcomes in this group of patients.
Methods: An analysis of the pathological material of a man who died from COVID-19 pneumonia associated with dissecting aortic aneurysm against the background of arterial hypertension is presented. Histological structures of the lungs, aortic walls were examined with haematoxylin-eosin and immunohistochemical methods.
Results: Macroscopically, on the posterior wall of the aorta, an atherosclerotic plaque in the stage of atheromatosis and calcification with ulceration was determined, measuring 1.5x1x0.5 cm, at the border of the plaque there was a stellate defect of the 1.1 cm wall with uneven edges, the gap led to the wall of the aorta and the thickness of the pericardium. T. intima is yellow with more than 50% of the aortic area affected by atherosclerotic plaques in the fibrosis stage. An immunohistochemical study of elastin showed pronounced fragmentation of elastic fibres. Inflammatory infiltrate in the area of t. adventicii aorta and vasa vasorum consisted of CD3, CD20, and CD68.
Conclusion: It is known that vasa vasorum macrophages, T-lymphocytes and endotheliocytes are of great importance in the formation of aneurysms. Thus, the main cause of death was a dissecting aortic aneurysm according to Stanford - type A, according to DeBakey - type II. The associated viral pneumonia aggravated the course of the disease and affected the death.

E-PS-01-011

Pericardial effusion leading to cardiac tamponade secondary to Graft-versus-Host Disease. Autopsy findings

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Background & objectives: Pericardial Effusion is a rare cardiac complication (occurring in 1% of patients)[1] described in patients undergoing Allogeneic Hematopoietic Stem Cell Transplant[2]. This complication is considered to be a manifestation of chronic Graft-versus-host disease[1], which may contribute to significant post-transplant morbidity.
Methods: The patient was a 36-year-old woman who presented to Hodgkin's Lymphoma in 2018, Nodular Sclerosis variant. After 5 cycles of chemotherapy without response, undergoes allogenic transplantation. Four months later, the patient is diagnosed by Graft versus Host Disease. In 2020, two days before admission, the patient began with disuria, haematuria and abdominal pain. At 24 hours after admission, hypertransaminasemia and decreased conscience level. The patient died 4 days after admission.
Results: Gross examination during autopsy revealed 200ml of clear serous fluid from the pericardium. The peritoneal surfaces were smooth and shiny. On microscopic examination revealed skin: histomorphological alterations compatible with graft-versus-host-disease(GVHD)grade II. Lung: Marked vascular congestión with intraalveolar hematic extravasation. Pericardium: reactive mesotelial cells and lymphocytic inflammatory infiltrate. Spleen: Intraparenchymal haemorrhage. COVID-19, Blood cultivation and cerebrospinal fluid were studied with negative results.
Conclusion: It is unlikely that an infection or drug toxicity had a role in the development of pericardial effusion. In this patient the median time to post-transplant pericardial effusion development was 2 years where the serosa and the skin were the only site of GVHD exacerbation without involvement of other organs. It's possible that the inflammatory process involving the pericardium was caused by immune-mediated mechanisms most likely associated with GVHD but no direct evidence exists to prove pericardial effusion were a manifestation of GVHD.

E-PS-01-012

A case report of giant-cell myocarditis diagnosed on autopsy

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Background & objectives: Giant-cell myocarditis is an unusual cause of death which often presents as rapidly evolving congestive heart failure. Histologic findings include myocardial necrosis, multinucleated giant cells, and mixed inflammatory cell-infiltrate. A case report of giant-cell myocarditis diagnosed on autopsy presents briefly.
Methods: A 68-year-old man who lived alone, with tablet-treated hypertension, was found dead at home after not having contact with his relatives for a few days. Circumstances of death raised no suspicion of crime, abuse, or suicide. Clinical autopsy was conducted to determine the cause of death.
Results: External body inspection revealed no injuries or scars. The findings of internal organs examination were the following: heart with symmetrical hypertrophy, weight 540gr. Small isolated whitish areas frontal and lateral in the right ventricle. Mild but not critical coronary atherosclerosis only focally. Regarding the other organs, mild pulmonary oedema, a few simple kidneys cysts, enlarged prostate without tumour and generalized moderate atherosclerosis were noticed. Microscopic examination revealed myocardium hypertrophy, perivascular fibrosis and focal myofiber break-up. Foci with fibrosis, sparse mixed inflammatory cells, and necrotic myocardial fibres with multinucleated giant cells were found. No vasculitis, no foreign material, and no evidence for systematic granulomatous or other inflammation or sarcoidosis were described.
Conclusion: Histological findings of heart described above gave rise to suspicion of giant-cell myocarditis, an unusual cause of death. The aetiology is unclear, idiopathic, drug-associated, or viral cause have been described. Multinucleated giant-cell formation can also occur rarely in myocardial infarction. Desmin immunostaining is then positive in the multinucleated giant-cells supporting multinuclear myogenic giant cell formation under myocardial infraction. In this case myocardial infraction considered less likely due to the absence of critical stenos in coronary arteries.

E-PS-01-013

Fatal invasive fungal infection 21 days after renal transplant: a case report

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Background & objectives: To report a case of fatal invasive fungal infection 21 days after renal transplant.
Methods: Review of autopsy report and medical record. The case was analysed both macroscopically and microscopically. The specimens were submitted to formalin fixation and all the histological processing. The stains used for the microscopic evaluation of this case were haematoxylin-eosin and Grocott-Gomori methanamine silver.
Results: Female, 58-year-old, with chronic kidney failure, interned for kidney transplantation, which occurred without complications. Immunosuppression was made with tacrolimus, mycophenolate and prednisone. On the thirteenth postoperative day, she presented dyspnoea and progressed to cardiorespiratory arrest. In the intensive care unit, there was no clinical improvement and she died 21 days after transplant. During the autopsy, native kidneys were markedly atrophic and irregular, while renal graft had usual macroscopic appearance. It was also observed lung congestion and oedema. Microscopic evaluation showed extensive areas of necrosis of lung parenchyma. Candida albicans were observed in the form of yeasts and hyphae at the oesophagus and lungs. There was a phenomenon of angioinvasion.
Conclusion: Approximately 5% of infections in renal transplant patients are caused by fungi. Candida, Aspergillus, Mucorales and Cryptococcus species are the most-common opportunistic fungi that causes infection. The most unusual and unexpected fact of this case is the time between kidney transplantation and infection. The data found in the literature indicate an average period for such an event which varies from 103 days to 18.35 months. On average, the gap between infection and an outcome (recovery/death/graft loss), is approximately 2 months.

E-PS-01-014

Two autopsy cases of HIV-negative Kaposi's sarcoma

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Background & objectives: Kaposi's sarcoma is a malignant vascular tumour which affecting elderly patients. This tumour is associated with herpes simplex virus type 8 and immunodeficiency (HIV). But sporadic HIV negative forms exist. We present two autopsies of patients with HIV-negative Kaposi's sarcoma.
Methods: Two autopsies of patients with HIV-negative Kaposi's sarcoma were performed. IHC studies were carried out with CD31, CD34, HHV-8 markers.
Results: Patient X attended to hospital with complaints of weakness and dyspnoea, later the patient died from pulmonary oedema. Autopsy results: hepatomegaly with multiple tumour formations, and large lymph nodes. Histological examination showed chaotic proliferation of spindle-cells around the newly formed blood vessels. IHC study showed diffuse expression of CD34, CD31 and focal granular staining of HHV-8.
Patient Y has been treated in a hospital for prostate cancer (Gleason 3 + 3 = 6), which became a cause of his death. Autopsy revealed tumour of the

toe of the left foot. Histological examination showed the proliferation of spindle-cells around young vessels. The IHC study was identical to the 1st case.
Conclusion: HIV-negative Kaposi's sarcomas are sporadically rare tumours that represent medical and social problems, which imply the importance of choosing a treatment strategy for patients with this disease. These 2 cases expand our understanding of these tumours, and also give hope for adequate diagnosis and treatment of these groups of patients.

E-PS-01-015
Covid-19 and visceral candidiasis mixed infection associated with Hodgkin's lymphoma
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Background & objectives: COVID-19 is a new coronavirus infection that is now worldwide. This disease is especially dangerous for the elderly and people with immunodeficiencies, including cancer patients. We present a case of mixed covid 19 infection and visceral candidiasis associated with Hodgkin's lymphoma.
Methods: An autopsy of patient with Covid-19 and visceral candidiasis associated with generalized Hodgkin's lymphoma were performed. IHC studies were carried out with CD20, CD30, CD45 markers.
Results: Patient X attended to hospital with complaints of weakness and dyspnoea, later the patient died from necrotic enterocolitis. Autopsy showed hepatomegaly, interstitial pneumonia, small subepithelial haemorrhages with white foci in the oesophagus. Necrotizing enterocolitis has also been observed.
Histological examination showed diffuse alveolar damage with peripheral candida-granulomas, diffuse liver infiltration with atypical lymphocytes, including Reed-Sternberg cells and Hodgkin cells, and candida-granulomas. In the oesophagus, superficial candidiasis is presented. There is necrotizing enterocolitis in the colon. There is also a lymphoid infiltrate of atypical cells, including Reed-Strenberg cells and Hodgkin cells In the lymph nodes.
IHC study was carried out. Positive expression of CD20, CD30 and CD45 markers was observed.
Conclusion: Covid19-associated mixed infections are of increased interest due to the novelty and prevalence of the disease. Patients with cancer require special attention to prevent adverse outcomes and improve treatment success.

E-PS-02 | Breast Pathology E-Posters

E-PS-02-001
Bilateral breast cancer; a five-year histopathological review of a rare entity in a resource limited setting
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Background & objectives: Bilateral breast cancer (BBC) can be synchronous and metachronous. It accounts for 2-6% of breast cancers. Before establishing BBC, metastatic carcinoma to the contralateral breast must be ruled out. We review five cases of BBC over a five-year period (2016-2020).
Methods: Five cases of BBC were retrieved from our archives. Information was extracted from the patient's case notes. Paraffin blocks were cut and stained with routine H&E stain. Four immunohistochemical markers were used (ER, PR, Her2 and E-cadherin). Data was analysed using SPSS version 24.
Results: The age range of patients with BBC was 45-65 years with a mean age of 55.6±8.2. Three cases were synchronous while two were metachronous base on duration of symptoms before diagnosis. Histology of both breasts showed only two patients with BBC had the same histology of invasive lobular carcinoma in both breast while, the remaining three had invasive ductal histology NOS in one breast and apocrine or neuroendocrine differentiation in the other breast. Hormonal profile was variable. Two patients had triple negative hormonal profile while two were Her2 positive with a single case of ER positivity. Metastasis to the axillary lymph node was seen in two patients.
Conclusion: BBC is rare in our setting, although it is difficult to rule out local metastasis to the contralateral breast in some cases, those with local or metastatic disease are at a higher risk of having metastatic disease. Genomic studies are needed in such cases since BBC are genetically likely to be non-identical.

E-PS-02-002
Encapsulated papillary carcinoma with axillary lymph node macrometastasis, diagnosed after COVID-19 vaccination
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Background & objectives: Encapsulated papillary carcinoma (EPC) of the breast is a rare entity accounting for 0.5 to 1% of all breast carcinomas. We report the case of a 66-year-old woman diagnosed with an EPC with axillary lymph node macrometastasis, post COVID-19 vaccination.
Methods: The patient was vaccinated in February 2021. The next day after the vaccination, she complained about pain in the left breast. The mammogram and CT showed a breast lesion classified as BI-RADS 4c, and an enlarged axillary lymph node. The patient underwent biopsy and lymph node FNA, both positive for malignancy, followed by radical mastectomy with axillary dissection.
Results: Gross examination showed a 9x6 cm mass consisting of aggregated nodules, displaying cystic spaces. Histologically, the tumour was composed of papillary structures, lined by a low-grade monomorphic population of neoplastic cells and scant mitotic figures, surrounded by a thick fibrous capsule. Myoepithelial cell lining was absent (confirmed by p63 and SMA). Tumour cells were positive for ER, PR, while negative for Her-2/neu. The ki67 index was 10%. One of 23 lymph nodes showed a macrometastasis. The morphological and immunohistochemical features were compatible with EPC (with no areas of conventional invasion), Oncotype DX showed 0 recurrence score and no chemotherapy benefit. On follow-up, the patient is disease-free to date (3 months).
Conclusion: EPC is usually characterized by slow growth and good prognosis. However, the indolent behaviour impairs early detection, and in the absence of noticeable symptoms, for the present case, the COVID-19 vaccine enabled uncovering the tumour. Notable features of the case include the large size, multinodular appearance of the tumour, and axillary lymph node metastasis. Tumour's overall management is adequate local therapy, but for high-grade lesions, triple-negative or HER2-positive phenotype, the management is similar to invasive tumours.

E-PS-02-003
Breast hamartoma in a young male patient, accompanying vascular and adipose tissue lesions
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Background & objectives: Hamartoma is a benign tumour of the breast, formed from all components of breast tissue. There have been less than 5 cases in men reported up to now. Gynecomastia may obscure this condition in men, and hamartomas could be overlooked.
Methods: A 21-year-old man consulted general surgery clinic with the complaint of gynecomastia. Bilateral breast reduction was applied. Histology of the biopsies revealed vascular lesions consistent with arteriovenous malformation, nerves and Pacinian corpuscles, accompanied by fibrous stromal and adipose tissue. Pseudoangiomatous stromal

hyperplasia was also present. Around the lesion, congested vascular structures were seen in groups of adipocytes.
Results: Histomorphologic evidences were interpreted as hamartoma with arteriovenous malformation and angiolipoma in both specimens.
In this case, the existence of bilateral hamartoma with arteriovenous malformation accompanying brought angiolipoma Cowden syndrome to our mind. Most of them are sporadic, but multiple hamartomas can be seen in Cowden syndrome as well. Cowden syndrome, (a. k. a.) PTEN hamartoma tumour syndrome (PHTS), is a group of disorders with autosomal dominant inheritance caused by PTEN germline mutation of the PTEN gene. It is characterized by multiple hamartomas and a predisposition to cancer such as breast, thyroid, renal cell and colon cancers.
Conclusion: Hamartoma is a benign tumour which has an excellent prognosis. However, it can indicate a high cancer risk especially for the patients having multiple hamartomas.

E-PS-02-004
A case report on metastatic ileal neuroendocrine tumour to the breast mimicking primary mammary carcinoma
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Background & objectives: Metastases from extramammary tumours to breast are rare and metastatic neuroendocrine neoplasms to breast account for approximately 1% of all metastatic breast neoplasms. These may be misdiagnosed as triple negative primary breast cancers if there is no relevant clinical history.
Methods: Case: We present an unusual case of a 72-year-old female patient with an 11mm mammography-detected lesion in the right breast (R4 U4). There was no additional background history was given. The core biopsies were sent for histology.
Results: Histological investigation revealed a malignant epithelial neoplasm with acinar and cribriform architecture and neuroendocrine morphology. There was no in-situ component and there was no lymphovascular invasion. Molecular markers (ER, PR and Her2) were all negative. An additional panel of immunostains revealed positive neuroendocrine markers (CD56, Chromogranin, and Synaptophysin) and positivity for the hindgut marker CDX2. The tumour cells were entirely negative for GATA3, TTF-1, CK7, and CK20. Further exploration of the patient's clinical history at the breast MDT revealed a previous sigmoid adenocarcinoma in 2006 and a history of ileal carcinoid tumour in 2012. The appearances were considered most in-keeping with metastatic ileal neuroendocrine neoplasm to the breast.
Conclusion: The take-home messages from this case were: To rule out breast metastasis to breast in triple negative carcinomas that arise in the breast but have no accompanying in-situ component. To explore the clinical history more fully and discuss at breast Multi-Disciplinary Team meeting. To use an appropriate panel of immunostains to clarify the diagnosis. Identifying metastatic tumours to breast on core biopsy is crucial for the subsequent management and avoiding unnecessary surgery.

E-PS-02-005
The role of immunohistochemistry in the diagnosis of lymphocytoma cutis in the breast – a rare and challenging entity
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Background & objectives: Lymphocytoma cutis (cutaneous lymphoid hyperplasia/cutaneous pseudolymphoma) is a rare disease which affect the dermis. Breast localization of this lesion is an extremely rare event and rise difficulties in established a correct diagnosis since its morphological features resemble with cutaneous lymphoma
Methods: We report a rare case of lymphocytoma cutis in the left upper-outer quadrant of breast, in a 7th decade woman. The patient presented with a poorly defined nodular lesion and with a BI-RADS score of 4 on radiologic evaluation. Tumorectomy was performed and surgical specimen was evaluated by morphological immunohistochemical characteristics. Immunohistochemistry was performed with a panel of seven antibodies.
Results: Morphologically, the tumour was composed by a lymphoid proliferation within the dermis of the skin and extended into the breast parenchyma and no involvement of the epidermis. There was a nodular, follicular pattern with polarized germinal centres. Immunohistochemistry was performed mainly to ruled out a low-grade cutaneous B-cell lymphoma diagnosis. Immunohistochemistry highlighted a B-cell lymphoid proliferation, a specific immunostaining for a normal germinal centre (CD20+, CD5-, CD10+, BCL6+, BCL2-) and a positive reaction for CD23, which highlighted the meshwork of follicular dendritic cells. It was also observed a population of reactive T lymphocytes and a normal pattern of KI67 expression. These immunoreactions established the diagnosis of follicular pseudolymphoma.
Conclusion: A diagnosis of lymphocytoma cutis or pseudolymphoma of Spiegler–Fendt in the breast is a difficult one that raises challenges in establishing a correct diagnosis, but immunohistochemistry is a major help and mandatory for excluding a malignant lymphoid proliferation. Its treatment consists mainly in surgical removal of the lesion and it has a favourable clinical evolution.

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E-PS-02-006
Metaplastic carcinoma: a study of 7 cases
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Background & objectives: Metaplastic carcinoma of the breast is a heterogeneous group of breast carcinoma characterized by squamous differentiation or mesenchymal looking elements, including spindle, chondroid and osseous cells. The aim of our study is to highlight the clinicopathological characteristics of MC.
Methods: We report a retrospective study of 7 cases of metaplastic carcinoma of the breast, over a period of 2015 and 2020, obtained from files of Pathology Department of Farhat Hached University Hospital, Sousse, Tunisia.
Results: The average age of patients was 49.2 years. The mean size of tumours was 4.56 cm with extremities ranged between 2.2 and 11 cm. There were 5 cases with squamous component, one case with chondroid component and one case with squamous, chondroid and osseous components. There were 4 cases of luminal B type. 4 tumours were classified as stage I and 2 were stage III.
Conclusion: Metaplastic carcinoma of the breast is a rare and aggressive tumour that occurs in 0.2% to 1% of all breast carcinomas. It affects females over 50 years. It is composed of a mixed group of neoplasms containing both glandular and non-glandular patterns with epithelial and/or mesenchymal components. Metaplastic carcinoma carries a poor prognosis with a low rate of axillary involvement and high potential for distant metastases.

E-PS-02-007
Ki67 in breast carcinoma: Relationship with other prognostic factors
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Background & objectives: Ki-67 in breast carcinoma is a biomarker that was demonstrated to be beneficial in determining the tumour behaviour including tumour size, stage, grading and patient survival. We aim to investigate to correlation between Ki-67 and the other prognostic factors in breast carcinoma (BC).
Methods: This retrospective study included all cases of invasive breast carcinoma diagnosed in the Pathology department of Habib Thameur Hospital between 2016 and 2020.All histopathology reports reviewed for data regarding age, tumour size, histological type, glandular differentiation, nuclear pelomorphism, mitotic count, SBR grade, tumour and lymph node stage, lymphovascular and perineural invasion, oestrogen, progesterone and HER2 status, and molecular classification.
Results: A total of 60 women was included. The average age was 52 ±13.28 years. The mean tumour size was 3.63 ±2.38 cm. We diagnosed 45 invasive BC of no specific type,9 lobular carcinomas, 6mixed carcinomas ductal and lobular and one papillary carcinoma. Ki67 was ≥20% in 34 cases (33.01%). The molecular status was luminal A in 19 patients, luminal B in 29 patients, HER2 in 6 patients and triple negative in 6 patients. A statistically significant association was revealed between ki67 index and SBR grade (p=0.004), mitotic count (p=0.04), perineural invasion (p=0.075), oestrogen status (p=0,036), progesterone status (p=0,037), HER2 status (p=0,039) and molecular classification($p<0.001$).
Conclusion: This single institution study showed that high expression of Ki-67 is associated with higher pT-stage, higher pN-stage, higher grade, lymphovascular invasion, ER/PR negativity, HER2 positivity and molecular classification. ThusKi67 index is a valuable biomarker of breast carcinoma. Its correct assessment is required for an optimal treatment. The prognostic impact of Ki-67 was only demonstrated for Disease Free Survival and longer follow-up time may be required to see its effect on survival outcome.

E-PS-02-008
Acinic cell carcinoma of the breast: a case report of a rare triple negative breast cancer with unusual clinical course
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Background & objectives: Acinic cell carcinoma (ACC) is an exceptionally rare triple negative breast cancer (TNBC). It shares morphological and immunohistochemical similarities with the counterpart tumour of the salivary gland, although molecular studies have shown that they probably constitute unrelated diseases.
Methods: A 37-year-old woman presented with a palpable breast lump. She had no previous history of malignancy. Ultrasonography showed three superficial hyperechoic heterogeneous nodules together spanning 40mm in the upper outer quadrant, U3. Following two needle core biopsies, mammography and MRI investigations, she proceeded to mastectomy with sentinel node biopsy.
Results: Histology showed an infiltrative neoplasm composed of tightly packed acini containing luminal secretions lined by atypical epithelial cells, with mitotic activity and eosinophilic granular cytoplasm. Atypical microglandular adenosis (MGA)-like areas were seen at the periphery of the neoplasm. The tumour was triple negative. The tumour was GATA-3, S100, SOX10, and lysozyme, alpha1 antitrypsin positive, with PASD positive cytoplasmic granules. Molecular analysis, including NTRK immunohistochemistry and RT-PCR for IDH1, IDH2 and PIK3CA were performed to exclude secretory carcinoma and tall cell carcinoma with reversed polarity, respectively.
Three months following the first biopsy the patient developed a chest wall recurrence and underwent a further wide local excision and axillary node sampling.
Conclusion: ACC is an exceedingly rare type of low grade TNBC that is generally associated with indolent behaviour. This case, however, showed an unusual clinical outcome with early recurrence.
The association with atypical microglandular adenosis is interesting as both lesions have been found to share similar molecular abnormalities, which supports their clonal relationship. Molecular testing can help establish the diagnosis of this challenging entity and differentiate from mimics particularly secretory carcinoma and tall cell carcinoma with reversed polarity.

E-PS-02-009
Breast carcinoma in a male with type 1 neurofibromatosis
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Background & objectives: Neurofibromatosis type 1 is an autosomal dominant disorder characterized by the appearance of cafe au lait spots, neurofibromas and Lisch nodules and it is associated with increased risk for several neural and non-neural malignancies, as breast carcinomas.
Methods: We present the case of a 55-year-old male with type 1 neurofibromatosis, with multiple resections of neurofibromas in skin and in spinal cord. This patient had a bleeding lesion in right nipple that was removed and sent to our department. We received fragments of breast tissue with skin ulcerated and under that, a white and solid lesion.
Results: Histologically, we saw a malignant neoplasm poorly differentiated with solid, tubular and ductal patterns, that ulcerated the skin surface and had vascular and perineural invasion, with a high mitotic index (25 mitosis/HPF) and high nuclear pleomorphism.
Immunohistochemically, the neoplasm was positive intense and diffuse for EMA, CK19, GATA3 and oestrogen receptors, focally for p40, p63, GCDFP-15, CEA and progesterone receptors and negative for CK7, CK20, CK5/6, D2-40, S100, CDX2, TTF1 and synapofisine, with a Ki67 index of 70 %. So, we diagnosed that neoplasm as a poorly differentiated breast carcinoma G3 with images of cribiform ductal carcinoma in situ grade II, without necrosis.
Conclusion: The link between NF1 and breast cancer has recently been established, with patients with NF1 being at higher risk for developing breast cancer, more likely to get breast cancer at a younger age, and more likely to have their breast cancer present with more adverse prognostic factors.
The concurrent presentation of type 1 neurofibromatosis and male breast cancer is a very rare phenomenon with only a handful of case descriptions in the literature.

E-PS-02-010
Fibroepithelial lesions of the breast: are we up to the challenge? A case report
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Background & objectives: Fibroepithelial lesions of the breast are a heterogeneous group of biphasic tumours that include the common benign fibroadenomas and the relatively rare phyllodes tumours (PT). They have a wide prognostic variability, being their management based upon histological diagnosis and classification.
Methods: A 46-year-old woman presented in mid-2019 with a palpable breast mass felt for over one year. She underwent radiological investigation that revealed a heterogeneous, polylobulated mass, with 6.7x4.5cm. A core needle biopsy was performed. It showed a fibroadenoma with pericanalicular pattern. She was lost to follow-up, reappearing in 2021 with an ulcerated extensive lesion occupying the totality of the breast.

Results: Grossly, the mastectomy specimen measured 20x13x6cm and weighted 1028g. The cut surface revealed a well-circumscribed multinodular solid grey tumour, with necrotic foci. It measured 12x12x8cm and was coincidental with the superficial, superior and internal margins. Microscopically, it presented as a biphasic proliferation, with epithelial and stromal components, with a leaf-like pattern and clefts, and benign chondroid heterologous elements. It had expansive growth, with mild-to-moderate nuclear atypia and 10 mitoses/10 High Power Fields. Stromal overgrowth was not identified. These histological parameters defined the lesion as a borderline PT (according to Breast Tumours WHO 5th edition - 2019).
Conclusion: We highlight the challenge in distinguishing between a PT and fibroadenoma. Although clear diagnostic criteria are established, their morphological similarities result in significant inter-observer variability, as reported in recent studies. Moreover, the inherent limitations of core biopsies specimens' favours surgical excision as the preferred procedure, as it allows negative margins to be obtained in the event that the final diagnosis is a PT, as margin status at excision is the most reliable predictor of recurrence. A close follow-up is mandatory.

E-PS-02-011
The problematic diagnosis of metastatic dyscohesive cell lesions: incidental finding in cholecystectomy specimen
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Background & objectives: Metastatic breast carcinoma in the gallbladder is an infrequent occurrence, strongly associated with the lobular type. Our purpose is to gain further knowledge about this phenomenon and dyscohesive cell tumours, emphasizing the importance of immunohistochemical staining for an accurate diagnosis.
Methods: The Department of Pathology received a cholecystectomy specimen, samples from which were fixed with 10% buffered formalin and were processed by conventional histopathological methods, using paraffin embedding, sectioning and Haematoxylin–Eosin (HE) staining. Afterwards, the sections were deparaffinized and prepared for immunohistochemical staining, the following markers having been used: Ki 67, PR, ER and HER2.
Results: We present a 65 years-old female with no significant medical history who presented with biliary dyskinesia for which she underwent a cholecystectomy. Gross examination revealed no particular aspects. The microscopic examination identified multiple small dyscohesive cells displaying a targetoid pattern in the muscular and serous layers. The aforementioned cells exhibited high N/C ratio, basophilic nuclei with moderate nuclear pleomorphism, visible nucleoli, eosinophilic cytoplasm, which could easily have been misinterpreted as chronic inflammatory infiltrate on a low power field. The immunohistochemical staining revealed positive oestrogen and progesterone receptors markers, negative HER2 and Ki67 positive in 16% of the malignant cell population. Thus, the diagnosis of metastatic lobular breast carcinoma was established.
Conclusion: Dyscohesive cell carcinomas seldom metastasize in the gallbladder, the most frequent metastatic cholecystic tumour being represented by the malignant melanoma. However, breast carcinoma, especially the lobular histological type, may be associated with such clinical events. Given the dyscohesive character of the cells in such lesions, we emphasize the importance of immunohistochemical staining, as well as the necessity of clinical and imaging data in the differential diagnosis with poorly cohesive gastric carcinoma.

E-PS-02-012
Metaplastic breast carcinoma with extensive chondrosarcomatous differentiation
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Background & objectives: Metaplastic carcinomas are aggressive heterogeneous groups of tumours characterized by a biphasic proliferation of adenocarcinoma with dominant areas of spindle cell, squamous, or mesenchymal differentiation. Metaplastic breast carcinoma is very rare, and metaplastic carcinoma with chondrosarcomatous differentiation is even rarer
Methods: In primary breast tumours, chondrosarcomatous lesions may occur in three different forms: a pure extra skeletal chondrosarcoma, as a heterologous component of a malignant phyllodes tumour or as a chondrosarcomatous differentiation in a metaplastic carcinoma. In rare cases, part or all of the carcinomatous epithelium is transformed into a nonglandular mesenchymal tissue.
Results: We report a case of a 67-year-old woman with metaplastic carcinoma with extensive chondrosarcomatous component that was challenging to diagnose. The tumour was characterized by major chondromyxoid matrix with few areas suggestive for peculiar osteosarcomatous differentiation. The area of classic high grade invasive ductal carcinoma was minimal. Tumour cells in the chondrosarcomatous areas were diffusely immunoreactive for S-100 protein, negative for cytokeratin and epithelial membrane antigen. Tumour cells in carcinomatous areas were diffusely positive for cytokeratin, had patchy S-100 expression and were triple negative for prognostic markers (ER, PR and Her2/neu). In both areas, tumour cells were negative for smooth muscle actin and CD34, while p53 was overexpressed.
Conclusion: Postoperatively, the patient received 6 cycles of chemotherapy and external radiation therapy. The patient was doing well at the 7-month postoperative follow-up, without evidence of tumour recurrence or metastasis.
We emphasize that careful and extensive sampling is mandatory when dealing with breast tumours with chondroid differentiation. Immunohistochemistry is essential. Immunomarkers such as cytokeratin, S100 and SMA are most helpful to differentiate metaplastic carcinoma from malignant phyllodes tumour and other primary sarcoma of the breast.

E-PS-02-013
Adenoid cystic carcinoma of the breast. A case report and literature review
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Background & objectives: Adenoid cystic carcinomas (ACCs) are malignant epithelial tumours that more often occur in salivary glands. Primary ACC of the breast occurs rarely, accounting for 0.06% of ACC cases. We report a case of mammary ACC.
Methods: A 59-year-old female patient presented with a painful right breast swelling. Ultrasonography and mammography showed a 13cm mass. FNA was positive and a total mastectomy was performed. The dissection of the right breast specimen revealed a 13cm multilobular mass below the nipple with a greyish white cut surface, resulting in partial ulceration of the nipple area.
Results: Histopathological examination revealed a tumour consisting of nests of cells with well-formed ducts and tubules, lined by inner epithelial and outer myoepithelial cell layer and pseudolumens filled with basophilic stromal matrix material, PAS- diastase resistant. Immunohistochemical stains were positive for CK7, c-kit regarding the epithelial component and positive for CK14, p63, calponin, CD10 regarding the myoepithelial cells. The Ki67 mitotic index was 5%. ER, PR and HER2 were negative. The morphological and immunohistochemical results established the diagnosis of ACC.
Conclusion: ACC is an unusual type of breast carcinoma accounting for <0.1% of breast malignancies. It is characterized by a biphasic population

of luminal and basaloid cells with pseudolumens filled with basement membrane material. The mean age at diagnosis is 66 years. Almost all cases are classified as triple-negative tumours. Nodal metastases are uncommon. The prognosis is excellent in contrast to the aggressive nature of the counterpart salivary gland tumours.

E-PS-02-014

Invasive Paget disease in young patient: a rare case report

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Background & objectives: Mammary Paget disease (MPD) is a well-known clinical and pathological neoplastic entity in the nipple. This disease may be associated with in-situ or invasive breast carcinoma. Invasion of mammary Paget cells into the dermis is extremely rare.
Methods: A 29-year-old woman patient presented with ulcerative and crusted changes of the nipple. Punch biopsy diagnosis was MPD. The patient underwent breast-sparing including the nipple-areola complex and sentinel lymph node biopsy.
Results: On histopathologic evaluation, scattered large tumour cells with abundant cytoplasm in the epidermis. These tumour cells had large nuclei and prominent nucleoli. The invasive areas had an identical feature to the intraepidermal tumour cells. The depth of Paget cell invasion was 4 mm. Some of the underlying lactiferous ducts showed ductal carcinoma in situ (DCIS) of solid type, with high-grade nuclei, central necrosis. MPD, invasive MPD and DCIS were negative for both oestrogen receptors and progesterone receptors and showed diffusely strong membranous immunoreactivity for HER2. There was no myoepithelial cell around the dermal tumour cells by three myoepithelial markers. Histomorphological and immunohistochemical findings were suggestive for invasive MPD + high grade DCIS.
Conclusion: Invasion of MPD tumour cells into the dermis is rare. A small number of patients have been previously reported with this entity. The clinical significance of this entity is unknown, and further studies are required.

E-PS-02-015

Adenoid cystic carcinoma, solid type with basaloid features. Case report

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Background & objectives: Adenoid cystic carcinoma (ACC) is a rare malignant tumour in the breast that constitutes less than 0,1 % of all breast cancer. It is a triple-negative breast cancer with favourable prognosis. We will report a case of breast ACC.
Methods: A 51-year-old woman, with no medical complaints, underwent a diagnostic ultrasound scan in which a hypoechoic mass of oval morphology, lobulated borders and hyperechogenic halo was detected in the internal interquadrants and superointernal quadrant of the right breast measuring 79 x 61.7 mm. The finding was highly suspicious of malignancy, so it was decided to perform a biopsy.
Results: Several cylinders of breast tissue with a solid neoplastic proliferation composed of large trabeculae and nests of basaloid cells with hyperchromatic nuclei and moderate cellular pleomorphism, frequent mitoses and a high proliferative index (30%) were observed. The cell nests are arranged in a focally myxoid stroma with areas of hyalinized stroma with spaces resembling reduplicated basement membrane material. No duct formation or microcystic spaces are detected and focally there are areas with a predominance of cells with clear cytoplasm. Immunohistochemical study of the lesion shows expression for cytokeratin 7 and p53, being focally positive for c-kit and p63. It does not show staining for CD56, HER2, oestrogen and progesterone receptors.
Conclusion: The diagnosis is adenoid cystic carcinoma, solid type with basaloid features. It is characterized by solid nests composed of basaloid cells, with marked nuclear atypia, high mitotic count, and necrosis. Axillary node metastases and perineural invasion can be observed. Differential diagnosis should be made with small cell neuroendocrine carcinoma and carcinomas with basaloid morphology. Negativity for neuroendocrine markers can be useful in order to exclude neuroendocrine carcinoma.

E-PS-02-016

Pure mucinous breast carcinoma in late twenties female: two case reports

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Background & objectives: Mucinous carcinoma is a rare variant among invasive breast carcinomas, representing 2% of them. These tumours mainly present in post-menopausal women. Only 1% present in women age less than 30 years.
Methods: We report two cases of mucinous carcinoma in a 29-year-old and a 26-year- old woman.
Results: Case 1 was a 29-year-old woman presented with a well-circumscribed, slow-growing right breast mass for six months. Ultrasonographic analysis showed a well-defined hypoechoic mass. Histologically, the tumour was pure mucinous carcinoma with micropapillary features. The tumours were positive for hormonal receptors and negative for HER-2. She was treated with surgical resection, then hormonal and radiation therapy. Case 2 was a 26-year-old woman who presented with right breast pain. Physical examination revealed dense breast tissue without any palpable mass. Mammography of the right breast showed amorphous and coarse heterogenous microcalcification (BIRADS 4B). Histology findings showed two mucinous carcinomas and one invasive ductal carcinoma. She moved to another hospital for further treatment.
Conclusion: Mucinous carcinomas frequently occur in post-menopausal women. Only a few cases reported this variant in women younger than 30 years old. Differential diagnoses from clinical findings and imaging analysis may include benign breast lesions, especially in young women. Due to slow progression with relatively benign clinical courses, clinicians and pathologists need to be aware of this rare entity.

E-PS-02-017

Economic evaluation of breast cancer pathology tests at an Algerian pathology department

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Background & objectives: Breast cancer is the most common in women in Algiers cancer registry (79 cases /100,000 / year), 1383 cases expected / year. Aim of this study is to assess the cost of pathology test at Douera university hospital in 2016.
Methods: 150 samples sent to our pathology department from 1st January to 31st December 2016, divided into 128 biopsies, 6 lumpectomies and 26 mastectomies
The evaluation, per patient, of the costs of pathological tests: Hematein Eosin stain, Immunohistochemistry (IHC) and in situ hybridization (ISH), was carried out on the basis of the prices for the year2016.
Results: 140 invasive carcinoma NOS (CI NOS) and 10 lobular carcinoma (CLI) were diagnosed out of 1383 cases expected at Algiers (11% of expected cases)
The total cost for CLI was 178 to 298 euros/ case and that of CI NOS 152.5 to 272.5 euros
The annual needs in our department for this pathology are estimated to 18,700 euros, i.e. 5% of the annual budget allocated for 1.66% of patients.

The real needs for ISH at Algiers would be 180-200 tests / year to be distributed among the 3-4 structures with ISH unit, which would represent 10 to 12% of the annual budget for < 2% of patients.
Conclusion: The increase in the incidence of breast cancer in Algeria requires efforts in terms of equipment and reagents in order to be able to meet the growing demand from clinicians and patients to offer the best chances of care to our patients.
Economic evaluation of pathology tests must be done to anticipate the future healthcare needs of our population. The increase incidence in the coming years could lead to an overload of the capacities of public services.

E-PS-02-018
Neuroendocrine tumour of the breast with extensive lymphatic and vascular infiltration
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Background & objectives: Recently, we reported an unusual case with hematogenous metastases due to a massive tumour embolus from a mammary neuroendocrine tumour. Herein, we describe, to our knowledge, the first case of an NE neoplasm with extraordinary intra-lymphatic embolization in the breast.
Methods: The patient, a 46-year-old premenopausal woman, presented with a painful mass in the upper outer quadrant of the left breast. There was no medical or familial history of breast disease. Ultrasonography revealed a geographic, hypoechoic left breast area and enlarged regional lymph nodes. We performed ultrasound-guided, core needle biopsy of the breast lesion, and the histologic diagnosis was invasive carcinoma.
Results: The cut surface of the mastectomy specimen contained an ill-defined, greyish-white solid tumour, measuring 23x22 mm. Histopathologically, the tumour was composed of a solid invasive growth of carcinoma cells and a highly vascular fibrovascular stroma. Polygonal carcinoma cells had finely granular cytoplasm and oval or irregularly shaped nuclei with fine-granular chromatins. Twenty-one mitotic figures were counted in 10HPFs (histological grade 2). Marked lymphatic permeation as well as vascular infiltration were detected. Metastases were identified in 9 of 17 excised left axillary nodes, with extracapsular extension. Immunohistochemically, the carcinoma cells in the primary invasive, in situ and intra-lymphatic and metastatic regions were diffusely positive for synaptophysin and focally positive for chromogranin A.
Conclusion: The rates of carcinoma cells showing reactivity for oestrogen and progesterone receptors were 99% and 30%, respectively. The HER2 score was estimated to be 1+, and the MIB-1 labelling index was 32.5%. Although neuroendocrine mammary carcinomas have long been considered to follow a less aggressive clinical course than unselected breast cancers, our present case showed the unusual feature of lymphangitic carcinomatosis, which is known to be closely associated with poor recurrence-free and overall survivals as well as a lymphogenous metastasis.

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E-PS-02-019
Review of breast cancer grading in a district general hospital
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Background & objectives: Accurate grading of breast cancer is important for patient management and prognosis. It should be undertaken for all types of breast carcinomas. Strict adherence to grading methodology improves the accuracy and reproducibility of breast cancer grading.
Methods: The distribution and completeness of breast cancer grades at the department was compared with the national distribution of breast cancer. The data was obtained using SNOMED codes for all the breast resections carried out from 1st Jan 2019 – 31st Dec 2019. The grade (either Grade 1, 2, 3 or not assessable) was recorded and collated on an Excel sheet.
Results: A total of 193 breast resections were done in the year with 125 resections carried out for cancer. There were 97 symptomatic and 39 screen detected cancers identified. The breast cancer grade was assigned in all of the cases (100% compliance). Majority of the cancers were grade 2 (62%) comparable with the national average of 53%, followed by grade 3 (29%). Grade 1 made up 9% of the total cases, below the national average of 25%. A Nottingham grading score was assigned in most cases with the exception of 27 cases (19.8%).
Conclusion: There was 100% compliance with recording of grade (where assessable) in all breast cancer cases. However, there are a lower proportion of grade 1 breast cancer cases being diagnosed in comparison with the national average, likely due to lack of record of Nottingham grading score in all cases. We rectified this by incorporating the grading score in the breast cancer reporting performa used in the department.

E-PS-02-021
Radiation-associated breast angiosarcoma: features of diagnostics and treatment (a clinical case)
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Background & objectives: Breast angiosarcoma is an extremely rare and agressive neoplasm from the endothelial cells of blood vessels. Radiation-associated angiosarcoma (RAAS)of the breast appears 4–7 years after treatment. We report this rare entity as an important complication after breast-conserving surgery (BCS)and radiotherapy (RT)for breast cancer.
Methods: We present a 62-year-old woman who had underwent BCS with adjuvant chemotherapy and RT (ROD-2Gy, SOD-50Gy,2D-planning) in 2015 for the left breast cancer, pT1N1M0, stage IIA, luminal B HER2-negative subtype. In 2020 she admitted thickening and discoloration of the skin in the area of the postoperative scar. The patient underwent a simple mastectomy after a biopsy diagnosis was established.
Results: Locally, the left mammary gland with signs of post-radiation fibrosis. Near the areola, in the area of the postoperative scar, a tumour of about 1.5 cm in diameter, with rounded edges, purple-cyanotic colour, towering above the skin surface, inactive, painless, is determined. Gross examination revealed a solid, well-circumscribed, reddish tumour with a 2x1.5 cm size. Histologically, it was composed of high-nuclear-grade spindle cells with hyperchromatic nuclei and scant cytoplasm. Immunohistochemically, the tumour was negative to ER, PgR, Keratin Pan, S100, and positive to Vimentin, CD31, FLI1, with a Ki-67 index of approximately 90%. The tumour was graded according to Rosen's method. The diagnosis was established as RAAS high-grade.
Conclusion: RAAS is an extremely rare and poorly studied tumour for which diagnostic and treatment standards have not been developed. The only radical treatment is its surgical removal. The course of the disease is extremely aggressive. The most important prognostic factors are the size of the tumour and the area of skin lesions. The effectiveness of chemotherapy for RAAS remains controversial. It is necessary to accumulate the experience of treating patients with RAAS to develop the most effective therapeutic and diagnostic algorithm.

E-PS-02-022
SOX10 expression in breast cancer and its correlation with clinicopathological features and lymph nodes status
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Background & objectives: SRY-related HMG-box 10 protein (SOX10) is a transcription factor characterising neural crest-derived cells. SOX10 was reported to be preferentially expressed in metaplastic BC. This study aimed to investigate correlation Sox10 expression with BC clinicopathological characteristics and lymph nodes status.
Methods: We tested the expression of SOX10 in 358 BC specimens with used immunohistochemistry (SP267, Spring bioscience, USA). The reactivity assessed was nuclear. SOX10>1% nuclear positivity was considered as positive. SOX10-positive expression was detected in 22 cases (6%). Loss of SOX10 expression was predominant in both comparing groups (with/without lymph nodes metastases - 97.7% and 91.6%, respectively).
Results: Statistical significant association was found between SOX10 overexpression and patient's age <50y.o.(HR=9.5,p=0.002); metaplastic type BC (HR=20.5,p<0.001); Grade3(HR=39.4,p<0.001); Ki-67≥50% (HR=76.7,p<0.001). There is loss of SOX10 expression in ER and PgR-positive BC (p<0.001). There was no statistically significant correlation of SOX10 expression with tumour size, number of tumour nodes, its localization, HER2/neu expression. The transcription factor SOX10 is expressed in TNBC and is not detected in luminal BC subtypes (p<0.001). A significant relationship was found between SOX10 expression and regional metastasis (p=0.0297). In the group without lymph nodes BC metastases the number of cases with SOX10 overexpression was higher (19 cases, 8.4%) than in the group with lymph nodes metastases (3 cases,2.3%).
Conclusion: Identification of specific biomarkers is very important for prediction of regional metastases. We demonstrated that SOX10 expression is associated with clinicopathological parameters of BC and its lymph nodes status. Loss of SOX10 expression statistically significantly reduced risk of lymph nodes metastases (p=0.0297). Sox10 may be used as a novel reliable putative marker for the diagnosis of metaplastic and high grade BC, TNBC and lymph nodes metastasis.

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E-PS-02-023
Pigmented papillary carcinoma of male nipple mimicking melanoma
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Background & objectives: Melanoma in nipple-areola complex is extremely rare and in differential diagnosis must be distinguished between Paget disease, melanoma from extramammary sites and invasive carcinomas. We present a case of invasive papillary carcinoma of male nipple with melanin laden tumour cells.
Methods: A 71-year-old male patient presents with lobulated greyish tumour of the right nipple measuring 2x1,3cm elevated above the skin surface 1cm. The lesion was surgically removed with skin excision 0,7x0,5x0,5cm. The specimen was formalin-fixed and paraffin-embedded, routinely stained with haematoxylin and eosin. Additional immunohistochemical analysis was performed with CK7, ER, SMA, S-100, and Melan A.
Results: The gross specimen on cut surface revealed solid, white to brown tumour, well demarcated at the base and ulceration of overlying epidermis. Histomorphology of the sections showed papillary structures with tall columnar cells overlying fibrovascular cores, as well as micropapillary formations. There were areas of solid and cribriform growth pattern. Microcalcifications were diffusely present. There were accumulated melanophages in subepithelial tissue and melanin granules were also found in tumour cells. Tumour cells were positive for CK7, with strong and diffuse nuclear stain for ER, with complete absence of myoepithelial cell on SMA stain. Melan A and S-100 were negative. Although rare, a diagnosis of pigmented papillary carcinoma was made.
Conclusion: Pigmented carcinomas of breast are rare. When they are localized in areolar region the diagnosis should be carefully made to exclude lesions with melanocytic differentiation. The pigmentation should be considered also as a result by proximity to epidermis. The distinction between benign and malignant papillary lesions is quite difficult in most cases. The prognosis of patients with solid papillary carcinoma is relatively favourable.

E-PS-02-024
Limitations of tru-cut biopsy in diagnosis of malignant phyllodes tumour
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Background & objectives: Malignant phyllodes is one of the rarest breast tumours and it is most commonly diagnosed in the elderly populations, but can also occur in young patients, as reported in this case.
Tru-cut biopsy is a sensitive diagnostic tool for breast cancer.
Methods: A 41-year-old female with no family history of breast cancer presented with enlarged tender mass which occupied most of the left breast. Imagistic examination of the left breast revealed a solid tumour formation with a diameter of 20 mm. Subsequently, an ultrasound-guided tru-cut biopsy of the left breast was performed for an accurate tissue diagnosis.
Results: The sample for tru-cut biopsy was processed. The histology revealed only the mesenchymal component without the epithelial one. The tumoral cells were atypical epithelioid cells with nuclear pleomorphism, mitotic activity-16 /10 HPF. The necrosis was present.
On immunohistochemistry the tumoral cells were positivity for vimentin, CK 7,CD117, and focally positive for S100, E-cadherin, and were negative for p63, Cd34 and oestrogen.
After corelation between the immunoexpression, histological features and imagistical features, our diagnosis was as follows, malignant mesenchymal tumour compatible with malignant phyllode tumour. Malignant phyllodes tumours can present dedifferentiations areas, which consists in liposarcoma, fibrosarcoma and malignant fibrous histiocytoma, all these entities should be consider for differential diagnosis of lesion.
Conclusion: The differential diagnosis of the phyllodes tumour involves the assessment of the malignant mesenchymal component with or without possible heterologous malignant elements; the evaluation of the epithelial component with the characteristic aspect of slits with leaf-like projections together with the appearance of the tumour demarcation. All of these aspects can be evaluated simultaneous on the excision specimen for the final diagnosis, tru-cut biopsy diagnosis should only be used in the first stages of a diagnosis.

E-PS-02-025
Corynebacterium caused cystic neutrophilic granulomatous mastitis
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Background & objectives: Cystic neutrophilic granulomatous mastitis with Corynebacterium affecting young women is a rare inflammatory disease that can mimic malignancy. Between 2002 and 2020, a total of 141 cases were documented in the literature.
Methods: We report a case of a 44-year-old female patient suffering from fever, chills, and palpable lesions in the left breast.
MR examination detected a pathological accumulation of contrast material from mamilla to pectoralis. Morphologically inflammatory or malignant process could not be differentiated.
The core biopsy sample was diagnosed as most probably cystic neutrophilic granulomatous mastitis caused by Corynebacterium.
Results: In 2021 February, the external quadrant of the left breast was excised. On HE stains perilobular mixed inflammatory infiltrate composed of lymphocytes, neutrophils and scattered multinucleated giant

cells were seen. Round to oval cystic spaces rimmed by neutrophils and nonnecrotizing granulomas were also present.
Conclusion: In summary, Corynebacterium caused cystic neutrophilic granulomatous mastitis is an entity that is clinically difficult to distinguish from breast carcinoma. On radiological examination, these lesions are highly suspicious for malignancy. Only careful histological evaluation can help in the correct diagnosis as Corynebacterium species are usually small in quantity and organisms can be difficult to culture.

E-PS-02-026
Unusual post radiotherapy breast sarcoma: a case report
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Background & objectives: Our patient, a 39-year-old woman was diagnosed and operated in 2016 of an infiltrating ductal carcinoma grade 3, triple negative. The patient received chemotherapy and radiotherapy and presented 5 years later a new mass at the same location.
Methods: Due to familial background, genetic analysis was undertaken, with a positive result for BRCA2 mutation. A biopsy of the latter was performed, showing sarcomatoid features. An ample immunohistochemistry battery was ordered to try to establish the correct diagnosis, and ample excision was recommended for definitive diagnosis.
Results: The current neoplasm was composed by a mesenchymal proliferation with myxoid stroma, and pleomorphic cells exhibiting high nuclear/cytoplasmic ratio, atypical mitosis and multinucleated bizarre nuclei. A vascular proliferation composed of curvy thin-walled vessels was also present. The malignant proliferation showed pectoral muscle and surrounding adipose tissue infiltration. Immunohistochemically, high proliferation index was observed with Ki67 antibody (80-90%), with focal p63 positivity. The remaining markers, including keratins, were negative, hence discarding metaplastic carcinoma as a diagnostic possibility. Differential diagnosis was therefore established between pleomorphic sarcoma and high grade myxofibrosarcoma, favouring the last one. Due to its complexity, the case was consulted to a senior pathologist, who certified our diagnosis.
Conclusion: We present the case of a post-radiotherapy high grade myxofibrosarcoma, in a patient with BRCA2 mutation. The presence of myxoid component, thin-walled curvy vessels together with the atypical pleomorphism and bizarre multinucleated nuclei with high number of atypical mitosis, made the myxofibrosarcoma diagnosis clear. According to our knowledge, myxofibrosarcoma has not been associated previously with the use of radiotherapy. We hence present a case report which shows that this tumour might also be associated with radiotherapy.

E-PS-02-027
Tumour budding as a predictive factor of breast carcinoma progression
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Background & objectives: Tumour budding is one of the independent prognostic factors of a tumour, first described in a colorectal cancer. it is not used in clinical oncology as a prognostic factor due to the lack of a standardized and easily reproducible assessment method.
Methods: The aim of study is to create a standardized method for assessing tumour budding in relation to breast carcinoma. We used such methods as IHC, light microscopy, analysis of scientific publications of materials on the topic "Tumour budding".
Results: Tumour buds are single cells or clusters of 4 or less cells in an invasive component of a carcinoma. The presence of the infiltrating margin of the tumour (the zone of invasive growth) and pseudopodies of tumour cells is noted.
Rare there is a weak or moderate lymphoid infiltration of the tumour.
Tumour budding is divided into peritumoral budding and intratumoral budding. Both are morphological manifestations of the epithelial-mesenchymal transition, as evidenced by the loss of adhesion of E-cadherin molecules and the expression of markers of the activated Wnt-signaling pathway, such as nuclear beta-catenin in tumour bud cells.
Conclusion: Tumour budding plays an important role in the prognosis of breast carcinoma. The study of tumour budding as a factor contributes to improving the management of patients with breast carcinoma.
It became possible to include this method in routine practice by the standardization of the method for assessing tumour budding. We have developed preliminary versions of recommendations for the evaluation of tumour budding as a prognostic factor in the development of breast carcinoma during routine histological examination of samples of the tumour.

E-PS-02-028
Lymphoid cell microenvironment in the stroma of invasive breast carcinoma of the non-specific type
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Background & objectives: Tumour infiltrating lymphocytes in breast cancer (BC) is relevant issue in the context of new possibilities of immunotherapy.
Objective of our study is to examine the structure of lymphoid cellular formations in the breast in invasive non-specific cancer.
Methods: TIL were studied by morphometry on material from 18 patients with invasive breast carcinoma luminal B type. Ki67 index was 40%
An IHC study was carried out with CD20, CD8, CD4, CD68, CD138, Ki-67 markers. Morphometry was performed using ImageJ1.5. Statistical data processing was performed using the nonparametric Mann – Whitney test. TIL was evaluated in the tumour stromal component (in%).
Results: Tight cellular infiltrates surrounding the tumour cells in the form of ridges were found directly in the stroma of the tumour. In interlobular connective tissue the diffuse leukocyte infiltrates and lymphoid nodules were detected. Lymphoid nodules contain more than 60% lymphocytes; CD20+ and CD4+ cells dominate over CD8+ lymphocytes. Plasmocytes and histiocytes also were detected here. Immunocompetent cells (small lymphocytes and plasmocytes) and fibroblastic cells were detected in diffuse intratumoral infiltrates in equal proportions. Among the lymphocytes, the predominant subpopulation here were CD8+ cells, CD20+ and CD 4+ lymphocytes were represented in almost equal quantities. The histiocytes content (CD68+) was reliably high in close proximity to tumour cells.
Conclusion: The severity and subpopulation composition of lymphoid tumour infiltration can be considered as a prognostic factor, but also can be important for the selection of personalised treatment, including modern immunotherapeutic drugs.

E-PS-02-029
A rare case of primary Hodgkin's Lymphoma presenting in the breast. Diagnostic challenges and catastrophic consequences from literature
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Background & objectives: Primary Hodgkin's lymphoma (PHL) of breast is an exceedingly rare entity (0.04%-0.5% incidence) among primary breast lymphoma with around 24 cases reported in literature. Histological diagnosis can prove challenging, owing to the morphological features resembling those of an inflammatory pathology.[1]
Methods: A 75-year-old woman presented with several months of right axillary swelling alongside a pre-existing breast lesion (U3) which had

been diagnosed as a reactive intramammary lymph node (B2). Ultrasound showed that the breast lesion had increased in size and the axillary swelling corresponded to abnormal-looking lymph nodes (U4). Core biopsies revealed primary classic Hodgkin's Lymphoma (CHL) of breast.
Results: Histological assessment of breast and axillary cores revealed effaced lymph nodal architecture with a mixed inflammatory background including scattered large atypical vacuolated cells abundant in clear cytoplasm with mononucleated and rare binucleated forms were seen. Immunohistochemical analysis confirmed a CHL being positive to CD15 and CD30 stains. Subsequent full-body imaging indicated the breast as primary site and excluded extramammary dissemination. In addition to the general B systems of lymphoma, the clinical presentation is mostly insidious and may present as screen detected lesion or skin changes. The morphological features may also mimic mastitis or inflammatory carcinoma [2][3]. Correctly identifying this lesion is imperative in ensuring the patient undergoes appropriate treatment pathway.
Conclusion: PHL in breast is extremely rare and can easily be missed. Radiology is less helpful as it may recognise the mammary lesion as suspicious at most however histopathology is crucial to make such a diagnosis. Careful consideration of a wide range of possibilities including lymphoma is important to ensure a correct diagnosis. The literature highlights such a diagnostic difficulty as both FNA and biopsies may be inconclusive. Indeed, inappropriate diagnosis could lead to unusual presentations, delayed or inappropriate treatment [1].

E-PS-02-030
KI-67 Expression in triple negative breast cancer (TNBC) patients and its significance
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Background & objectives: Triple-negative breast cancer (TNBC) is a subset of breast cancer with a poor prognosis because of lack of targets for hormonal therapy. Research has focused in recent years on discovering biomarkers of TNBCs, which will aid in its management.
Methods: We analysed the expression of KI-67 Labelling Index (LI), a nuclear protein that play diagnostic and prognostic roles in many cancers, by immunohistochemistry, in TNBC cases from the King Khaled University hospital. This expression was cross-checked against clinical-pathological criteria of TNBC patients, and against Vimentin expression in TNBC patients with significant KI-67 expression.
Results: KI-67 LI was significantly expressed in the majority of TNBC cases. This expression was significantly correlated with lymph node metastases, tumour invasion, high tumour nuclear grade, advanced stage and failure to achieve complete remission. TNBCs' KI-67 LI expression was also correlated with Vimentin expression, the mesenchymal chief marker of the EMT phenomenon.
Conclusion: Collectively, our study presents a strong argument for the use of KI-67 LI as a biomarker of aggressive, metastatic TNBC disease with poor outcome. This study, along with mounting evidence in the scientific literature, presents a case for the use of this nuclear protein in diagnosis, prognosis and follow-up of patients with this difficult diagnosis.

E-PS-02-031
Primary breast angiosarcoma: a case report
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Background & objectives: Primary angiosarcoma of the breast is an extremely rare tumour (0.04% of all malignant breast tumours) and one of the most aggressive type. Its diagnosis is challenging since has a variable and non-specific clinical and radiological presentation.
Methods: We herein report the case of a 54-year-old Caucasian woman presented at the emergency department of our Centro Hospitalar e Universitário de Coimbra with a lump in the left breast, which over the last 6 months had become bigger and itchy. Positron emission tomography-computed tomography (PET-CT) imaging confirmed a space-occupying lesion with high metabolic activity in the left breast.
Results: The tumour histology, in the initial core needle biopsy, showed papillary formations and vascular structures lined by atypical cells with a hyperchromatic nucleus and eosinophilic cytoplasm. The tumour cells expressed CD34, CD31, ERG and Fli-1 but were negative for cytokeratin. The angiosarcoma grade I was made.
Conclusion: The patient was treated with neoadjuvant systemic chemotherapy based on doxorubicin and carboxamide. After treatment completion, the patient underwent radical mastectomy. Pathologic complete response in the breast and axillary lymph nodes was achieved. The patient has no evidence of disease recurrence.

E-PS-02-032
Prognostic value of elastic fibres in breast invasive ductal carcinoma microenvironment after chemotherapy
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Background & objectives: The tumour microenvironment substantially influences cancer pathogenesis and progression. A prognostic role of stromal elastic fibres remains unclear. The aim of study is to estimate the prognostic value of stromal elastic fibres in breast invasive ductal carcinoma after neoadjuvant chemotherapy.
Methods: The residual tumours after standard neoadjuvant chemotherapy from 31 patients were resected. A breast invasive ductal carcinoma of no special type (not otherwise specified") was diagnosed. Histochemical studies for Russell-Movat pentachrome stain was done. A deposition of elastic fibre (EF) around vessels in tumour microenvironment was evaluated as a weak (a weak EF network) and severe (massive EF conglomerates).
Results: Patients who had a weak EF deposition (3/9.7%) or did not have thickened elastic fibres (14/45.2%) around vessels in microenvironment of residual tumour was included in the first group (n=17). Women who had a severe EF deposition (14/45.2%) around vessels in microenvironment of residual tumour was included in the second group (n=14). The average follow-up time after operation was 44.6±5.2 months (from 3 to 80 month). A 3 (2.5%) patients from the first group and 7 (50%) from the second group had tumour recurrent. The average time of disease-free survival was 58.15±5.0 months for the first group and 37.46±8.0 months – for the second group (p=0,0137).
Conclusion: This study showed that the change in the thickness of an elastic fibres around vessels in residual tumour microenvironment of breast invasive ductal carcinoma is related to disease-free survival time. A severe deposition of elastic fibre around vessels in tumour microenvironment after neoadjuvant chemotherapy can be used as an additional predictor of tumour behaviour.

E-PS-02-033
Mucinous cystadenocarcinoma of the breast – a very rare case
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Background & objectives: Mucinous cystadenocarcinomas (MCA) of the breast are very rare tumours.
Methods: An 86-year-old woman with a history of papillary breast carcinoma of the left breast (T4bN0, 4 years ago), presented to our hospital with two palpable masses at the left breast. A resection of two lesions measuring 8cm and 1,4cm was performed. The first was well circumscribed, partial cystic and partial solid, with mucus content.

Results: The microscopic examination of the largest lesion revealed a high grade cystic invasive carcinoma, with papillary projections, lined by tall columnar cells with stratification and abundant intracytoplasmic mucin. Necrosis was present. The immunochemistry revealed CK7 (+), mammoglobin (+), CK20 (-), CDX2 (-), WT-1 (-) CA-125 (+) with apical stain, ER (-), PgR (-), Her-2 (CISH) (+). The smaller lesion was a high grade papillary invasive carcinoma with a high nuclear grade in situ carcinoma component and displayed cribriform/ papillary architectural pattern. The immunochemistry showed ER (+), PgR (+), Her-2 (-).
Conclusion: The MCA has distinct clinical behaviour with a favourable prognosis which is unrelated to the tumour size, metastasis to the lymph nodes or molecular subtype. Differential diagnosis includes metastasis from an ovarian cystadenocarcinoma or pancreatic carcinoma and is based on the immunophenotype.

E-PS-02-034
Giant phyllodes tumours of the breast: are they always malignant?
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Background & objectives: Phyllodes Tumours (PTs) account for 0.3–1% of all primary breast neoplasms and are classified into benign, borderline, and malignant. PTs larger than 10 cm in size are considered giant and are most commonly malignant in nature.
Methods: Here we describe two cases of giant PTs, the first in a 38-year-old female who presented with a 22 cm lump in the right breast, and the second in a 55-year-old female with a 45 cm, fast-growing, ulcerated mass in the left breast. Both patients underwent radical mastectomy and axillary lymphadenectomy.
Results: In both cases, histopathologic features of PTs were observed. In the first case, the stroma was moderately cellular with mild-moderate atypia, low mitotic activity (<5/10HPFs), and absence of stromal overgrowth, pointing to a diagnosis of borderline PT. The patient remains free of disease for 2 years in follow-up. In the second case, stromal cellularity ranged from moderate to focally increased with marked nuclear pleomorphism and cellular atypia, high mitotic activity (>13/10HPFs), areas of stromal overgrowth, and foci with heterologous chondrosarcomatous differentiation. The diagnosis of malignant PT was established, after which radiation therapy was initiated. One year and four months later, the patient presented with widespread metastatic disease.
Conclusion: Giant PTs represent an uncommon entity. Clinical suspicion should be high in patients with a rapidly enlarging breast mass. The majority of the cases are malignant with a high probability of metastatic disease, whereas giant borderline PTs are exceptional. Although FNA and core biopsy are helpful, definitive diagnosis is established after complete surgical excision and detailed histopathologic examination. The establishment of specific therapeutic guidelines is required to ensure the appropriate management of this type of tumours.

E-PS-02-035
Triple negative breast carcinomas: correlation between TILS and classic prognostic factors
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Background & objectives: Triple negative (TN) BC, represents 15–20% of BCs and it usually is an aggressive tumour. Tumour infiltrating lymphocytes (TILs) seems to have an important prognostic significance in TNBC. This study aims to evaluate TILS as a prognostic marker in TNBC.
Methods: We selected from the Pathology Department of SCJUPBT database TNBC cases corresponding to the following inclusion criteria: histopathological evaluation in our department, ER/PR/HER2-; exclusion criteria: core-needle biopsy specimens. Stromal TILS were digitally evaluated on a single H&E scanned slide; TILs were analysed in correlation with other clinico-pathological parameters: age, tumour size, lymph node involvement, histologic subtype, lymphovascular and perineural invasion.
Results: We identified 24 patients that meet the inclusion criteria, aged 29-84 years (mean age – 63 years). The TILS percentage, evaluated according to the International TILs working group guidelines, varied from 0% to 70% (average - 21%), with higher percentages in women < 65 years. Out of 24 cases, 19 were NST carcinomas, and 5 cases metaplastic carcinomas; 22 carcinomas were GIII and only 2 GII. A high TILs score has been identified in all 3 carcinomas with medullary differentiation. Low TILs scores have been associated with higher tumour stages, lymph node metastases, perineural invasion and lymphovascular invasion.
Conclusion: Our results suggest a correlation between the presence of TILs and a potentially better outcome of patients with TNBC after chemotherapy or biological therapy. The pathologist must be familiar with TILs and the quantification method from the perspective of introducing this parameter in the pathological report of TNBC.

E-PS-02-036
Metastatic papillary serous carcinoma should be considered in cases of high-grade encapsulated papillary carcinoma of the breast. An extremely rare case and a possible pitfall
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Background & objectives: Encapsulated papillary carcinoma (EPC) of the breast has a favourable prognosis. High-grade EPCs, triple-negative or HER-2-positive, are managed as invasive carcinomas. Breast metastasis from serous carcinoma represents a late-stage event. The distinction between the two could be very challenging.
Methods: A 68-year-old woman underwent a total left mastectomy and sentinel lymph node biopsy (SLNB). A specimen with the indication of 'tumour of the left breast' was received in our Pathology Department. A peripheral nodular mass of 3cm was found.
Results: Microscopically, the appearances were of large intracystic papillary stalks, with high nuclear grade, surrounded by collagenous tissue. The diagnosis was of infiltrated encapsulated papillary carcinoma, ER+. One year later, the woman was diagnosed with a cervical mass, possible pathologic lymph node, which on FNB was consistent with metastatic serous papillary carcinoma. According to clinical history, the patient was diagnosed elsewhere with high-grade serous papillary carcinoma of the peritoneum, four years earlier. Immunohistochemical stains were similar in both specimens, ER+, WT1-, PAX8+, p53+ (wild type) and high Ki-67 (80%). GATA-3 was weakly, scarcely expressed. The findings were consistent with metastatic SPC in the breast, mimicking primary carcinoma of the EPC type.
Conclusion: Pathology of breast metastases and differentiation from primary breast cancers is based on a combination of morphological and IHC features. In our case, the lack of clinical history, the type of surgical approach (mastectomy and SLNB), the solitary lesion, the EPC pattern of growth and the diffuse ER+ staining, were more in favour of primary breast lesion. Different morphologic features of metastatic PSC have been described. EPC growth pattern should be considered among them.

E-PS-02-037
Undifferentiated pleomorphic sarcoma of the breast. Presentation of an exceedingly rare case
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Background & objectives: Sarcomas are exceptionally rare primary breast tumours, arising within breast parenchyma, the skin and

subcutaneous tissue overlying the breast. Undifferentiated pleomorphic sarcoma (UPS) of the breast is a high grade malignant soft tissue neoplasm with no specific line of differentiation.
Methods: A 62-year-old woman was admitted to our hospital due to a palpable lump of the right breast of approximately 4cm in mammography and bloody discharge from the nipple. A partial mastectomy and sentinel lymph node biopsy (SLNB) was originally performed, complemented by total mastectomy, due to originally infiltrated breast margins.
Results: Breast parenchyma was occupied by a circumscribed solid, white-grey tumour with friable haemorrhagic necrotic area. Microscopically, the tumour consisted of myxofibrosarcomatous areas alternating with areas of pleomorphic giant cell type with brisk mitotic activity and areas of necrosis. There was a nodular pattern of growth and a continuous histological spectrum from hypocellular, myxoid and spindle cell areas to highly pleomorphic with bizarre giant cells and high mitotic activity. There was positive immunohistochemical staining expression in VIM, Kp1 (CD68) and CD10. The diagnosis of UPS of the breast was made. The patient underwent chemotherapy and is scheduled to begin adjuvant radiotherapy. Ten months after diagnosis the patient is free of disease.
Conclusion: UPS occurs as a primary lesion in breast parenchyma, with the prerequisite of location within breast parenchyma and without chest wall involvement. Extensive tumour sampling, attention to morphologic detail and the use of appropriate immunohistochemical markers lead to the correct diagnosis. Surgical resection with a negative margin is the standard treatment. SLNB is not warranted. Adjuvant radiation is utilized in large tumours or following incomplete surgical resections. Adjuvant chemotherapy may be used in patients with large, unresectable or metastatic tumours.

E-PS-02-038
A rare entity, Invasive Lobular Carcinoma, Apocrine subtype with aberrant E-cadherin pattern – a case report
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Background & objectives: Invasive lobular carcinoma accounts for 5-15% of all breast cancers, which has a classic type (55%) and different architectural and cytological variants. One rare cytologic variant is apocrine or histiocytoid, which represents about 3% of all invasive lobular carcinomas.
Methods: A 62-year-old female depicts on self-palpation a nodule in the upper-outer quadrant. The ultrasound and mammography examination confirms a breast lesion, with a BI-RADS score of 5, highly suggestive of malignancy. Intraoperative examination revealed a white, firm nodule of 18/15 mm, with features of invasive carcinoma. Further breast excision and microscopic examination were performed.
Results: Microscopic evaluation illustrates a malignant tumour proliferation formed by large cells, with abundant eosinophilic cytoplasm, with vesicular nuclei and multiple eosinophilic nucleoli. The pattern of distribution is targetoid, around ducts, with single-cell file infiltration. Immunohistochemically, the tumour revealed an aberrant membranous E-cadherin pattern, with faint or granular positivity and focal cytoplasmic positivity. Oestrogen and progesterone markers were negative. Her2 showed a weak/moderate positivity, with an equivocal 2+ score. Androgen receptor had nuclear positivity in about 99% of tumour cells and GCDFP-15 was positive just focally. There was a proliferation index of 5-7% with Ki-67. All these features were consistent with a diagnosis of Invasive Lobular Carcinoma, Apocrine subtype, moderately differentiated.
Conclusion: This particular case highlights the importance of immunohistochemical examination, especially in distinctive invasive breast carcinomas, with rare features. Invasive lobular carcinoma, the apocrine subtype is a rare entity and one has to make a differential diagnosis with other entities with apocrine differentiation, in terms of the tendency to recur and metastasize.

E-PS-02-039
A case report of a breast implant-associated anaplastic large cell lymphoma
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Background & objectives: To report a case of a Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL), an entity that has been recognizes in the 2017 on revision of the WHO Classification of the Tumours of Haematopoietic and Lymphoid Tissues.
Methods: A 48-year-old woman 2 year after the 2nd silicone breast implant placement, complained for pain and swelling in the right breast. She went for clinical, MRI and ultrasonography examination which they revealed a peri implant fluid collection and rupture of right implant. The patient underwent surgery and both implants were removed and fibrous capsules sent to pathological department for examination.
Results: The microscopic of right capsulectomy specimens showed mild degree diffuse chronic inflammation, but a more careful examination revealed also large pleomorphic cells at the surface of capsule in a fibrinous material. These cells had anaplastic nuclei, abundant pale cytoplasm and prominent nucleoli. The nuclei were eccentric with horseshoe morphology. Mitotic figures were recognized. There were some areas that tumour cells infiltrated into the capsule. The immunohistochemical analysis gave negative results for AE1/AE3, CD20, CD43 and positive reaction for EMA, CD30, CD45 and CD3 (focal). The tumour cells were ALK negative.
Based on morphological and immunohistochemical evaluation the diagnosis of the Breast Implant- Associated Anaplastic Large Cell Lymphoma was made.
Conclusion: BI-ALCL is a newly, very rare described entity which is usually developing 10 to 13 years after placement of the breast implant. The neoplasm has common morphological and immunophenotypical features with systemic ALK negative ALCL. The mean age of patients is 50 years. The treatment of choice is implant removing and capsulectomy. The outcome of the most patients is excellent.
The differential diagnosis of BIA-AL from chronic inflammation associated with breast implantation it may be a challenge.

E-PS-02-040
Agreement between core biopsy and surgical specimen, regarding breast cancer histological degree; a Brazilian study
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Background & objectives: Scarff-Bloom-Richardson classification modified by Ellis and Elston (SBR) is a well-known scale used worldwide to classify breast carcinomas. The aim of this study was to compare the agreement between histological graduation obtained through the core biopsy (CB) and surgical specimens.
Methods: A retrospective observational study performed in a tertiary service in the Brazilian countryside. The comparative histological graduation was based on the three morphological characteristics from SBR. The Kappa index was the coefficient of agreement used to verify the possible correlation. The rates of overestimation and underestimation were also assessed.
Results: One hundred fifty-seven patients had their medical records reviewed. Sixty-one years old was the mean age. The mean number of fragments obtained by CB was 3.8. The tumour's size ranged from 0.5 cm to 8.5 cm. In TNM staging 38% of patients were pT1c and 34% were pT2. There were not lymph node metastasis in 59% of them. The agreement between CB and surgical specimens was 78.98% (n=124). CB underestimation index was 19.75% (n=31) and overestimation 1.27% (n=2). There was no difference between

both groups of cases (with agreement and without agreement between CB and surgical specimen) in relation to tumour size, patients' age, number and length of biopsy fragments.
Conclusion: CB when compared to the excision specimens predicts moderate agreement when analysing by Kappa index. In the studied population tumour size, patients' age, number and length of CB fragments did not influence the rate of agreement between CB and surgical specimen.

E-PS-02-041
A rare case of solitary fibrous tumour of the breast in a man
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Background & objectives: Solitary fibrous tumour (SFT) is a spindle-cell fibroblastic neoplasm that usually occurs in the pleura, but it can appear virtually anywhere. SFT is very uncommon in the breast, with around 15 cases reported in the literature (13 women, 2 men).
Methods: A 78-year-old-man, with familial history of breast cancer, and evidence of gynecomastia. A mammogram and ultrasound were performed showing a solid nodule of 10 mm, hypoechoic, defined margins, smooth edges, slightly lobulated, BIRADS-3. Ultrasound-guided core-needle biopsy was performed, the diagnosis of a mesenchymal spindle cell tumour, consistent with SFT/Miofibroblastoma, was suggested. The patient underwent to surgical excision of the nodule.
Results: The surgical specimen revealed a well circumscribed mass of 1x0.9 cm, whitish and firm-gelatinous consistency. Histologically showed a neoplasm mesenquimal expansive, unencapsulated, multilobular growth, made up of bundles of bland-looking ovoid to short spindle cells, within an oedematous and myxoid stroma, with perivascular reinforcement. Nuclear pleomorphism, necrosis, mitosis and haemorrhages were absent. Immunohistochemically, was positive for oestrogen (ER), progesterone (PR) and androgen (AR) receptors; patchy staining with Vimentin, CD34, Actin, Caldesmon, CD10, BCL-2, and strong and diffuse nuclear immunoreactivity (>90%) with STAT6; negative for CKAE1/AE3, EMA, Desmin, S-100, SOX10, HMB45 and MIFT. The diagnosis of SFT was rendered. Clinically there is no evidence of local recurrence after a 1-year-follow-up period.
Conclusion: SFT of the breast is a rare neoplasm included in "the benign-spindle-cell-tumours" which representing less than 1% of all mammary tumours. Although SFT is suspected on characteristic morphologic features, immunohistochemistry revealing reactivity for CD34, BCL2 and STAT6, is crucial in the differential diagnosis of potential benign and malignant mimics. Regarding ER, only two studies have addressed this issue, in one they were positive, in the other negative. More studies are needed to clarify it.

E-PS-02-042
IgG4-related sclerosing mastitis with metachronous invasive lobular breast carcinoma
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Background & objectives: IgG4-related disease (IgG-RD) is a fibroinflammatory disease that can involve various organs. IgG-RD is a systemic disease characterized by specific histopathological findings of an intense lymphoplasmacytic infiltrate, storiform fibrosis, and obliterative phlebitis in the presence of predominant IgG4-positive plasma cells.
Methods: Our case is a 72-year-old woman with rheumatoid complaints. Eight years ago, she underwent left radical mastectomy because of breast cancer which pathologic diagnosis was reported as invasive lobular carcinoma. She is being followed in the rheumatology department with skin lesions.
Results: One year ago, a distorted area was detected in her right breast and a lumpectomy was performed with preliminary diagnoses as breast cancer and tuberculosis. Histopathological examination showed lobular intraepithelial neoplasia areas within sclerotic stroma with dense ducto-centric lymphoplasmacytic inflammation, in routine haematoxylin-eosin stain. This inflammation pattern raised the suspicion of a sclerosing mastitis which might be related to IgG4. On immunohistochemical assessment, most of the plasma cells were stained for IgG4 (cut-off value as 50 plasma cells per HPF), without any monoclonality with kappa and lambda. Recently, during clinical follow-up, a rectal adenocarcinoma was detected and segmental colon resection was performed.
Conclusion: The IgG4-RD with lobular intraepithelial neoplasia and with metachronous invasive lobular breast carcinoma has not been reported until today and the probable relationship between the two entities has not yet been discussed. This is a unique case with benign immune-based breast disease with lobular neoplasia, invasive breast cancer history and recently developed rectal cancer. So, it is found to be important to be shared.

E-PS-03 | Cardiovascular Pathology E-Posters

E-PS-03-001
Primary undifferentiated pleomorphic cardiac sarcoma – a case report
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Background & objectives: About 25% of primary cardiac tumours are malignant, and of those 75% are sarcomas. Primary cardiac sarcomas are rare but often fatal. These tumours are generally incidental findings, as they are usually asymptomatic until locally advanced.
Methods: A 49-year-old female, with known history of atrial fibrillation, was found to have a left atrial mass during a routine CT-scan.
Cardiac MR revealed a mass within the posterior and superior wall of the left atrium, suspicious for malignancy, measuring 32 mm. Due to the extent of invasion into the pulmonary vein, the mass was incompletely resected.
Results: Grossly, the tumour was a 50 mm, infiltrative, fibrous mass, with no necrosis or myxoid change. Histologically, a pleomorphic sarcoma with epithelioid features and collagenous stroma was observed. Mitotic activity was conspicuous and atypical mitoses were present. MDM2 and vimentin positivity was seen by immunohistochemistry and the proliferative index (Ki-67) was approximately 40%. No amplification of MDM2 gene was identified by FISH analysis. A diagnosis of primary undifferentiated pleomorphic cardiac sarcoma was rendered. The patient is alive 4 months after surgery, undergoing adjuvant radio and chemotherapy.
Conclusion: Cardiac sarcomas are a rare subset of soft tissue sarcomas with aggressive, highly invasive behaviour and a poor prognosis, with median survival of less than 1 year. As in this case, clear surgical margins are often difficult to obtain and tumours can easily recur. MDM2 positivity by immunohistochemistry may not indicate MDM2 gene amplification, as this case showed. Surgery, followed by adjuvant chemotherapy with or without radiation, is the standard care.

E-PS-03-002
Cardiac hibernoma in a new-born
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Background & objectives: Hibernoma is a tumour that develops out of remnants of foetal brown fat tissue, occurring in subcutaneous soft tissue

of thigh, upper neck and trunk. Its localization to cardiac cavities is extremely uncommon. Its occurrence in newborns is more uncommon.
Methods: A 2-day-old new-born was extracted in emergency after discovery on echography of a 38*29 mm polylobed tumour of the right atrium and ventricle compressing left ventricle. The new-born underwent heart surgery.
Results: Multiple fragments measuring 4 to 18 mm were received. On microscopy, it is formed out by lobules of multivacuolated adipocytic cells, mature adipocytic cells and fat brown cells. These cells are distributed in variable proportions. Tumour cells displayed CD34 immunostaining. No PS100, MDM2 and CD68 expression was identified. Histopathology report confirmed the diagnosis of benign cardiac hibernoma.
Conclusion: Hibernoma is a rare and benign tumour accounting for about 1% of all adipocytic tumours. It occurs frequently in adults with a mean age of 38 years old. Its localization to cardiac cavities is extremely uncommon. It is a painless slow-growing mass. Due to its rare localization in cardiac cavities, immunochemistry is needed to eliminate other more frequent and aggressive tumours. Treatment consists on surgical removal.

E-PS-03-003
Benign metastatic leimyoma: unusual heart location
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Background & objectives: the smooth muscle tumours of the heart are extremely rare. this is only the fifth reported case of benign metastasizing leiomyoma to the heart with histological proof and the first case of cardiac metastasis without associated pulmonary metastasis localization.
Methods: A 56-year-old woman presented with dyspnoea and shortness of breath. On imaging, she was found to have a right atrial mass initially thought to be a thrombus, Cardiac magnetic resonance imaging (MRI) showed a monolobed, pedunculated, mobile, well-circumscribed mass attached to the intra-atrial septum. The resected tumour was sent to us for histological confirmation.
Results: The 8 cm x 5 cm x 3 cm resected cardiac tumour was solid, grey-white, and homogeneous fasciculate with no haemorrhage or necrosis.
Microscopically, the tumour was composed of bundles of bland spindle cells no nuclear atypia or necrosis, and only rare mitoses (less than 1/10 high-power fields).
Immunohistochemically, the spindle tumour cells expressed hcaldesmon and desmin and were negative for S100 protein. MIB-1 immunohistochemical staining showed low proliferative activity, with less than 1% MIB-1-positive cells. The tumour cells were strongly positive for oestrogen receptors (ER) and for progesterone receptors (PR), supportive of uterine origin.
Conclusion: It illustrates that benign metastasizing leiomyoma should be included in the differential diagnosis of cardiac tumours in patients with a history of surgery uterine leiomyoma perfectly benign,

E-PS-03-004
Oncocardiopathology and endomyocardial biopsy
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Background & objectives: Cardiac tumours are rare entities. Most are benign and, if malignant, the majority is metastatic. Heart involvement topology and characteristics are diverse, and its investigation may be assisted by Endomyocardial Biopsy. The authors present such a case.
Methods: A 78-year-old male was submitted to endomyocardial biopsy, at a Reference Centre, due to an infiltrative myocardial disorder, without familial or personal known nosologic antecedents. Clinico-imagiological workflow did not find other pathological involvement. Eight endomyocardial fragments, measuring 1-2 mm, were procured and sent to Anatomo-Pathological evaluation.
Results: Microscopic examination revealed a diffuse infiltration by atypical lymphoid cells, whose immunohistochemical phenotyping showed marked positivity for pan-B lymphocyte marker CD20; leading to the diagnosis of cardiac involvement by lympho-hematopoietic neoplasia, with features of Diffuse Large B Cell Non-Hodgkin Lymphoma (primitive versus metastatic). Additional cardio and haematological investigation, as well as clinical follow-up excluded other tumoral sites, favouring the diagnosis of primitive cardiac lymphoma.
Conclusion: 'Primary Cardiac Lymphoma' (restricted to heart and/or pericardium, by definition) is reported to account for 1-2% in surgical heart specimens and for 0.15-1% autopsy studies, while metastatic involvement ranges 20%. It is responsible for 0.5% of extra-nodal lymphomas. It is prone to affect immunocompromised persons, namely heart transplanted individuals. The clinical behaviour is aggressive, including cardiac failure, arrhythmias, pericardial effusion, sudden death. 'Percutaneous Endomyocardial Biopsy' is an important tool in the diagnosis and follow-up survey of cardiac oncologic settings.

E-PS-03-005
Primary cardiac lymphoma in a 62-year-old female
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Background & objectives: Primary cardiac lymphoma (PCL) is a rare type of non Hodgkin's lymphoma. It accounts for less than 0.01% of all cardiac tumours. We report a case of PCL and define its clinical and pathological features.
Methods: We presented a 62-year-old female patient with clinical signs of cardiac right insufficiency which progressing for 2 months. The patient underwent a cardiac ultrasound in which a tumour of the right atrium was found. Further cardiac MRI confirmed the presence of this tumour. An ultrasound-guided biopsy was performed.
Results: Microscopically, the sample corresponded to a proliferation made up of sheets of large rounded cells. Some tumour cells had a finely pitted or clumped chromatin nucleus and often a single large, centric nucleolus. Other tumour cells had a marginal nucleus, pressed against the nuclear membrane. An immunochemical study was then carried out, showing diffuse and intense labelling of tumour cells by CD45 and CD20. Immunostaining for CK 7, CD34, desmin, myogenin, synaptophysin and chromogranin was negative. The diagnosis of diffuse large B-cell lymphoma was made. As staging revealed no evidence of disseminated disease or bone marrow involvement, this was considered to be primary cardiac diffuse large B-cell lymphoma.
Conclusion: Primary cardiac lymphoma is a rare localization of extra-lymph nodes non-Hodgkin lymphomas. It more frequently affects immunodeficient patients with an affinity for the right heart. It is diagnosed at an advanced stage when they involve either the myocardium or the pericardium. Morphologically, PCL can pose diagnostic problems with any round cell tumour, hence the importance of immunochemical analysis which remains a gold standard to determine the nature of the tumour.

E-PS-03-006
Autopsy case of chronic COVID-19 confirmed with positive PCR RNA and viral proteins in the organs
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Background & objectives: Anatomic pathology of post-COVID-19 syndrome is discussed in the literature. We describe the autopsy case of a 46-year-old female patient who had undergone COVID-19 (pneumonia - CT2) six months before her death.
Methods: We present the data of morphological study of autopsy case including histological, immunohistochemical study of virus proteins (nucleocapsid protein and spike protein of SARS-CoV-2) and determination

of the characteristics of the cellular infiltrate in the heart (CD3, CD20, CD45, CD68, TLR4, TLR9, perforine). Detection of coronavirus RNA in myocardium was performed by PCR.
Results: Within 6 months after COVID-19, clinically, the patient had significant signs of chronic myocarditis (decompensation of heart failure, arrhythmia, increase in anti-cardiac antibody titre). She died of chronic cardiovascular failure. The virus RNA was detected in myocardial tissue, kidney, intestine, liver, brain and ovary, but not in lung tissue. Histology revealed in the heart chronic lymphocytic myocarditis with giant multinucleated cells, collaptoid glomerulopathy and necronephrosis, steatohepatitis, oedema and vascular stasis in the brain. Virus proteins were identified in macrophages of the inflammatory infiltrate, cardiomyocytes, neurons of the brain, epithelium of the proximal convoluted tubules of the kidney, which suggests virus persistence in the body.
Conclusion: Post-COVID-19 syndrome may be the result of a chronic COVID-19 infection.

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E-PS-04 | Cytopathology E-Posters

E-PS-04-001
Fine needle aspiration primary squamous cell carcinoma of the parotid gland
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Background & objectives: Primary squamous cell carcinoma of the Parotid gland is a rare aggressive malignancy (<1% of all salivary gland tumours). A case of primary parotid gland squamous cell carcinoma by fine needle aspiration (FNA) is presented.
Methods: A 82-year-old man, non-smoker presented with a progressively increasing painless mass in parotid region of 3 months duration. There was no history of prior mass in same region or in the neck. Tumour measuring 4x3 cm in the right parotid, non-tender, fixed to skin. An FNA was performed and conventional smears, were stained with Papanicolaou and Giemsa stains.
Results: (FNAC) from the lesion was composed mainly of individual or small clusters cells with large polymorphic and hyperchromatic nuclei. Cellular overlapping and moderate disturbance nuclear cytoplasmic (N/C) ratio were observed. Immunocytochemistry showed reactivity to p63. Based on the above findings, the cytological diagnosis was consistent with a primary parotid gland squamous cell carcinoma. The followed histopathological diagnosis confirmed it.
Conclusion: The cytological diagnosis of primary parotid gland tumour is effective, when the morphological, as well as the immunostaining results are taken into account and may contribute to the patient's clinical treatment.

E-PS-04-002
Fine Needle Aspiration of breast cancer in a male patient with multiple symmetrical lipomatosis
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Background & objectives: Benign symmetrical lipomatosis is characterized by multiple lipomatous nodules in the trunk or limbs that coexist with increased alcohol consumption. The nodules have extremely benign behaviour and a family predisposition.
Methods: 82 years old male with multiple nodules in the chest and abdomen, compatible with the diagnosis of multiple symmetrical lipomatosis. During physical examination a nodule with different characteristics was revealed near to the left breast nipple that was immobile and fixed to the surrounding skin. He has a history of heart failure and alcoholism. FNA conventional method using Papanikolaou stain.
Results: Microscopy examination revealed a lot of epithelial type neoplasmatic cells. These cells appeared single or in monolayer and papillary form clusters. The clusters appeared disorder of cell orientation, loss of cellular cohesion and loss of myoepithelial cells. Neoplasmatic cells have enlarged, variably hyperchromatic and usually eccentric nuclei that can vary considerably in size and shape, with coarse granular chromatin pattern and small or prominent nucleoli. All of the cells are in a bloody background. The immunocytochemistry revealed intense positive nuclear stain for ER and PR in many neoplasmatic cells.
Conclusion: The cooperation between the laboratory and clinical department is a prerequisite for the correct diagnosis in the setting of coexistence of multiple nodular lesions.

E-PS-04-003
Atrophic cervico-vaginal smears in young women: challenges and pitfalls
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Background & objectives: Intrinsic or extrinsic oestrogen produces maturation of cervical and vaginal squamous epithelium, while complete absence of oestrogen activity causes the atrophy of the squamous epithelium. Our study aims to assess various cytomorphological profiles of atrophic cervico-vaginal smears in young women.
Methods: A total of 19 conventional cervico-vaginal smears were reviewed, of women between 22-42 years old, routinely stained by the Papanicolaou method, evaluated and classified according to the Bethesda system, and interpreted as atrophic. The assessment considered the patient clinical data such as site of material collection, age, menstrual history, hormone therapy, surgery procedures, history of lesions and malignancies, radiotherapy.
Results: 7 out of 19 cases (36.84%) were between 22-30 years old, and 12 patients (63.16%) were between 31-42 years old. All of the cervical smears (100%) were cytological diagnosed as atrophic. 12 cases (63.15%) presented an inflammatory background. No smear had intraepithelial squamous or glandular associated lesions. The smears presented incomplete maturation or complete atrophy, due to low supply of oestrogen. 6 patients (31.57%) were previously diagnosed with infertility. 4 cases (21.05%) presented an associated polycystic ovarian syndrome. All cervico-vaginal smears showed small parabasal type cells, with less intermediate or mature cells. When a certain degree of nuclear irregularity was present, it raised the problem of an existing dysplastic lesion.
Conclusion: The assessment of the endocrine status of a reproductive age woman represents one of the most difficult tasks for cytological diagnosis. The interpretation of morphology and patterns of squamous cells should be cautiously made regarding endocrine status and therapeutic strategy. Endocrine cytology is a useful tool for diagnosis and treatment in particular clinical contexts.

E-PS-04-004
Improved analysis of tumour-associated circulating rare cells: simultaneous quantification of ploidy and highly multiplexed fluorescence immunostaining on standard laboratory slides
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Background & objectives: Aneuploidy is a defining feature of malignancies. We isolated circulating tumour-associated rare cells from the blood of cancer patients on standard laboratory slides, quantified their ploidy status and correlated it with immunocytomorphology on the single-cell level.
Methods: Whole blood was processed by hMX high-gradient magnetic cell separation to remove red and white blood cells. Remaining atypical

cells were characterised by Cryoimmunostaining, using antibodies directed against leukocyte (CD45), epithelial (cytokeratin, EpCAM), mesenchymal (vimentin) and proliferation antigens (H3Ser10). Aneuploidy was computed by determining integrated nuclear fluorescence intensity (DRAQ5), modifying the flow-cytometric method previously described by Darzynkiewicz.
Results: When normalising DNA content of white blood cells to 1.0 (euploidy), tumour-associated circulating cells showed hypoploidy as low as 0.3 and hyperploidy as high as 3.5 (CD45-negative cells with single nuclei) in the blood of prostate cancer patients. Coincidental findings in cancer-negative patients included CD45 and H3Ser10 positive cells with tetraploidy (DNA content 2.0±0.2), pointing to circulating leukocytes undergoing mitosis. Moreover, vimentin was diffusely overexpressed in aneuploidic CD45-negative cells in cancer patients, markedly different from very fine, filamentous vimentin morphologies observed in both euploidic and tetraploidic white blood cells.
Conclusion: Tumour-associated circulating rare cells have attracted widespread attention as potential biomarkers in cancer. However, basing diagnosis and prognosis of cancer on samples usually containing extremely limited numbers of circulating rare cells continues to pose significant challenges. The present method is amenable to automated DNA quantification as well as artificial intelligence-based immunocytomorphological analysis. It may therefore contribute to a more detailed but clinically robust characterisation of circulating rare cells on laboratory slides, improving reproducibility and scalability of cytology-based liquid biopsy diagnostics.

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E-PS-04-005
Thymoma exhibiting pleural effusion at disease progression: case report
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Background & objectives: Thymomas are uncommon neoplasms. Relapse after aggressive locoregional treatment is unfrequent. Metastatic pleural dissemination can occur. However, malignant pleural effusion is rare. We present a case report, with emphasis on differential diagnosis and relevance of cell blocks use for immunocytochemistry.
Methods: 53-year-old woman suffering from miastenia gravis was found to have a mediastinal mass. B3 thymoma diagnosis was made. Margins were affected. She underwent locorregional radiotherapy. After 4 years of follow-up, disease relapsed as pleural nodules. She started systemic chemotherapy. Stable disease was achieved. 10 months later, she developed pleural effusion. Cytospins and cell blocks were evaluated.
Results: Small/medium size atypical cells were commonly seen in between scattered mesothelial cells. They showed high nuclear/cytoplasm ratio, anisonucleosis and clumsy chromatin. Immunophenotype was positive for CD99 and TdT. It was negative for P40, PAX8, CK19 and CK20. Pleural cavity involvement by thymoma was established.
Conclusion: Thymomas can rarely give rise to pleural effusions. Diagnosis can be challenging. Detailed review of the patient's personal history and immunocytochemistry remains crucial to clarify differential diagnosis. Cell blocks, if available, can be very useful.

E-PS-04-006
Cytomorphological and clinical features of liposarcoma in peritoneal effusion
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Background & objectives: The metastasis or dissemination of sarcomas to the pleural and peritoneal effusions are very challenging for diagnosis because they can mimic carcinomas and mesotheliomas. Here a case of a liposarcoma dissemination in peritoneal effusion was presented.
Methods: A 78-year-old female patient presented complaining of abdominal pain and swelling for 3 months. Free fluid and implants were detected in the peritoneum. The sampling was made from the free fluid and send our laboratory without medical history. A PAP staining slide and a cell block obtained from peritoneal fluid by prepared with liquid-based cytology (Surepath, BD®).
Results: Cytologic examination of the peritoneal fluid demonstrated discohesive tumour cells with large, hyperchromatic nuclei, with mostly multiple nucleoli, showing prominent pleomorphism and a small number of mesothelial cells, histiocytes, mixed type inflammatory cells. When the patient's medical history explored we found that she had been operated for liposarcoma twice before and now had a mass extending to the femoral area. In the immunohistochemical examination of cell block tumour cells were positive for CDK4, S100, Calretinin and negative for BerEp4. With these findings the case was reported as "Tumour infiltration with marked pleomorphism, liposarcoma dissemination in peritoneal effusion".
Conclusion: Cytologic diagnosis of metastasis or dissemination of liposarcoma to the effusions is difficult due to its rarity and resemblance to carcinoma or malignant mesothelioma. It should be kept in mind in the differential diagnosis of malignant effusions. Workup on cell blocks helps in the differential diagnosis.

E-PS-04-007
PD-L1 expression in cell blocks
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Background & objectives: Programmed death-1 ligand 1 (PD-L1) have become an important option in the treatment of advanced cancers. In our study, we aimed to evaluate the PD-L1 staining properties and adequacy of cell blocks obtained by fine needle aspiration.
Methods: The 14 cases were included the study that PD-L1 performed to cell blocks immunohistochemically. PD-L1 (22C3)[Dako ®(22C3)] antibody was applied in an automated immunohistochemistry device (Ventana BenchMark XT.®) Membranous staining of any intensity above 1% in tumour cells was accepted as positive. The percentage of severity of staining was noted. Demographic and clinical data were obtained from pathology reports.
Results: In total of 14 cases were consisted of 11 lung non – small cell carcinoma (NSCC), 1 pancreatic ductal adenocarcinoma, 2 pleural malignant effusion (lung adenocarcinoma metastasis).
In 4 cases cell blocks were prepared with alcohol-formalin method, in 10 cases cell blocks were prepared with liquid-based cytology (Surepath, BD®) fixative (LBC-F).
PD-L1 staining results: 1 case (7.1%) was unsatisfactory, 6 cases (42.9%) were negative, 7 cases (50%) were positive (in varying degrees). The unsatisfactory case belonged to a malignant pleural effusion. The 2 of the negative cases cell blocks prepared with alcohol-formalin whereas the 4 of negative cases' cell blocks prepared with LBC-F.
Conclusion: The cell blocks prepared from cytological specimens are suitable for evaluation of PD-L1 expressions. Our number of cases is restricted, but no difference was found between the cell blocks prepared with the conventional method (alcohol-formalin) and the liquid-based cytology method in terms of adequacy and negative or positive PD-L1 staining.

E-PS-04-008
CSF diagnosis of leptomeningeal carcinomatosis as the first sign of gastric carcinoma
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Background & objectives: Cytologic examination of cerebrospinal fluid (CSF) is a diagnostic modality useful in differentiating between infectious and malignant diseases of the central nervous system. We present a case of leptomeningeal carcinomatosis from gastric carcinoma, with neurological deficits as its initial manifestation.
Methods: A 60-year-old man with no medical history, other than recent headaches, presented due to an episode of loss of consciousness without loss of bladder or bowel control. Physical examination, echocardiogram, cranial CT and MRI, intracranial arteriography and CT scan of neck, chest and the abdomen demonstrated no pathological findings. Ophthalmoscopy revealed bilateral papilledema and a lumbar puncture was carried out.
Results: CSF pressure was up to 40 cmH20 (with an upper limit of 20 cmH2O) and biochemical analysis showed an elevated protein content (1196 mg/L, normal range 150-450 mg/L). Cytologic examination of CSF revealed the presence of numerous malignant cells, single or in groups, that exhibited large, often lobulated nuclei with distinct nucleoli, high nuclear pleiomorphism and elevated nuclear to cytoplasmic ratio with rare mitotic activity. Immunocytochemical positivity for pankeratin and BerEp4 was observed in malignant cells. Gastroscopy was conducted, and histological examination of a small ulcerative lesion in the angular incisure revealed the infiltration from a poorly differentiated, poorly cohesive gastric adenocarcinoma with signet ring morphology.
Conclusion: CSF cytology may be very efficient in diagnosing secondary malignancy, even at the rare setting of unknown primary gastric carcinoma.

E-PS-05 | Dermatopathology E-Posters

E-PS-05-001
Angiomatoid fibrous histiocytoma ALK positive: a case report
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Background & objectives: Angiomatoid fibrohistiocytoma (AFH) is a rare tumour representing about 0.3% of soft tissue tumours. The biological behaviour and histogenesis are uncertain. The article aims to describe and discuss a case of ALK positive AFH that was first diagnosed as an inflammatory myofibroblastic tumour.
Methods: A 34-year-old female presented with a heterogenous solid expansile formation measuring approximately 5.0 cm with regular limits and in close contact with the adjacent muscle planes in the left superior member.
Results: A first biopsy was performed, which showed proliferation of spindle cells with light nuclear pleomorphism, with a centre presenting an organized haemorrhagic process and hemosiderin deposits. An immunohistochemical study was recommended, with positivity for desmin, vimentin and smooth muscle actin, which favoured a diagnosis of inflammatory myofibroblastic tumour. However, after a request for revision by the assistant physician, and the absence of clinical response, the panel was expanded and positivity for ALK was observed, which allowed, together with the morphological findings, to close the diagnosis of AFH ALK positive.
Conclusion: Positivity for ALK in AFH cases was unknown until the current year (2019), and very recent studies have appeared that confirm this finding. Until then, these cases showing positivity for ALK were considered to be inflammatory myofibroblastic tumour. This is a strong example of how advances in molecular and biomarker studies are accompanied by evolution and even changes in the diagnostic criteria of some diseases over time.

E-PS-05-002
Palmoplantar lichen nitidus: case report
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Background & objectives: Lichen nitidus (LN) is located mainly in the trunk and genitalia. The presence of LN in others parts of body, such as palmoplantar region and nails is rare. The article aims to describe and discuss a case of LN in an unusual region.
Methods: Female, 59 years old, reported scaly lesions on palms and plants, asymptomatic, about five months ago. The clinical hypotheses were contact dermatitis, psoriasis and dehydrosis. There were no injuries elsewhere.
Results: Histopathological examination shows a dermis containing a well-defined focal lichenoid infiltrate, composed of lymphocytes and histiocytes and located just below the epidermis, between two elongated epidermal ridges. The cornea shows hyperparaceratosis just above the affected dermal region.
Conclusion: Cases like this tend to be underdiagnosed and can be a diagnostic hint for lichen nitidus lesions in other parts of the body, as they may appear isolated or accompanied by a classic condition. So, when there is a picture of palmoplantar hyperkeratosis, one must remember and look for lichen nitidus palmoplantar.

E-PS-05-003
Fungus mycosis rich in spongiosis: a case report
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Background & objectives: Mycosis fungoides(MF)is the most common type of cutaneous T-cell lymphoma, and can present with a wide spectrum of clinical and pathological manifestations and mimic different dermatoses, such as eczema and interface dermatitis. The article aims is describe and discuss case of spongiotic MF.
Methods: Female, 32 years old, for more than 15 years with a picture of hypochromic macules disseminated in the upper and lower limbs, asymptomatic, associated with discretely scaly erythematous plaques in the trunk. The clinical hypotheses were mycosis fungoides, nevus, indeterminate leprosy and pityriasis alba.
Results: The patient presents previous biopsies with diagnoses of spongiotic dermatitis. Failing to respond to treatment, a new biopsy was performed. The new histopathological exam shows an epidermis with elongation of the epithelial ridges accompanied by moderate lymphocytic epidermotropism and the presence of extensive moderate spongiosis.
Conclusion: Among the histological variants of MF, mild spongiosis can be seen in MF in the plaque stage, but it is an uncommon finding. We present this case to show the diagnostic pitfall associated with spongiotic presentations of MF, reinforcing, once again, that the pathological clinical relationship in cases like this is of cardinal importance, as they can be routinely conducted as a reactive eczematous process.
Key words: Mycosis fungoides; Eczema; Cutaneous lymphoma.

E-PS-05-004
Necrotizing infundibular crystalline folliculitis: case report
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Background & objectives: Necrotizing infundibular crystalline folliculitis (NICF) is a rare disorder, of unknown aetiology, which was first described by Lucke et al in 1999. The article aims to describe and discuss a case of necrotizing infundibular crystalline folliculitis mimicking another follicular condition.
Methods: Female, 41 years old, with papules in the anterior trunk region. Diagnostic hypotheses were made of Grover's Disease, Miliaria and

Folliculitis. The initial biopsy was interpreted as suppurative folliculitis and after revision, deep cuts and polarized light, a definitive diagnosis was made.
Results: Histopathological examination revealed a dilated follicular ostium containing crystalline material associated with parakeratosis and the analysis of polarized light showed birefringence and special staining (Alcian Blue) detected deposition of mucin.
Conclusion: NICF presents itself as folliculocentric papules with a predilection for seborrheic areas and histologically contains deposits of birefringent crystalline material, in addition to partially necrotic follicular epithelium and parakeratosis. Previous studies suggest that NICF may be caused by complex interactions between surface microorganisms and skin-derived lipids. So, it can be concluded that NICF is a rare disorder that should be remembered as a differential diagnosis of folliculitis when seeing a deposit of crystalline material in an enlarged follicular ostio.

E-PS-05-005
Undifferentiated Pleomorphic Sarcoma: a case of unexpected histology of a forehead cutaneous lesion
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Background & objectives: Malignant fibrous histiocytoma is a neoplasm believed to originate from primitive mesenchymal cells, arising from soft tissue or bone, usually in the extremities. It is now referred to as undifferentiated pleomorphic sarcoma and is classified under the undifferentiated/unclassified sarcomas group.
Methods: We present the case of a 76-year-old woman, with multiple comorbidities, who addresses the dermatology department for a big forehead tumour. The inspection revealed a mass, highly attached to the skin, which also involved the left eyebrow, having a nodular form, increased consistency, with variable crusts on the surface, thus considering a presumptive diagnose of squamous cell carcinoma.
Results: At gross appearance it was described a skin excision that on the surface presented a nodular, ulcerated, whitish nodular formation, with the dimensions of 3.5 / 3 cm. Microscopic examination revealed the fragment of the skin showing a tumour proliferation in the form of nodules that have infiltrative appearance in the adipose and adjacent striated muscle tissue, the proliferation being consisted of fibroblastic and histiocyte-like cells, single or multiple nuclei, bizarre/monstrous nuclei, with high mitotic rate (> 10/10 HPF). The nodules have various aspects with a fasciculate or storiform pattern with the following immunohistochemistry profile: AE1/AE3-, Vimentin+, CD68+, SMA focal+, Desmin-, S100-, CD34-. Tumoral necrosis absent and clean surgical margins.
Conclusion: Undifferentiated pleomorphic sarcoma located at the head and neck is very rare and uncommon and it should be a differential of a deeper lying cutaneous/subcutaneous lesion. It frequently presents in an advanced stage in older patients. Regarding histologic diagnose, with highly undifferentiated cells, it requires a wide immunohistochemistry panel to determine tumour cell lines.

E-PS-05-006
A rare presentation of cutaneous Rosai-Dorfman disease
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Background & objectives: Rosai-Dorfman disease (RDD) is a rare benign proliferative disorder of histiocytes in the lymph nodes with or without extranodal involvement. RDD limited to the skin without nodal involvement is a very rare condition.
Methods: We report a new case of RDD of the skin over the abdomen diagnosed in the department of pathology of the University Hospital of Monastir with a review of the literature.
Results: We describe the case of a 65-year-old female with a history of cholecystectomy presenting with a nodule of 2cm in the abdominal scar. Physical examination showed no lymphadenopathy or any extracutaneous lesions. The nodule was excised for histopathological examination. Microscopically, the dermis and the subcutaneous tissue were composed of fibrosis including many clusters of large histiocytes exhibiting emperipolesis, among many plasma cells, lymphocytes and neutrophils. Immunohistochemically, the histiocytes were positive for S-100 protein and CD68 but negative for CD 1a.
Conclusion: RDD is a rare, benign condition especially difficult to diagnose due to lack of general symptoms and lymphadenopathy. Histopathologic examination with immunohistochemical staining, exhibiting characteristic and reproducible findings play a key role in establishing an accurate diagnosis.

E-PS-05-007
Multicentric reticulohistiocytosis: a rare but histopathologically and clinically distinctive non-Langerhans cell histiocytosis
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Background & objectives: Reticulohistiocytosis is a group of rare conditions, included in the C(utaneous)-group of the 2016 classification of histiocytosis. According to the most recent revision, it encompass five different clinical syndromes all characterized by a common and distinctive histopathological picture.
Methods: We describe the case of a 39-years old woman with a history of primary biliary cholangitis and diffuse severe symmetric arthralgia with synovitis, presenting to our attention with a progressive erythematous and itchy papular eruption on her ears, trunk, and limbs, worsening especially above the hand joints, after pregnancy. A cutaneous biopsy concludes for a diagnosis of reticulohistiocytosis.
Results: Histopathological examination of the skin biopsy revealed a monomorphous dermal infiltrate made of CD163+, CD68R/PGM1+, S100p+/-, CD1a-, large-sized mono-, bi- and multinucleated cells with abundant deeply eosinophilic ground-glass cytoplasm dissecting the collagen bundles and admixed with T cells and granulocytes. Occasional figures of emperipolesis of granulocytes were seen. No foamy, Touton, or Langhans cells were seen. The Ki67 index was 3%. The histopathological findings together with the history of arthropathy and the dermatological picture lead to a final diagnosis of multicentric reticulohistiocytosis.
Conclusion: First described in 1957 by Goltz and Laymon, multicentric reticulohistiocytosis is a distinctive clinical syndrome, generally affecting young women with a history of autoimmunity. In up to a third of patients, multicentric reticulohistiocytosis associates with epithelial neoplasms, contrarily to the more typical association with haematological neoplasms of multisystem non-Langerhans cell histiocytosis such as Erdheim-Chester disease. Therefore, the pathologist should be aware of the implication of this diagnosis allowing a correct and rapid clinical evaluation with exclusion of underlining neoplastic conditions.

E-PS-05-008
Benign cephalic histiocytosis: a forgotten self-healing condition of childhood
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Background & objectives: Benign cephalic histiocytosis (BCH) is an exceedingly rare dermatological disorder characterized by a papular

eruption over the head and neck region, in the first years of life, with the tendency toward spontaneous involution within three years after the clinical presentation.
Methods: An otherwise healthy 2-months-old Hispanic boy come to our attention with a skin eruption characterized by few erythematous-yellowish papules spread over his face, neck and upper trunk. Darier sign was negative. This lesion increased in number over the first year of life and later started to involute and disappear leaving only an hypopigmented halo. A diagnostic biopsy was performed.
Results: The skin biopsy revealed a cupoliform dermal proliferation made of benign-looking medium-sized mononuclear cells with ovoidal nuclei with prominent nucleoli, a small amount of nondescript cytoplasm, and poorly defined cell borders admixed with few perivascular CD3+ T-cell. No foamy, ground-glass of multinucleated histiocyte were seen. The mononuclear cells were CD163+, CD68R/PGM1+, fXIIIa+, CD14+, S100p+, CD1a-, CD117-. Although the same histological picture may be seen in the early phases of generalized eruptive histiocytosis, the clinical-pathological correlation allows concluding with a diagnosis of BCH.
Conclusion: First described by Gianotti et.al in 1971, BCH is a distinctive paediatric skin-limited histiocytosis characterized by the specific localization in the upper part of the body and a self-limiting disease course. Most patients are under a year of age and sexes are equally affected. Histopathologically BCH overlaps with generalized eruptive histiocytosis and the early phase of xanthogranuloma but displays typical comma-shaped bodies and coated vesicles at the ultrastructural examination. Correct diagnosis of BCH prevents unnecessary and possibly harmful treatment.

E-PS-05-009
Eccrine porocarcinoma of the scalp: a case report
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Background & objectives: Eccrine porocarcinoma is a rare malignant tumour of eccrine sweat gland tumour, comprising 0.005% of all malignant epithelial tumours. In this case report, we are presenting a rare case of eccrine porocarcinoma of the scalp in a 62-year-old male.
Methods: He presented with gradually increasing painless lobulated mass at the parietal region of the scalp. It was 4,5x4x3 cm in dimension and not fixed with underlying structures. CT scan of the brain did not show any intracranial extension and no calcification was noted in the tumour. Wide local excision was applied with a 1 cm margin around it.
Results: Grossly, the specimen was exophytic, pigmented, and irregular in appearance with surface ulceration. The cut surface of the tumour showed a grey-white appearance. Microscopic examination revealed an epidermis with an ulcerated appearance in the focal area. Malignant cells in lobular masses and islands were composed of large, basaloid neoplastic cells with hyperchromatic nuclei. Lobular masses or islands with cystic cavities connected with the epidermis and infiltrated the dermal tissue. The islands were separated by thick fibrous septae. There were many mitotic figures along with duct formation. Immunohistochemistry showed positive immunostaining for P63, P16, p53 and negative immunostaining for BEREP-4, CD10. CEA and EMA were positive in the duct formation.
Conclusion: The case was diagnosed as eccrine porocarcinoma. Eccrine porocarcinomas even rarer but pathologists should consider this neoplasm in the differential diagnosis of malign skin tumours.

E-PS-05-010
Angiolymphoid hyperplasia with eosinophilia with multinucleated cells: a different histomorphologic presentation
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Background & objectives: Angiolymphoid hyperplasia with eosinophilia (ALHE), also known as epithelioid haemangioma is a benign disease presenting with red-brown papules or nodules, usually located at the head and neck region.
Methods: Here we report a 61-year-old female patient presented with multiple nodules located at the scalp which were present for several years. These nodules were diagnosed clinically as dermatofibroma. Three of the nodules were excised and examined pathologically.
Results: Histopathologic examination revealed ill-circumscribed, evident vascular proliferation with noticeably plump epithelioid endothelial cells with intracytoplasmic vacuoles. These endothelial cells were positive with CD31 and CD34. There were inflammatory infiltrate dominated by eosinophils with lymphocytes, isolated plasma cells, and histiocytes around the vessels. Mitoses and pleomorphism were not seen as expected. In this case, besides these common histomorphologic appearances there were several interstitial multinucleated giant cells. These multinucleated cells were positive with CD68 therefore histiocytic origin was proved. The presence of multinucleated giant cells in ALHE has rarely been described, we were able to find only three previous case reports.
Conclusion: ALHE is a benign lesion, so complete surgical excision is recommended as the optimum treatment, without negative surgical margins recurrences might occur. ALHE's aetiology is not clearly known, infection, hormonal factors, and trauma are the suspected reasons. The uniqueness of this case was the presence of multinucleated giant cells, therefore we should be aware of different histomorphological features in these lesions.

E-PS-05-011
A rare phenomenon: aesthetic complaint reveals undiagnosed metastatic colonic adenocarcinoma in asymptomatic patient
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Background & objectives: Cutaneous colonic adenocarcinoma metastases are extremely rare clinical events and they pose a diagnostic problem, as their histomorphology highly resembles that of adnexal adenocarcinoma NOS. Our purpose: gaining further knowledge about the differential diagnosis of skin tumours with glandular differentiation.
Methods: Our Department of Pathology received a cutaneous fragment, samples from which were fixed with 10% buffered formalin and were processed by conventional histopathological methods, using paraffin embedding, sectioning and Haematoxylin–Eosin (HE) staining. Afterwards, the sections were deparaffinized and prepared for immunohistochemical staining, the following markers having been used: CDX2, GATA3, CK7, CK20 and HER2.
Results: We report a 68-year-old female patient with no significant history, who presented with a 1 cm ulcerated skin nodule localised on the frontal right hairline. Upon gross examination, the lesion exhibited elevated, poorly circumscribed margins and solid consistency. The microscopic findings consisted of a poorly circumscribed malignant proliferation of atypical epithelial cells, exhibiting duct and gland formation affecting the superficial and deep dermis. In order to differentiate between an adnexal adenocarcinoma NOS and a metastatic lesion, an MRI scan was performed which showed a colonic tumoral mass and hepatic and vertebral metastatic nodules. Intensely positive CDX2 immunohistochemical staining confirmed the diagnosis of colonic adenocarcinoma metastasis.
Conclusion: Cutaneous tumours with glandular differentiation represent rare entities that require a thorough and diligent examination by means of histopathological and immunohistochemical study. Cutaneous colonic adenocarcinoma metastasis are also exceptionally identified, but always

indicate an advanced stage of the disease that accounts for a poor prognosis.

E-PS-05-012

Atypical Spitz nevus – the childhood dilemma – a case presentation

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Background & objectives: Atypical Spitz nevus, defined as borderline lesions from the histological point of view, are described as Spitz tumours with at least one atypical feature, which can resemble the histological characteristics of the melanoma. The lesion is mostly found in childhood.
Methods: We present the case of an 11-year-old female patient which was clinical diagnosed with low extremities haemangioma. The tumour was surgical removed and sent to the Pathology Laboratory for histopathological diagnostic. We have performed H&E staining and immunohistochemistry (S100, SOX10, Melan A and HMB45) on the received tissue samples.
Results: Grossing revealed a tumour of 13x12x5mm with a cell proliferation in the entire dermis and hypodermis in the form of nests with vertical disposition towards the basement membrane, consisting of spindle, rhomboidal and epithelioid cells, the cell nests varying in size. Cells in the superficial dermis are large and rhomboidal, in the middle dermis are slightly discoid and have a polygonal shape and in the deep areas become oval with a deep maturation phenomenon and no pagetoid migration. About 3-6mitoses 10HPF/(40x) are present in all layers of the dermis. Immunohistochemically, cells are SOX10,S100 positive and HMB45 negative. MelanA is focally positive in superficial and middle dermis. Ki67 is below 1%.
Conclusion: Due to the fact that the tumour does not present the histopathological features of Spitz nevi and neither the criteria for melanoma, and also taking in consideration the tumour dimensions, patients age (11 years), the localization on the low extremities, the nodular aspect, the extension to the deep dermis and hypodermis and the presence of mitoses, the lesion described as atypical Spitz tumour must be clinical and paraclinical supervised for possible recurrences and adequate treatment.

E-PS-05-014

Osteo-nevus of Nanta (complete osseous metaplasia in a benign melanocytic nevus): an uncommon phenomenon

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Background & objectives: Nanta's osteo-nevus is a rare tumour characterized by osseous metaplasia in a nevus. Heidesfield described it in 1908, and it was published in 1911 by French dermatologist André Nanta. Very few cases have been reported so far in the literature.
Methods: We present the case of a 31-year-old woman who presented to her general practitioner with a mole in the chin region. The tumour was surgically excised and submitted to the Pathological Anatomy department for microscopic evaluation using suitable techniques. The "en dome" tumour had an irregular surface of brown-grey colour, was round-oval, measuring approximately 8/8/3 mm.
Results: The tumour showed a proliferation of medium and large nevus cells with no cyto-nuclear atypia or mitotic figures. Nevic cells formed nests, clusters and cords of varying sizes in superficial and deep dermis with focal involvement of the dermo-epidermal junction. Some nevus cells were highly pigmented, while others are multinucleated. Tumour proliferation is characterized by the maturation of nevus cells from the deep dermis to the surface, with multiple Wagner-Meissner type neurotization, pseudolymphatic spaces, and unusual lipomatous dystrophy of some nevic cells. A large region with complete bone metaplasia was found in the deep area of the tumour proliferation, composed of haversian-type bone lamellae and dystrophic calcified bone spikes.
Conclusion: The histological diagnosis was osteonevus of Nanta. The immunohistochemical study confirmed the benign nature of the lesion, with positivity for the markers such as S-100, MART-1, SOX10 and a low Ki67 index. The phenomenon does not appear to be related to a poor prognosis, even though bone metaplasia has been described in other skin tumours, some malignant such as melanoma. Therefore, the findings of ossification in excised melanocytic lesions should not be underestimated.

E-PS-05-015

Bednar tumour with peculiar fibrosarcomatous features

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Background & objectives: Bednar tumour is an uncommon pigmented variant of dermatofibrosarcoma protuberans. This tumour is mostly seen in adults and has a predisposition to affect the shoulder region. We report a rare case of Bednar tumour in a 72-year-old female patient.
Methods: A 72-year-old female presented with right shoulder swelling present since few months and gradually increasing in size. A complete excision was performed. The tumour was just beneath the skin, uncircumscribed, non-capsulated extending into the deep subcutaneous fat and measuring 6.3 × 4 × 5.7 cm. Grossly, focal areas of pigmentation were noticed towards the periphery of the tumour.
Results: The tumour was a spindle cell lesion abutting the epidermis and invading the underlying dermis and subcutaneous fat. The tumour cells had a storiform grow pattern. There were scattered pigment-laden cells throughout the lesion. On higher magnification, the spindle cells were monomorphic with eosinophillic cytoplasm and plump nuclei with tapering edges. A tumour contingent has been identified consisting of cells with high grade nuclear pleomorphism and relatively common monstrous-looking bizarre cells. The tumour was mitotically active. Also, areas of necrosis or haemorrhage were noted. The above-mentioned features lead to the diagnosis of Bednar tumour with fibrosarcomatous features. Currently the patient is on regular follow-up without any recurrences.
Conclusion: To conclude, though rare, it is important for the histopathologists to be aware and recognize this unusual entity and distinguish it from other pigmented spindle cell lesions. It is also important to mention the fibrosarcomantous transformation of these lesions to correctly estimate the risk of recurrence.

E-PS-05-016

Atypical hidradenoma; a rare case report

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Background & objectives: Hidradenomas are benign dermal, adnexal neoplasms that are nodules with cystic foci in the dermis; however, atypical hidradenomas are lesions that are thought to have borderline characteristics including cytological atypia or lack of circumscription, higher rate of recurrence, and malignancy.
Methods: 57-year- old male patient presented with a subcutaneous mass on his left arm. Excisional biopsy was performed with a clinical diagnosis as a benign haemorrhagic cyst.
Results: Grossly, 4x3x2,1 cm sized, subcutaneous mass, with a central cyst containing papillary structures on the inner surface was observed. Histological examination revealed, a dermal tumoral lesion with lobules consisting of cystic and solid areas There was no obvious infiltrative growth pattern. Tumour cells had clear eosinophilic cytoplasms, round nuclei, and prominent nucleoli. Immunohistochemical studies revealed positivity with EMA and p53. Ki67 index was 5-6%. The final diagnosis was Hidradenoma, but it was noted that it should be managed clinically as

atypical hidradenoma/hidradenoma of uncertain malignant potential due to the mitotic index> 2/10 HPF, the presence of suspicious lymphovascular invasion, and the progression of small irregular tumour layers in one area.
Conclusion: Atypical hidradenomas may exhibit worrisome histological features for increased risk of recurrence and possible malignant potential. Therefore, if focal atypical features such as focal border irregularities, nuclear pleomorphism, and increased mitotic activity are observed, atypical hidradenoma should be kept in mind.

E-PS-05-017
A rare variant of lichen planus; lichen planus pigmentosus-inversus; a case report
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Background & objectives: Lichen planus pigmentosus (LPP) is an uncommon variant of lichen planus. However, LPP-inversus, is an extremely rare variant of LPP and occurs as dark-brown macules and patches in the axilla, inguinal creases, flexural areas.
Methods: A 52-year-old woman presented to the dermatology clinic with a 5-months history of asymptomatic, hyperpigmented, unilateral lesions in the groin. Physical examination revealed 2 brownish patches with well-defined borders on the left inguinal fold. A skin punch biopsy was performed from one of the patches.
Results: Histopathological examination revealed, orthokeratotic atrophic epidermis, ill-defined rete ridges (loss of rete ridges), vacuolar basal cell change in the basal layer. There were mild spongiosis and necrotic keratinocytes (Civatte bodies) in the epithelium. Band-like mild mononuclear infiltration was observed at the dermo-epidermal junction, while perivascular inflammatory infiltration, disperse pigment incontinence, and melanophages were observed in the upper part of the dermis. The diagnosis of lichen planus pigmentosus inversus (LPP-inversus) was confirmed on account of clinical appearance and histopathological findings.
Conclusion: LPP-inversus is a rare variant among all clinical subtypes of lichen planus. Quite a few cases were reported since this clinical entity had been defined. LPP-inversus should be noted in the differential diagnosis of cutaneous pigmentation, especially in the flexural regions. Histopathological findings are almost similar with LPP; therefore, the diagnosis should be made by histopathological and clinical correlation. Briefly, one more LPP-inversus case report has been added to the literature known to date through our case report.

E-PS-05-018
Primary extramammary Paget's disease: a case report
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Background & objectives: Primary extramammary Paget's disease is a rare cutaneous malignancy that accounts for 6,5% of all cutaneous Paget's disease. It originates in the epidermis or apocrine sweat glands and is not associated with an underlying carcinoma.
Methods: A 75 years-old woman presented to our hospital having an erythematous lesion on the scalp for 3 years, that lately has enlarged. Surgical excision was performed.
Results: The skin specimen revealed a tumour measuring 1,8cm in greatest diameter, with a white cut surface. Microscopical examination showed malignant glandular epithelial cells with abundant and clear cytoplasm, usually containing mucin and pleomorphic hyperchromatic nucleus, organized in nest-like or gland like structures located intradermally, with invasion of the papillary and reticular dermis, invasion of adnexal structures and pagetoid spread to the epidermis. Immunohistochemically the tumour cells stained positive for CK7, Cam5.2, EMA, pCEA, GCDFP-15, ERBB2(3+), GATA3 and for S100, Mart-1, HMB45,CK5/6, CK20, ER, PgR, Ca125, p63, NF were negative.
Conclusion: Given to the location, the histological-morphological and immunohistochemical features and the free history of malignancy, a diagnosis of primary extramammary Paget's disease was performed. The patient underwent wider local excision and 8 months after is free of recurrence.

E-PS-05-019
EBV-positive lymphoproliferative disorder MTX-related in a patient with ankylosis spondylitis
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Background & objectives: Ankylosing spondylitis (AS) is a chronic systemic inflammatory disease of the axial skeleton. Recent meta-analysis has calculated an increased risk for lymphoma in patients with AS. The main theory about lymphomagenesis linking rheumatic diseases is the continued immune stimulation.
Methods: We present the case of 86-year-old woman with erythematous subcutaneous nodules on her right arm. Careful anamnesis revealed 35-year history of ankylosis spondylitis (AS), with negative HLA-B27, treated with corticoids and methotrexate (MTX). Four consecutive skin punch biopsies were obtained with a diagnosis of no-necrotizing granulomatous dermatitis and panniculitis. The treatment given was unhelpful and another biopsy was performed.
Results: Histologically, the last skin punch was characterized by no-ulcerated epidermis, dermal proliferation of medium-sized lymphocytes accompanied by abundant histocytes in perivascular and periadnexal areas. Some scattered eosinophils were also seen. Hypodermis showed a panniculitis pattern with small granulomas. Immunohistochemically neoplastic cells were: CD20(+)/EBV(+)/CD56(-)/CD10(-)/BCL6(-), with confirmed monoclonality. The diagnosis of EBV-positive polymorphic lymphoproliferative disorder MTX-related was made. Withdrawal of MTX was decided with skin lesions improvement.
Conclusion: MTX is probably the most common antirheumatic drug, causing a iatrogenic immunosuppression and reactivate latent EBV infection. Even though the fact that multiple research groups concluded that MTX is not associated with increased risk of lymphoma, spontaneous regression of these lymphoproliferative disorders in some cases after drug withdrawal underscores the putative pathogenic role of MTX in EBV positive-LPD.
This case shows the relevance of conducting multiple biopsies in a patient treated with immunosuppression therapy, to rule out a lymphoproliferative disorder.

E-PS-05-020
Music box keratoderma: an odd tune
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Background & objectives: Music box keratoderma or spiny keratoderma is a rare dermatosis characterized by multiple discrete papules of the palms and soles, rendering an appearance similar to old music boxes. Hereditary and paraneoplastic cases were reported but aetiology is still largely unknown.
Methods: We present the case of a 68-year-old female without relevant personal medical history. She was referred to our institution due to small lesions in her hands, associated with sensation of roughness, since 5 years ago. There was no known family history of similar complaints. Physical

examination revealed several punctiform and keratotic papules in her palms and soles, which were biopsied.
Results: On histopathological examination, skin with orthokeratosis and focal columns of parakeratosis arising predominantly from the interadnexal epidermis could be found. These columns were associated with depression of the underlying epidermis. Additionally, a decrease in both the thickness of the granular layer and in the number of keratohyalin granules was identified in these areas, without any dyskeratosis or vacuolar changes. There was no significant inflammatory infiltrate and no signs of malignancy. From these findings, the patient was diagnosed with music box keratoderma. This is a rare and still mysterious entity and we reviewed the most recent findings in medical literature, especially regarding its possible aetiologies.
Conclusion: Music box keratoderma is a curious entity which has been mainly associated with malignancies, including lung and colon cancer, although there is still debate if it constitutes a true paraneoplastic condition. Some other cases are hereditary or associated with non-neoplastic diseases, such as type IV hyperlipoproteinemia and Darier's disease. Differential diagnosis includes arsenical keratosis, porokeratosis, multiple filiform verrucae and Buschke-Fischer-Brauer disease. Patient complains are essentially cosmetic and a feeling of palmar rugosity. No malignization of these lesions has been reported.

E-PS-05-021
Post-transplant Squamous Cell Carcinoma with Rhabdoid Phenotype, a case report
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Background & objectives: A 63-year-old man with history of deceased donor renal transplantation four years previously due to chronic kidney disease. He was immunosuppressed on Ciclosporin and Mycophenolate Mofetil treatment. He presented with a recent 10mm keratotic nodule on the crown.
Methods: Microscopically it showed an ulcerated solid nodular tumour composed of dyscohesive large nonkeratinizing round plasmacytoid/rhabdoid cells with abundant eosinophilic cytoplasm containing filamentous hyaline inclusions, eccentric nuclei and prominent nucleoli, few osteoclast-like giant cells and desomosomes. There was a focal area of a moderately-differentiated squamous cell carcinoma (SCC). Atypical mitotic count was up to 20 per 10 HPF. No necrosis was seen.
Results: Immunohistochemical stains AE1/AE3, CK5, p63 and CD138 were diffusely positive in the tumour. CD10, Calponin, CD117 and CD68 had scattered pattern. CD31, CD34, S100, Desmin, SMA and Melan A were negative. INI stain was retained. Ki67 was high (>70%). The diagnosis of post-transplant squamous cell carcinoma with rhabdoid phenotype was made. Previously he also had one SCC and a keratoacanthoma. Later on he developed two SCCs, no specific type, of the scalp three years later and in the forehead four years later. Six years later he developed basal cell carcinoma in his forearm. On literature review, six cases of the skin and four of the oral cavity were reported.
Conclusion: We present a rare case of immunosuppression-associated SCC with rhabdoid phenotype (ten previous cases reported) and osteoclast-like giant cells (reported in one previous case). Their clinical behaviour is noted to be more aggressive than their usual counterparts. In our case the patient remains alive after six years. It is advisable to look for unusual patterns of SCC in post-transplant patients on immunosuppression. Desmosomes and areas of squamous differentiation may or may not be present within the tumour.

E-PS-05-022
Trichoblastoma with malignant transformation arising in a young patient, a case report
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Background & objectives: A 28-year-old flight hostess presented with a lesion in the vertex, enlarging in size over two years. She was sent home by her GP with the diagnosis of seborrheic keratosis. There was no family history of similar lesions.
Methods: Clinical details received from the dermatology clinic stated a nodular dermal tumour in the scalp vertex arising in a background of naevus sebaceous measuring 15mm in diameter. No palpable regional lymph nodes were felt.
Macroscopically it was a skin ellipse measuring up to 21 mm with a hair-baring well-circumscribed keratotic pinkish surface nodule measuring 13x10mm.
Results: Microscopy showed an infiltrating tumour, partly connected to the epidermis and hair follicles with nests of basaloid cells expressing central necrosis and areas of hyalinised globules. It had intermediate-sized cells with basophilic nuclei and frequent mitosis with no peripheral palisading, retraction artefact or mucin deposition. No melanocyte colonisation, ductal or sebaceous differentiation was noted. The deeper part of tumour showed infiltrative smaller nests and cords of cells with no significant atypia and foci of calcification surrounded by fibrotic stroma, representing the begin background of a trichoblastoma.
Immunohistochemistry showed staining of the tumour with CK7 and CAM5.2.
It was negative for EMA, CEA, CK20, S100, SMA, CD56, Chromogranin A and Synaptophysin.
Conclusion: We presented a case of a young woman with trichoblastic carcinoma arising in a trichoblastoma. Trichoblastic carcinoma is a rare follicular tumour with only a handful of cases reported, arising from longstanding trichoblastomas (mean age of 70 years) including cases of Brooke-Spiegler's syndrome. It is rarer in young patients. They can metastasise to regional lymph nodes. Wide local excision and long term follow up is advised. Our patient is well and alive after two years and no metastasis is reported.

E-PS-05-023
Case of melanocytic neurofibroma associated with neurofibromatosis
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Background & objectives: Melanotic (pigmented) neurofibroma is a rare tumour of neural crest origin demonstrating schwannian differentiation, with production of melanin granules. The authors report a case of melanotic neurofibroma arising in neurofibromatosis.
Methods: A 17-year-old girl with neurofibromatosis type 1 is presented with a large hyperpigmented plaque on the leg. Significant infiltration and thickening of the foot dorsum and ankle were present. Also she had many café au lait spots and numerous neurofibromas. Incisional biopsy was performed.
Results: In histological examination, the tumour was characterized by benign spindle cells with schwannian differentiation and located dermis and subcutaneous fat tissue. In some areas, Wagner–Meissner-like bodies were visible. Immunohistochemistry demonstrated staining with antibodies to S100, SOX10, Melan-A, HMB45, and CD34.
Conclusion: Final diagnosis was melanocytic neurofibroma. It is very important to distinguish this tumour from other pigmented tumours, especially blue nevus and malignant melanoma.

E-PS-05-024
Histopathological outlook for BAP1 tumour predisposition syndrome - case report
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Background & objectives: Germline mutations in the BRCA-1 associated tumour protein 1 (BAP1) increase susceptibility to mesothelioma and other cancers. The prevalence of germline BAP1 mutations in the general population is not known.
Methods: We present the case of a 30-year-old woman who presented to the dermatologist with a few, similarly looking cutaneous lesions located on her face. On examination, the patient had three skin-coloured papules located preauricular, on her cheek and on the upper lip. Affirmatively, they appeared during adulthood, approximately 2 and a half years prior and have increased in size.
Results: On gross examination, the first two lesions were polymorphic: brown to pinkish, dome-shaped nodules and papules. Histopathological examination reveals an intradermal melanocytic proliferation with two populations of cells. The first one consists of small mature-appearing melanocytic cells resembling common intradermal nevi, and the second one is a proliferation of large epithelioid (spitzoid) melanocytes. Immunohistochemistry shows checkerboard p16 staining pattern, Ki-67<1%, HMB-45 positivity and loss of BAP1 in the large epithelioid cells. The genetic tests exposed a germline deletion in the BAP1 gene. Family history reveals that the patient's mother died at 44 years old from a meningioma. In addition, the patient's aunt was diagnosed with mesothelioma.
Conclusion: To conclude, we have reported histopathological features of two cutaneous melanocytic tumours with loss of BAP1 expression together with a germline BAP1 mutation in a case of BAP1-associated cancer susceptibility syndrome. If a Wiesner nevus is revealed and the patient has both multiple cutaneous tumours, with or without relevant family history, genetic tests for tumour predisposition syndrome are recommended.

E-PS-05-025
Metastatic malignant melanoma on 7-year-old Indonesian girl: a rare case report
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Background & objectives: Malignant melanoma in childhood being even rarer in those younger than 10 years of age. The diagnosis of melanoma in childhood is based upon histopathology and immunohistochemical can be challenging because of its clinical presentations possibly differing from adult melanoma.
Methods: We report a 7-year-old girl presenting with skin nodule that developed on the congenital melanocytic nevus on her left femur and an inguinal lymph node enlargement on the right side, suspicion of a metastasis malignancy. Histopathology examinations, as well as immunohistochemical, were performed on the skin nodule and FNAB was performed on the inguinal lymph node to establish the diagnosis.
Results: Histopathology and FNAB examinations revealed pleomorphic cells with occasional cytoplasmic pigment and positive expressions of immunohistochemical melanocytic marker consistent with the diagnosis of metastatic malignant melanoma in childhood.
Conclusion: Given the rarity of malignant melanoma in childhood, it is important to keep in mind that careful analysis of histologic features, as well as additional information provided by immunohistochemistry, should allow for a correct diagnosis.

E-PS-05-026
Cutaneous myxoid perineurinoma: a case report and a review of literature on a rare entity
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Background & objectives: Perineurioma is a peripheral nerve sheath tumour that rarely develops in the dermis. It presents mainly on the lower limbs of middle-aged adults, with female predilection. Perineuriomas remain underrecognized due to variable morphology and low frequency reporting in the skin.
Methods: Here we present a case of a 33-year-old male that was referred by the primary care doctor due to a 2cm buttock nodule with a year of evolution, that experience a recent growth. Surgical resection of the lesion was performed with the clinical suspicion of a haemangioma.
Results: We received a 2x1,4x0,6cm cutaneous specimen with 1,4x1,2cm epidermal nodular lesion, gelatinous-yellowish cut surface. Histological examination shows a polypoid unencapsulated tumour centred in the dermis. The lesion is composed by myxoid areas of bland epithelioid cells with roundish nuclei, indistinct nucleoli and moderately abundant eosinophilic cytoplasm and loose collagenous areas of bland elongated spindle cells with tapered nuclei and scant bipolar cytoplasm. In the spindle cell component, the neoplasia has a storiform growth pattern, with focal perivascular whorls and less myxoid stroma. Immunohistochemically, the tumour cells are EMA and CD34 positive and S100-protein negative.
Conclusion: Perineurioma is a benign peripheral nerve sheath tumour with perineural differentiation that develops commonly in subcutis or deep soft tissue and rarely in the dermis, which lowers the awareness for this entity. Furthermore, cutaneous myxoid perineurinoma is a lesion easily confused with other diagnoses, such as myxoid fibrous histiocytoma, low-grade fibromyxoid sarcoma or myxoid neurofibroma. The knowledge for this entity is important for correct diagnosis and to avoid inappropriate therapy.

E-PS-05-027
Sclerosing cellular neurothekeoma: a case report
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Background & objectives: In the last WHO classification of skin tumours (2018) the cellular variant of neurothekeoma was distinguished as a separate entity, which is negative for S100 and GFAP. We present a tumour with unusual morphological features resembling a cellular neurothekeoma.
Methods: A 20-year-old male patient was operated on for painful node of the skin of the left ankle joint measuring 1.0 cm in diameter. The tumour was slightly protruding above the surface without altering the surface of the skin itself. A clinical diagnosis of fibroma was made.
Results: Microscopically, the tumour was located in the dermis and subcutis. It did not have a capsule but had fairly well defined boundaries. Uniform spindle cells with indistinct cell borders without atypia were arranged in bundles (being longitudinally oriented), lobules, sometimes creating a network-like pattern around the sweat glands and blood vessels. They were regularly high-cellular along the periphery of the cell streams, and fibrosis and hyalinosis increased towards the centres. Cords of tumour cells were separated by fibrous stroma with irregular myxomatosis. Immunohistochemical staining was positive for CD34, Vimentin, β-catenin and negative for Desmin, SMA, S100, GFAP, Calponin, CK, EMA. The proliferative index determined by Ki-67 was up to 10%.
Conclusion: In our opinion, the presented tumour is a rare variant of cellular neurothekeoma with unusual ordered sclerosis and is worthy of discussing by specialists. We were unable to find analogs in the available literature. The retiform «neurotic» growth pattern around the appendages of the skin and blood vessels in combination with histological structure and the immunophenotype, which suggests a fibroblastic differentiation, are more consistent with the cellular neurothekeoma.

E-PS-05-028
Laser cosmetology imitation via rat's model
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Background & objectives: Laser equipment is intensively developing and used in dermatology and cosmetology. It needs an animal-based model for practicing new techniques. The purpose of the investigation is to establish a rat-based model for the study of laser impact on skin.
Methods: 12 black-coated laboratory rats and 6 white-coated ones were used to test three following power modes of Erbium: Yttrium, Aluminium, garnet (Er:YAG) Fotona laser (wavelength 2940 nm). Single pulses with power 1,2, 2,0, 3,0 J/cm2 were used. Macroscopic estimation and a histological methods on the 7th day after exposure were used.
Results: We found laser effects to be individual, thus 8 rats with black coating optimal exposure were obtained with 3,0 J/cm2 power and 4 rats with 2,0 J/cm2 impact power. 2 black rats were discharged from the experiment because of excess, traumatic laser impact on the skin. White rats obtained 2,0 and 3,0 J/cm2 power. Macroscopical changes were similar to clinical appearances with humans after depigmentation and peeling applications of the laser. Histologically we observed acanthosis with 2-3 rows of cells within stratum spinosum, granulosis with the appearance of the more prominent granular layer, and increased amount of fibroblasts in papillary derma, which correspond to known therapeutic effects of Er:YAG laser.
Conclusion: 1. Rat's model can be used for further investigation of laser impact on skin. 2. Each particular type and model of laser appliance need to be practiced with a rat line. 3. Establishing laser pulse properties may be challenging and requires genetically close rats, used in the model; otherwise, laser dose needs to be established individually.

E-PS-05-029
Collision tumour of an invasive squamous cell carcinoma and atypical fibroxanthoma
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Background & objectives: Collision tumours are tumours where two histopathologically distinct tumours develop adjacently maintain distinct borders. To our knowledge, we present the first case in the literature of a collision tumour between an atypical fibroxanthoma and an invasive squamous cell carcinoma.
Methods: Clinical case review and review of the topic in published clinical literature.
Results: We present a case of an 83-year-old man with a four-month history of a rapidly progressive nodule on the vertex of the scalp and underwent wide local excision. Histological examination showed two adjacent tumour morphologies within the nodule. The first tumour was a well differentiated crateriform squamoproliferative lesion with al keratin horn. This showed diffuse expression of AE1/AE3, CK5/6 and p63 and was diagnosed as a keratoacanthoma-like squamous cell carcinoma. The second tumour was composed of fascicles of atypical spindle cells. This tumour was negative for AE1/AE3, CK5/6, p63, S100, Melan-A, desmin, SMA, CD31 and CD34 and positive for CD10, and was diagnosed as an atypical fibroxanthoma (AFX).
Conclusion: Collision tumours in skin are uncommon. Our case represented a collision tumour between an atypical fibroxanthoma and an invasive squamous cell carcinoma. This case demonstrates the importance of detailed histological examination and the role of immunohistochemistry in making the final diagnosis.

E-PS-05-030
Cancer of unknown primary site may always be melanoma disregarding morphologic appearance – case report and review of literature
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Background & objectives: Cancer of unknown primary site remains a demanding condition, as it is by definition metastatic, has a wide range of biological activity and it is often therapy-resistant. This case report aims to document a challenging diagnosis.
Methods: A 46-year-old man with no previous history presented to our hospital with fast-growing axillary and inguinal masses, which were diagnosed as adenopathies, were surgically removed and sent to the Pathology Department. The PET-CT showed multiple osseous, pulmonary and adrenal metastases.
Results: Histopathological examination revealed two massive nodal metastases composed of malignant sarcomatoid and epithelioid cells, resembling a poorly differentiated carcinoma. Both components had a common and a distinct immunophenotype. The sarcomatoid component stained positive for HMB45, T311, MelanA, with a weak-to-absent CK7 expression. The epithelioid component was AE1/AE3, CAM5.2, CD56, synaptophysin, inhibin positive, with a weak-to-absent HMB45, T311 and calretinin expression. All tumour cells were positive for S100, SOX10 and MiTF. Various antibody panels were performed to rule out haematolymphoid, smooth muscle, skeletal muscle, pulmonary and mammary origins. The final diagnosis was metastatic amelanotic melanoma with aberrant cytokeratin expression and unknown primary site.
Conclusion: This case report serves as a reminder that melanoma is the great mimicker. Malignant melanoma with abnormal cytokeratin, intermediate filament or neuroendocrine marker expression can be easily confused with carcinomas, sarcomas or neuroendocrine tumours. It is essential to be aware of the existence of unusual immunophenotypes in order to make an accurate diagnosis.

E-PS-05-031
Polypoid Merkel cell carcinoma of the eyelid
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Background & objectives: Merkel cell carcinoma (MCC) is an uncommon skin tumour usually arising in the head and neck of elderly people. Although clinical presentation is diverse, polypoid configuration has been rarely reported and may pose diagnostic difficulties.
Methods: A 93-year.old man presented with a 1.5cm reddish, pedunculate lesion on his right upper eyelid, hindering his vision. Histological examination revealed a densely cellular neoplasm of small, round cells, with high proliferative activity. Immunohistochemistry showed diffuse staining for synaptophysin and chromograninin, while TTF1 was negative. Cytokeratin-20 showed the characteristic dot-like pattern. Final diagnosis was polypoid MCC of the eyelid.
Results: MCC is a rare but aggressive neuroendocrine carcinoma of the skin, which usually affects older Caucasian men on the head and neck. Main risk factors are sun exposure, immunosuppression and advanced age, but Merkel cell polyomavirus is also known to play a role in its pathogenesis. Palpebral involvement accounts only for 2.5% of cases an it usually presents as an asymptomatic, solitary, erythematous lesion located on the upper eyelid. Differential diagnosis includes both benign and malignant lesions, such as chalazion, basal cell carcinoma, lymphoma or keratoacanthoma. Polypoid presentation has been described only exceptionally and may be easily interpreted as a banal lesion, mainly a large skin tag.
Conclusion: These cases are usually diagnosed only after histological examination, which demonstrates the typical features of MCC. Immunohistochemistry is confirmatory. In our case, clinical differential diagnosis included MCC among many other options. Both histopathology and immunohistochemistry were typical of this condition. In conclusion, we report an unusual case of polypoid MCC arising on the eyelid. This unusual configuration is not usually diagnosed clinically and it is only confirmed after histopathological examination.

E-PS-05-032

Squamoid eccrine ductal carcinoma (SEDC) of the right foot with locoregional lymph node metastasis

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Background & objectives: SEDC is a rare skin carcinoma with biphasic histological appearance, characterized by squamous and adnexal (sweat duct) differentiation. SEDC has usually a plaque or nodular appearance and develops at sun-exposed skin areas of elderly men.
Methods: A 43-year-old woman, ballet dancer, presented with an ulcerated lesion at the great toe of her right foot, growing slowly for three years. The lesion had a maximum diameter of 1,7cm and was localized at the nail bed with extension to the skin of the distant phalanx. Biopsies were taken from these sites.
Results: Histological examination revealed the presence of Bowen disease and invasive squamous cell carcinoma (SCC) in the superficial dermis. However, the presence of two tumour foci with ductular-glandular morphology and CK7/EMA-positive immunophenotype in the deep dermis raised the suspicion of SEDC. A wide excision with locoregional lymphadenectomy was subsequently performed and metastatic spread was identified in two regional lymph nodes. The metastatic foci was representative of the biphasic nature of SDEC; it consisted of a moderately-differentiated SCC component and an adenocarcinoma component. The latter had prominent nuclear and cytological atypia, numerous mitoses and focal presence of mucin. The glandular tumour cells were immunopositive for CK7, EMA and CEA.
Conclusion: This is a case of SEDC in unusual location and age It highlights the difficulty of diagnosing SEDC in superficial biopsies where the ductal component may not be clearly represented. In contrast with the skin biopsies, the two components of SEDC were evident in the lymph node metastasis, confirming our initial diagnosis. Although distant metastasis is very rare, there is considerable chance of local lymph node metastasis and recurrence. The patient underwent radiotherapy and is disease-free, two years after treatment.

E-PS-05-033

The many faces of cutaneous spindle cell tumours: when should we consider melanoma?

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Background & objectives: Spindle cell melanoma is a rare and insufficiently described lesion, hence easily confused with other more frequent spindle cell neoplasms of the skin. In such cases, extensive immunohistochemical analysis should be performed in order to establish the diagnosis.
Methods: The aim of this report is to gain further insight into this rare variant of melanoma, in order to provide a correct diagnosis and the best strategy therapy. As standard histopathological examination cannot accurately identify spindle cell melanomas, extensive immunohistochemical analysis is crucial for the differential diagnosis.
Results: We report the case of a 75-year-old male who presented to the hospital with a latero-cervical pigmented lesion. Standard histopathological exam revealed a spindle cell neoplasia with a low mitotic index and a mild lymphocytic infiltrate. Neither perineural nor lympho-vascular invasion were noticed. The suspicion of a melanoma was raised due to areas of regression and the presence of intracytoplasmatic brownish pigment. Further immunohistochemical tests confirmed the diagnosis of a spindle cell melanoma.
Conclusion: Albeit rare among spindle cell neoplasia of the skin, spindle cell melanoma should be regarded as a possible diagnosis, particularly in macroscopically pigmented lesions. As melanomas are especially aggressive tumours and early diagnosis is of outmost importance in such cases. Therefore, comprehensive immunohistochemical tests must be performed in order to establish the correct diagnosis.

E-PS-05-034

A rare case of digital papillary adenocarcinoma that challenged the pathologist during Mohs micrographic surgery

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Background & objectives: Digital papillary adenocarcinoma(DPA) is a rare and histomorphological challenging malignant eccrine tumour with a high tendency to local recurrence and metastasis, often presents as a painless mass on the digits or toes. We've reached reported 219 cases in the literature.
Methods: We aimed to discuss the histopathological and intraoperative diagnostic pitfalls of DPA with a literature review. A 62-year-old female presented with a painless swelling in the thumb. A subcutaneous nodular 1.5cm-mass was found. No ulceration, colour change or loss of function was observed. A cystic lesion, thought to be compatible with infectious processes, was detected in MRI and excised.
Results: Macroscopically, a partially well-circumscribed mass containing cystic and solid components was observed. Microscopically, epithelial neoplasm consisting of tubular structures with back-to-back arrangements was noticed. The lining epithelium of cystic component was composed of a single row of flattened mild atypical cells; sometimes it contained double-layered cuboidal/columnar cells with mild atypia, with micropapillary extensions to the lumen. Immunohistochemistry revealed, double-layered neoplastic epithelium contains two different types of cells; basaloid/myoepithelial and luminal. Ki-67 index was 15%. Tumour was infiltrating surrounding adipose tissue and present at the deep surgical margin. The findings were consistent with DPA and, re-excision was recommended. Axillary sentinal-lymph-node(SLN) dissection and re-excision with Mohs-micrographic-surgery(MMS) were performed. SLN metastasis wasn't detected.
Conclusion: In our experiment, 2 additional MMS steps were required due to suspicious positivity, unlike previously reported 5 DPA cases who underwent MMS. Although the diagnosis is known preoperatively, because of the innocent histomorphology of DPA, suspicious positivity was reported in frozen sections and the operation was advanced despite the risk of loss of function. Whereas, residual tumour was only in a microscopic focus in the permanent sections. Our case was considered worthy of presentation regarding drawing attention to this pitfall.

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E-PS-06-001

IgG4-related disease of the colon: a case report

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Background & objectives: IgG4-related disease (IgG4-RD) is a chronic fibro-inflammatory syndrome related to immunomodulation. Histological examination is required to diagnosis. The diagnostic criteria are: storiform fibrosis, dense lymphoplasmacytic infiltrate, obliterative phlebitis, high number of IgG4+ plasma cells/HPF and IgG4+/IgG+ plasma cell ratio >40%.
Methods: An 83-year-old man presented with intestinal obstruction. CT scan showed a tumour-like mass in the transverse colon. The same neo formed tissue was observed even inside a right inguinal hernia. Due to the suspicion of peritoneal carcinosis and severe symptoms, exploratory

laparotomy was performed. A solid mass with a hard consistency of 7x4x3 cm was detected. IgG4 serum level was normal.
Results: Histological examination of both lesions, colonic and inguinal, showed the same features. At histology, a subserosal nodular dense lymphoplasmacytic infiltrate was found. Focal abscesses were detected. Focally, storiform fibrosis was observed. Fibrous septa were found in the adipose tissue, giving rise to nodules of different sizes. Scattered arterial and venous vessels were interested by a strong inflammatory infiltration. At immunohistochemistry, 80% of the CD38+ plasma cell component was formed by IgG4+ elements. Dense lymphoplasmacytic infiltrate, storiform fibrosis and high number of IgG4 positive plasma cells (210 per HPF) led to IgG4-related disease diagnosis. At 7 months of follow-up, the patient is free of disease.
Conclusion: IgG4-RD may affect multiple organs. Less than 10 cases of gastrointestinal involvement have been reported to date. The colonic IgG4-RD is extremely rare. Usually, surgery is not necessary. In our case, the surgical approach was mandatory due to intestinal occlusion and allowed us to better study this lesion.
This event may induce to considerate IgG4-RD in the differential diagnosis of mass-forming lesions. Our aim is to turn a "rare disease" into a "less rarely diagnosed disease".

E-PS-06-002
Gastric squamous cell carcinoma showing diffuse EBER positivity: a case report
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Background & objectives: Gastric squamous cell carcinoma (SCC) is a rare neoplasm with less than 100 cases reported, usually diagnosed at advanced stage and associated with poor prognosis. Aetiology is largely unknown. We present a case of SCC associated with EBV.
Methods: Case report of a 69-year-old female presenting with nausea and vomit. Upper endoscopy showed a vegetating, ulcerative lesion of the gastric body, which was biopsied. The patient has no relevant past history, namely no known immunodeficiencies or immunosuppression.
Results: Histological examination showed a solid neoplasm, formed by large, eosinophilic cells in aggregates, showing moderate nuclear pleomorphism as well as foci of acantholysis and dyskeratosis. Immunohistochemically, there was positivity for CK7, EMA and P40 and negativity for CD56, CK20 and CDX2. There was no loss of mismatch repair proteins. EBER in situ hybridization was performed, showing diffuse positivity. A tentative diagnosis of squamous cell carcinoma (SCC) of the stomach, with EBER positivity, was made. The patient (stage cT4N+) was submitted to preoperative chemotherapy and surgical resection. The tumour was predominantly localized next to the cardia without connection to the gastroesophageal junction. No evidence of glandular differentiation or regression were present.
Conclusion: Neoplastic cells retained diffuse positivity for P40 and EBER ISH, confirming the original diagnosis. The patient did postoperative chemotherapy, remaining disease free 12 months after treatment. Our case shows that EBER positivity is possible, albeit uncommon in SCC of the stomach. Cases of stomach SCC associated with EBV infection are rare and very few are described in the literature. Further studies are needed to determine the prevalence of EBER positivity in SCC and what role EBV plays in their carcinogenesis.

E-PS-06-003
Dodging bullets in a cachectic patient: fat atrophy versus metastatic signet ring cell carcinoma
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Background & objectives: Starvation fat can appear incidentally in surgical pathology and the dystrophic cells may have a signet ring-like morphology that raises the possibility of metastatic signet ring cell carcinoma.
Methods: A 35-year-old female with compulsion neurosis and cachexia (anorexia nervosa) was admitted due to abdominal pain. On examination, she was cachectic (39 kg with a body mass index of 13,6 kg/m2). A CT scan showed extensive peritoneal free air and pneumatosis of the cecum raising the hypothesis of perforation. A right hemicolectomy was performed.
Results: On macroscopic examination, a thickened intestinal wall and crepitus were present. The mesentery was described as "bubbly" and the fat was thin. The mucosal surface was oedematous, and it had congestion foci. No perforation was detected.
Histologic examination demonstrated signet ring-like cell aggregates throughout subserosa and mesocolon. These cells were surrounded by a myxoid fibrovascular stroma. This appearance raised suspicion for metastatic signet ring cell carcinoma, myxoid liposarcoma or mucophagocytizing histiocytes in a mucinous neoplasm.
Immunohistochemical staining of the signet ring-like cells demonstrated these cells to be negative for CAM 5.2 and CD68, and positive for Vimentin and S-100. This profile was most consistent with atrophic adipocytes rather than carcinoma.
Conclusion: The changes of cachexia in fat cells are rarely seen in routine surgical pathology. If a thorough history is not provided or sought, these features can be alarming, including involvement of subserosal region, intimate association with nerves and lymphoid tissue. The distinction is critical for exclusion of malignant conditions.
The clinicopathologic features and immunohistochemical staining were essential to reach the correct interpretation.

E-PS-06-004
Immunohistochemical evaluation of possible therapeutic targets in colorectal carcinoma (CRC) with microsatellite instability (MSI)
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Background & objectives: CRC with microsatellite instability is a distinct entity with different prognosis, therapeutic response (lack of response for some chemotherapy regimens) and clinical features. This study aims to assess immunohistochemical expression of other markers potentially useful for targeted therapy.
Methods: We included in this study 10 cases of CRC with MSI, subsequently performing immunostaining for BRAF, CDX2, CD117, Ki-67 and HER2. Except for the HER2 marker which was scored based on membrane positivity as 1+, 2+ or 3+, the results were evaluated based on the percentage of positive tumour cells.
Results: 60% of the tumours were moderately differentiated (G2) and 40% poorly differentiated (G3). BRAF was positive in one case (15%), CD117 in 30% of the cases (ranging from 10% to 40% positive in tumour cells), CDX2 in 70% (over 50% being positive in >60% of tumour cells), HER2 scored 3+ in only 2 cases (20%) and high Ki-67 expression (>40%) was seen in 90% of the cases. All cases positive for CD117, HER2 and BRAF were G2 tumours. CD117 positivity was seen in cases with HER2 and/or BRAF positivity and loss of CDX2 expression. Also, Ki67 index was significantly higher in CD117 negative tumours.
Conclusion: Personalized treatment approach in CRC requires evaluation of the possible therapeutic targets that emerged in recent years. Tumours with HER2, BRAF, CD117 expression are probably more aggressive and should benefit of targeted molecules or clinical trials.

E-PS-06-005
Serrated polyposis: increasing awareness through a report of 2 cases
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Background & objectives: Serrated polyposis (SP) is a rare condition in which serrated polyps develop throughout the colorectum. 30% of sporadic colorectal cancer (CRC) arises following the "serrated pathway". Patients with SPs are subjects to a high, yet ill-defined risk of malignant transformation.
Methods: We report 2 cases of SP diagnosed according to the 5th edition of the WHO classification of digestive tumours, one of which ultimately transformed into a serrated adenocarcinoma (SA).
Results: The first case is an 85-year-old male requiring surgery for a sigmoidal volvulus. Macroscopically, the colon was embedded with 60sessile polyps. Histologically, these were non-dysplastic lesions: goblet-cell-rich hyperplastic polyps (GCRHP) and sessile- serrated-lesions(SSL). The SP was a type2 phenotype. The 2nd patient is a 58-year-old male whose colonoscopic follow-up found an ever-growing number of polyps. Biopsies concluded to GCRHPs. He underwent a colectomy to remove a stenosing tumour of the sigmoid. Gross examination found a 4cm tumour and 21polyps between it and the distal resection edge. Histologically, the polyps were either GCRHP or SSL. The tumour showed a serrated glandular architecture and was diagnosed as a SA. The SP is a type 3 phenotype.
Conclusion: The various denominations given to serrated lesions made SP records harder to track. No accurate evaluation of its transformation risk is documented. As for CCR arising following the "serrated pathway" serration is almost always missing making SA a rare entity.

E-PS-06-007
The need to know more about gastric cancer: prevalence and features in a retrospective study
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Background & objectives: Gastric cancer (GC) is one of the most frequent neoplasm worldwide. Based on GLOBOCAN 2020, GC is the 5th most common malignancy and the 4th cause of death. We determined the features of GC among the patients who undergo gastrectomy.
Methods: We assessed a retrospective cohort representing all stomach cancer diagnoses on gastrectomies from a single institution (University Emergency Hospital of Bucharest, Romania), from January 2013 until February 2020. For each case we gathered demographic data, such as age and gender, histological type of the tumour, grade of differentiation, location, grade of invasion, lymphovascular and perineural invasion and also nodal status.
Results: From a total of 130 patients with GC, 34.61% were females with age between 47 and 85 years old and 65.38% were males with age between 34 and 84 years old. The mean age for women was 67.7 years old and for men was 65.7 years old. Considering Lauren classification, 60% were intestinal type and 40% were diffuse type adenocarcinomas. Regarding the WHO latest classification, 54.61% were adenocarcinoma NOS, 6.15% mucinous adenocarcinoma, 29.23% poorly cohesive carcinomas (including signet ring cell) and 10% were mixed carcinomas. Poorly differentiated tumours were the most frequently (54.61%) and most of the carcinomas were invading the subserosal space (57.69%).
Conclusion: Gastric cancer is more common in men and tends to develop at a younger age than women. The results of this study indicate an increasing incidence for the poorly cohesive carcinoma (diffuse type) which has more aggressive behaviour than adenocarcinoma NOS (intestinal type). Also, at the time of gastrectomy (partial or total), only 1.53% were pT1 and 11.53% were pT2. Therefore, there should be a need to provide even more comprehensive screening controls among the population.

E-PS-06-008
Unpleasant surprise of diagnosis - gastric adenocarcinoma with yolk sac tumour
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Background & objectives: Yolk sac tumours (YST) are rare malignant GCT that usually originate in the gonads. They rarely arise in extragonadal sites (mediastinum, retroperitoneum, lung). Yolk sac differentiation of gastric adenocarcinomas is rare with only a few cases reported in the literature.
Methods: We report a case of primary gastric adenocarcinoma with YST differentiation and liver metastases of the YST component in a 49 y/o female presented with unspecific symptoms. Abdominal tomography showed wall thickening of the gastric lesser curvature and perigastric/retroperitoneal lymph node enlargement. Total gastrectomy with lymph node dissection and oesophagojejunostomy and an incisional biopsy of a liver tumour were performed.
Results: Grossly, we found an elevated tumour of 10/7/6cm, with ulceration and haemorrhage, located in the antral lesser curvature of the stomach. Histopathological examination of resected specimens revealed the presence of a G2 intestinal type adenocarcinoma, with features of YST. In the yolk sac component, tumour cells showed immunoreactivity for CK8/18, AFP and PLAP and focal staining for β-HCG. Lymph node (1/18) and liver metastasis had morphological and immunohistochemical features similar with the YST component of the gastric tumour.
Conclusion: Yolk sac differentiation in gastric adenocarcinoma represents a major diagnostic challenge with significant impact on patients' prognosis, since the YST component is more aggressive and has a higher risk of metastasis. Reporting rare tumours is a helpful tool for pathologists, since the key of diagnosis, in this case, is the recognition of YST morphology.

E-PS-06-009
Inflammatory myofibroblastic tumour – a rare mesenchymal entity in the colon
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Background & objectives: Inflammatory myofibroblastic tumour is an unusual mesenchymal neoplasm, occurring usually in children and young adults, rarely arising in extrapulmonary locations. Herein, we present a case of an inflammatory myofibroblastic tumour diagnosed in the colon.
Methods: A 39-year-old man, smoker with clinical background of essential hypertension, dyslipidaemia and biliary lithiasis, presented to the emergency department after repeated episodes of melena since December 2020. Colonoscopy and abdominal computed tomography revealed the existence of a circumferential vegetant tumour in the proximal transversal colon near to the hepatic angle; biopsies were inconclusive, and a right hemicolectomy was performed.
Results: Macroscopically, there was a 4cm firm whitish tumour within the colon wall, with a fascicular and nodular cut surface, ulcerating the mucosa. Histologically, the tumour was composed of loose fascicles of uniform, plump spindle cells with pale cytoplasm, vesicular chromatin and small nucleoli, within a collagenous stroma and a prominent inflammatory infiltrate constituted mainly by lymphocytes, plasma cells and a few eosinophils; pleomorphism, mitoses and necrosis were absent. The neoplastic cells showed diffuse staining for vimentin and ALK (cytoplasmic pattern), focal staining for smooth muscle actin and HHF35 and were negative for CD117, DOG-1, desmin, STAT-6, cytokeratins and EMA. These features were consistent with the diagnosis of inflammatory myofibroblastic tumour.
Conclusion: Inflammatory myofibroblastic tumour is a neoplasm of intermediate biological potential with only 60 cases described in the

colorectal region. Grossly, its fascicular aspect usually resembles the gastrointestinal stromal tumour (GIST), the most common mesenchymal tumour of the digestive system. Even histologically, the differential diagnosis with GIST and other described mesenchymal tumours of the gastrointestinal tract is fundamental and immunochemistry evaluation is needed to establish the final diagnosis.

E-PS-06-010

Case report of gastrointestinal stromal tumour with signet-ring cells

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Background & objectives: We report a case of gastrointestinal stromal tumour (GIST) of the stomach, with abundance of signet-ring cells.
Methods: A 73-year-old male arrived at our hospital with nonspecific gastric symptoms. During gastroscopy, a submucosal mass was found. Partial gastrectomy was performed. We received an oval shaped segment of the stomach, with a circumscribed, brown submucosal mass of maximum diameter >4.7cm.
Results: Microscopically, it was a sharply demarcate mass consisting of epithelioid cells with clear cytoplasm and signet-ring cell morphology at the majority of the tumour cells. Focally, at the periphery of the tumour, there were also spindled cells with eosinophilic cytoplasm. Mild cytologic atypia and rare mitoses (<1 mitosis per 5mm2) were observed. Necrosis was not found. Immunohistochemistry showed diffuse and strong positivity for Cim, CD117, Dog1, CD34 whereas immunostaining for CKAE1/AE3, S100, SOX10, Mart1, HMB45, SMA, Desmin was negative. Similarly, the histochemical stains AB/PAS and PAS/PAS-D were negative. Ki67 (MIB1) was 3-4%. Thus, the diagnosis of GIST was made, category 2 according to WHO classification.
Conclusion: GISTs are a relatively common tumour, with approximately 54% of the cases arising in the stomach. Epithelioid morphology is less common in stomach. Rarely, a signet-ring cell pattern can be observed. The differential diagnosis includes gastric adenocarcinoma with signet-ring cells, melanoma, metastatic adenocarcinoma, gastric schwannoma with signet ring cells and any other tumour with clear cell features or mucin production.

E-PS-06-011

Case report: primary diffuse large B-cell lymphoma (DLBCL) arising in colonic adenoma

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Background & objectives: We report a case of primary diffuse large B-cell lymphoma, arising in the stem of a villous adenoma of the sigmoid colon, with no clinical indications.
Methods: A 71-year-old male was routinely evaluated endoscopically. During colonoscopy, several polyps of diameter 0.4-0.5cm were found and excised. One polyp located at sigmoid colon was pedunculated with diameter >4cm.
Results: Histologically, it was a villous adenoma with high grade dysplasia. The stem and the mucosal interstitium were infiltrated by diffusely arranged polymorphous large neoplastic cells, with absence of starry sky pattern. Immunohistochemical study revealed positivity for LCA, CD20, Bcl-6 and CD10 whereas it was negative against CKAE1/AE3, CgA, SYP, S100, CD3, CD30, bcl-2, CyclinD1, HHV8. C-myc was positive in 30% of the neoplastic nuclei. Ki67 (MIB1) was estimated positive in about 90% of the cells. EBER was positive in sparse nuclei. Thus, the diagnosis of composite DLBCL and villous adenoma was made. The smaller polyps were either hyperplastic or adenomas.
Conclusion: DLBCL is quite common in the gastrointestinal tract. Nevertheless, lymphomas coexisting with adenomas are extremely rare with only 4 reported cases in PubMed, consisting of an Epstein-Barr Virus-Associated B-cell lymphoproliferative Disorder, two DLBCLs and a marginal zone lymphoma. Although it is far more common for an adenoma to coexist with carcinoid, it is important to always keep in mind a lymphoma in the differential diagnosis of small blue round cell tumours.

E-PS-06-012

Gastric mesenchymal tumours resembling other entities: report of two cases

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Background & objectives: Schwannomas are nerve sheath tumours that usually affect the skin and subcutaneous tissue of the extremities, followed by the head and neck region. However, they can sometimes be found in uncommon locations, such as the gastrointestinal system.
Methods: From a total of 65 cases of peripheral schwannomas retrieved from our hospital records between 2005 and 2020, 3 (4,61%) were located in the stomach. In this retrospective study, we present two cases of gastric tumours that were clinically misdiagnosed as metastasis from colon adenocarcinoma in the first case and malignant tumour of the gastric cardia in the second one.
Results: CASE 1: A 72-year-old male underwent surgery after CT revealed a mass in the transverse colon and additional tumours initially diagnosed as metastases were found, including one on the anterior gastric serosa. CASE 2: A 57-year-old male underwent total gastrectomy after CT confirmed an interhepatogastric neoplasm. In both cases, microscopic examination revealed a nodular proliferation of spindle cells, with abundant, eosinophilic cytoplasm and vesicular nuclei, mostly organized in dense, cellular areas. Nuclear palisading was also present, with few mitoses and no nuclear pleomorphism, highly suggestive of schwannoma. In the first case the tumour cells were S100-, c-KIT+, CD34+ (GIST–prognostic group 1). In the second case, they were only S100+(gastric schwannoma).
Conclusion: Histopathologically, both cases were diagnosed as schwannomas. However, after immunohistochemical testing, the first case turned out to be a GIST. In conclusion, mesenchymal tumours with morphological appearance of neural differentiation may belong either to the nerve sheath tumours group or to the gastrointestinal stromal tumours one. Immunophenotyping is mandatory in order to establish a proper diagnosis, no matter how bland looking the tumour cells are or how suggestive of a certain tumour type the morphology is.

E-PS-06-013

Neuroendocrine carcinoma of the extrahepatic bile duct: case report of a rare entity in biliary tree

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Background & objectives: Neuroendocrine tumours and neuroendocrine carcinomas (NET) can arise in various systems throughout the body. But biliary tree is a very uncommon localization for such tumours. We herein report a case of NEC in the extrahepatic bile duct (EHBD).
Methods: 67-year-old male patient with diabetes and a pace maker was admitted to our hospital with jaundice. The patient had a history of cholecystectomy due to cholelithiasis. Endoscopic retrograde cholangiopancreatography revealed near-total luminal obstruction at bile duct until junction of cystic duct. Segment proximal to the area appeared dilated. With clinical preliminary diagnosis of cholangiocarcinoma, patient underwent EHBD resection.
Results: Gross examination revealed wall thickening of 2,8 cm segment of bile duct. Upon histopathological examination of specimen, infiltrative solid sheets of tumour cells with scant cytoplasm and high nuclei-

cytoplasmic ratio was seen in the bile duct wall. Tumour cells had irregularly shaped, hyperchromatic granular nuclei. Chromogranin A, synaptophysin, CD56, TTF-1 and pancytokeratin immunohistochemical stains were positive. Ki-67 index was >%80. With these findings, diagnosis of NEC was established. Surface epithelium of bile duct showed focal areas of low-grade dysplasia in the proximal parts of the specimen. But no identifiable adenocarcinoma component was present. The patient also had local lymph node metastases. PET scan of patient revealed no other primaries.
Conclusion: Preoperative diagnosis of NEC in the biliary tree can be quite challenging. Due to the localization, it can be hard to acquire biopsies to make a definitive diagnosis. NECs are aggressive tumours with a tendency for distant metastasis, thus leading to a very poor prognosis.

E-PS-06-014
Uncommon case of giant gastric lipomatous polyp: what prognosis? what therapeutic?
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Background & objectives: Gastric lipoma account for <1% of all gastric tumours encountered. Giant gastric lipoma, defined as ≥10 cm. We hereby present a case of a giant gastric lipomatous endoluminal polyp resulting in excision preserving gastric continuity.
Methods: Our patient is 49-year-old presented as a symptomatology epigastric pain, dyspepsia, and bloody vomiting. A fibroscopy gastroduodenal and CT scan revealed a gastric mass antral site with endoluminal growth, measuring 12× 7,5 × 7.3 cm. He underwent an exploratory laparotomy with transverse anterior gastrotomy and primary closure.
Results: Pathologic examination objective a mass of 12 cm of major axis submucosal, well-circumscribed, non-encapsulated comprised of mature adipose tissue without atypia or mitotic figures, consistent with lipoma. The over-stretched gastric mucosa is moderately inflammatory, helicobacter pylori are absent without dysplasia without metaplasia.
Conclusion: Obstruction gastrointestinal and bleeding secondary to a giant gastric lipoma is a rare finding of a rare disease. The majority of cases in the literature result in major gastric resection, if malignancy is carefully ruled out. stomach preserving surgery is an optimal treatment option. As it was in our case was managed by simple enucleation following a preoperative certainty diagnosis.

E-PS-06-015
Leiomyosarcoma of duodenal wall
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Background & objectives: Leiomyosarcoma is one of the most common type of sarcoma seen in adults. Primary gastrointestinal(GI) sarcomas in general are very rare, accounting for 1-2% of all GI malignancies but in this group leiomyosarcoma is one of the most common.
Methods: Forty-nine years old female patient presented with abdominal pain and discomfort. On physical examination no specific finding was observed. Imaging studies revealed a 9 cm mass on duodenal wall by the ampulla. Ampullary carcinoma being the preliminary diagnosis, surgery decision was given.
Results: The tumour was sent in pieces to the pathology laboratory. On gross examination of pancreaticoduodenectomy material, tumour was situated on the opposite site of ampulla with above mucosa being mostly intact. Cut surface was tan to grey, solid and rubbery. Morphologically tumour consisted of spindle to highly pleomorphic cells with eosinophilic cytoplasm on a myxoid background. Immunhistochemical studies showed SMA, Desmin and H-caldesmon positivity. Myogenin and MyoD1 were negative, Ki67 index was 65-70%. Proving true smooth muscle differentiation, case was reported as Leiomyosarcoma.
Conclusion: Primary GI leiomyosarcomas are very rare. Most important entity on differential diagnosis is Gastrointestinal Stromal Tumour (GIST). In addition to this pathologist must always keep in mind leiomyosarcoma on the differential diagnosis of GIST's. In this case weak-nonspecific CD117 and DOG1 staining were observed and molecular analysis was done for definitive diagnosis.

E-PS-06-016
CD3 and CD7 lymphocytes in the microenvironment of colorectal cancer and their influence on the progression of tumour growth
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Background & objectives: Currently, the incidence of colorectal cancer is growing steadily. By assessing the immune response to tumour growth, it is possible to predict the outcome of the disease and choose the most effective therapy.
Methods: Analysis of the data of patients who underwent primary tumour resection: life expectancy, gender, age, stage of the disease, presence of metastases in regional lymph nodes, degree of tumour differentiation, quantitative assessment of the prevalence of CD3, CD7 lymphocytes.
Results: The presence of lymphocytes was revealed in all cases. Their greatest density is observed in the invasive margin of the tumour. In the group of patients with early death, the density of CD3 lymphocytes in the tumour stroma is increased compared to long-lived ones, and the number of CD7 lymphocytes is reduced in the invasive margin. Metastases in regional lymph nodes leads to decrease of CD3 lymphocytes in invasive margin in long-lived persons, and in patients with early death it increases both in the stroma and in the invasive margin; the number of CD7 lymphocytes in the invasive margin decreases in long-living patients and increases in patients with early death.
Conclusion: Subpopulations of CD3 and CD7 lymphocytes are one of the main representatives of the tumour microenvironment in colorectal cancer, and the patterns of their distribution, as well as the volumes of representation in the tumour stroma and in the invasive margin, can be criteria for predicting the course of the disease for a particular patient.

E-PS-06-017
To be or not to be: Crohn's disease or sarcoidosis with only gastro-duodenal and pancreatic involvement
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Background & objectives: Sarcoidosis and Crohn's disease are multisystemic non-caseating granulomatous inflammatory diseases, with rare involvement of the GI tract in the case of sarcoidosis. Crohn's disease can affect any part of the digestive tract, but pancreatic involvement is rare.
Methods: A 31-year-old male was admitted for dyspepsia, anorexia and weight loss. Upper digestive endoscopy revealed diffuse infiltration of the gastric wall (linitis plastica-like appearance) and multiple ulcerations in the duodenum. MRI scan was suggestive of acute pancreatitis.
Results: The gastro-duodenal biopsies showed epithelioid, non-caseating granulomas in the background of chronic active inflammation. ACE, sIL2r and ASCA IgA levels were elevated, and IgG class 4 level was normal. Under high-dose of corticosteroids, symptoms have disappeared. A differential diagnosis between sarcoidosis involving the digestive tract and Crohn's disease with autoimmune pancreatitis was made, in favour of the former, due to the abnormal levels of biomarkers and clinical presentation. Other conditions were excluded: malignancy, infections, foreign body reaction, CVID, vasculitis, Whipple disease. On follow-up, we found normal values of ACE and sIL2r, complete remission of the pancreatic lesions and persistence of granulomas in an otherwise non-atrophic gastric mucosa.

Conclusion: Symptomatic involvement of the GI tract can be the first manifestation of sarcoidosis. Even if rare, finding non-caseating granulomas in the GI tract may guide the diagnosis toward sarcoidosis, but other granulomatous disorders must be excluded. Because histologically sarcoidosis and Crohn's disease are difficult to differentiate, serology can be helpful. Gastric sarcoidosis can grossly mimic malignancy. The acute management of both sarcoidosis and Crohn's disease involves corticotherapy, but differentiation between them is important for long-term case management and prognosis.

E-PS-06-018

Appendiceal goblet cell adenocarcinoma: a series of cases

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Background & objectives: Goblet cell adenocarcinoma (GCA) is a rare tumour almost exclusively seen in the appendix, composed of goblet-like mucinous cells, neuroendocrine cells and Paneth-like cells that infiltrate the appendiceal wall circumferentially, without desmoplastic stromal reaction.
Methods: We undertook a retrospective review of a series of GCA diagnosed and treated between 2018 and 2020 in two centres, analysing histological characteristics, immunohistochemical and molecular features, along with a clinical follow up. The diagnosis was reviewed considering the new WHO classification. The study included 5 cases (2men and 3 women) with a median age of 62 years.
Results: A classical morphology of GCA was present in all cases. The histological grade was G1 in 2pts, G2 in 1 and G3 in 2. Perineural and vascular invasions were identified in 4 and 1cases. TNM score was pT3N0 in 4cases and pT4N0 in 1. Chromogranin and synaptophysin highlighted variable numbers of neuroendocrine cells in all cases. p53 staining was wild-type in all but 1case with a total loss of expression. DNA-mismatch-repair genes and BRAF were preserved in all tumours analysed. Four pts are alive free from disease (median follow up: 21 months). One patient corresponding to a G3-case with p53 loss, is currently alive but with disease and undergoing chemotherapy.
Conclusion: Herein, we describe the histological, immunohistochemical and molecular characteristics and clinical evolution of a series of CGA. We found a p53 aberrant expression in the case with poorer outcome, suggesting a possible mechanism involving TP53 gene in the histogenesis of this tumour and a possible association with aggressiveness. However, it is well known that alteration in p53 is not always associated with TP53 gene mutation, and more studies are needed to find the genetic profiling of GCA.

E-PS-06-019

Medullary adenocarcinoma of colon. A case report

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Background & objectives: Adenocarcinoma of the colon is the third most-common type of cancer worldwide, with a 4% incidence in both men and women. We present a rare case of a recently recognized subtype of colorectal cancer, the medullary adenocarcinoma of colon (MAC).
Methods: A 63-year-old female patient was admitted with weakness, weight loss and left lower quadrant abdominal pain for a period of months. Colonoscopy revealed an ulcerated 5cm-long circumferential lesion located in the ascending colon and a right hemi-colectomy was performed.
Results: Histopathological examination showed a malignant neoplasm with solid and insular growth pattern. The tumour consisted of medium-sized polygonal cells with eosinophilic cytoplasm, vesicular nuclei and prominent nucleoli. A prominent lymphocytic infiltration within and around tumour was also evident. Immunohistochemical staining was positive for CK20 and CEA and negative for CDX2, CK7, Ca19-9, Ca125, synaptophysin and chromogranin. Further molecular analysis revealed a microsatellite stable tumour (MSS-pMMR) with a BRAF-V600E/E2/D mutation. KRAS and NRAS mutations were absent. These findings established the diagnosis of MAC.
Conclusion: MAC is a very rare colorectal cancer subtype, accounting for <1% of cases and mostly affects women (mean age 70 years). It is often associated with hereditary non-polyposis colorectal carcinoma (HNPCC) syndrome. Most MACs present microsatellite instability, though MSS tumours can also occur. In comparison to undifferentiated and poorly-differentiated adenocarcinomas of the colon, MACs are believed to have a relatively favourable prognosis.

E-PS-06-020

Colorectal carcinoma with divergent differentiation: clinicopathologic and molecular study of an aggressive variant

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Background & objectives: Colorectal carcinoma (CRC) is the most common type of gastrointestinal cancer, with approximately 1,931,950 worldwide new cases in 2020. Carcinomas exhibiting more than two lines of differentiation are unusual, and only sporadic reports of this phenomenon have been described.
Methods: An 81-year-old man with history of abdominal pain and positive result of faecal occult blood test. Abdominal examination showed a right-upper-quadrant palpable mass. Computed Tomography revealed a colonic exophytic mass measuring 27x46 mm and pathological regional lymph nodes without evidence of metastatic disease. The colonoscopy demonstrated a stenosing and ulcerated lesion in the hepatic angle. Right hemicolectomy was performed.
Results: The specimen measuring 40x6 cm with an invasive tumour of 7x4cm with extension into pericolorectal tissue and visceral peritoneum. Histological examination showed a carcinoma with conventional glandular differentiation, undifferentiated areas with rhabdoid features and pools of extracellular mucin and signet-ring cells. By immunohistochemistry, the conventional carcinoma showed expression of CKAE1/AE3, CK8, CK20, CDX2, SATB2, chromogranin and synaptophysin. The undifferentiated area expressed CKAE1/AE3, CK8, SATB2, chromogranin, synaptophysin, vimentin, with variable expression of βHCG. Nuclear SMARCB1 (INI1) expression was retained in the different tumour components. P53 showed a null-pattern. Analysis for mismatch-repair-proteins showed nuclear expression in both non-neoplastic and tumour cells. Molecular analysis revealed a BRAF(V600E/E2/D) mutation without alteration in KRAS/NRAS genes.
Conclusion: Although most cases of CRC are adenocarcinoma NOS, several histopathological subtypes have been described. Tumours with rhabdoid features are extremely rare, have poor prognosis and represents a pathway of dedifferentiation shared by heterogenous neoplasms and might or might not be associated with SMARCB1 (INI1) alterations. Some authors suggest that βHCG expression is associated with aggressive behaviour in non-trophoblastic tumours. Our case suggests that an integrated analysis of morphological, immunohistochemical and molecular traits help to recognize these uncommon tumours.

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E-PS-06-021

Gastrointestinal stromal tumour metastasis to the lung with chondrosarcomatous differentiation. Report of a case

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Background & objectives: Gastrointestinal stromal tumour (GIST) is the most common mesenchymal tumour of the digestive tract. We herewith present a case of a gastric GIST with pulmonary metastasis showing chondrosarcomatous differentiation after therapy with imatinib mesylate (IM).
Methods: A 67-year-old patient with a previous history of gastric GIST 15 years ago and a local recurrence four years later, was admitted due to a small tumour found in the lower lobe of the left lung on chest computed tomography. Wedge resection was performed.
Grossly, a well-circumscribed, solid, elastic, grey-white, 1.3cm. large tumour was found in the lung parenchyma.
Results: Microscopically, the neoplasm consisted of an epithelioid component with a solid architecture, high-grade atypia, and numerous mitotic figures, with an abrupt transition to a mesenchymal component showing chondrosarcomatous differentiation. The epithelioid component expressed CD117 and DOG1, whereas Vimentin was positive in both. CKAE-1/AE-3, CK5/6, p63, TTF1, Napsin A, and CD99 were uniformly negative. Our diagnosis was malignant neoplasm consistent with GIST metastasis with heterologous chondrosarcomatous differentiation. A review of the literature revealed 25 cases with unusual morphological and immunohistochemical findings in GIST, either de novo or after therapy with IM showing heterogeneous differentiation (epithelioid sarcoma, rhabdomyosarcoma, angiosarcoma, etc.) and loss of CD117, CD34, and DOG1 expression in the dedifferentiated component.
Conclusion: GIST showing disease progression or resistance to imatinib mesylate (IM) may present with unusual morphologic and immunohistochemical characteristics. Knowledge of these changes is essential to avoid a severe diagnostic pitfall.

E-PS-06-022
Gastric adenocarcinoma with lymphoid stroma: a rare case report
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Background & objectives: Gastric adenocarcinoma with lymphoid stroma, also known as medullary carcinoma or lymphoepithelioma-like carcinoma, accounts for 1-7% of all gastric carcinomas. Most of them arise in the proximal stomach and have been associated with either latent EBV infection or microsatellite instability.
Methods: A 68-year-old male with a medical history of class 3 cardiac condition and diabetes mellitus presented to the emergency department with marked fatigue and dizziness. He underwent an oesophagogastroscopy, which demonstrated a large mass, involving the lesser curvature near cardia. Biopsies were taken and the initial diagnosis was high-grade intraepithelial neoplasia, without the certainty of an invasive tumour.
Results: The patient was then referred to our institution for additional work-up and underwent a total gastrectomy. The microscopic examination of the gastric resection specimen showed moderately differentiated carcinoma on the surface with obvious dedifferentiation towards deeper levels. The lesion had an organoid growth pattern diffusely consisting of irregular sheets, trabeculae, syncytia, and ill-defined tubules of polygonal pleomorphic tumour cells with vesicular nuclei. There was an abundant peritumoral and intratumoral lymphocytic response. The proximal and distal margins were negative, but the lesser omental margin was involved by invasive carcinoma. One of the 14 extracted regional lymph nodes presented carcinomatous metastasis. Immunohistochemical stains and in situ hybridization for EBV are pending.
Conclusion: Our case was diagnosed as gastric adenocarcinoma with lymphoid stroma, which by some has been reported to have a favourable prognosis compared with usual gastric adenocarcinoma. Specifically, EBV-positive, as well as MSI-high tumours in general, have been variably associated with a survival advantage. On the other hand, lesions composed of lymphocytic infiltration may be mistaken for an intense reactive lymphoid infiltrate or even lymphoma and one has to pay attention to these differential diagnoses.

E-PS-06-023
Current dysplasia grading guidelines in colorectal adenomas do not seem to be valid among pathologists in Turkey: a nation-wide survey
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Background & objectives: Dysplasia grading is important in colorectal adenomas(CRAs)given its effect on polypectomy surveillance. We aimed to investigate the terminologies used for HGD in routine practice, if any and the agreement of dysplasia grading among Turkish pathologists with reference to current guidelines.
Methods: A survey including 7 images of CRAs with low-grade dysplasia (LGD) and HGD was sent to pathologists in Turkey via e-mail and social media. The images were selected from the Canadian National Polyp Guidelines. The pathologists were asked to grade the dysplasia as in their routine practice. For this purpose, the multiple choices not only included LGD and HGD but also adenocarcinoma in-situ and intramucosal adenocarcinoma.
Results: A total of 324 pathologists (including 48 senior residents and 176 gastrointestinal pathologists) participated in the survey. The majority of the staff-pathologists had an experience more than 5 years. Among staff-pathologists, the rate of agreement of dysplasia according to the guidelines was as follows; for CRAs with LGD, Image 1(with low-grade cytology)-97%, Image 2(with focal cribriformity)-6,2%, Image 5(with high-grade cytology)-26,8%, and for Image 6(with slightly high-grade cytology)-48,9%. For CRAs with HGD (Images 3,4, and 7), the agreement ratio was>91%. However, intramucosal adenocarcinoma was the preferred terminology by 43,8%,68,5%,and 50% of the participants, respectively and in-situ adenocarcinoma was used by 21%, 5,4% and 16,3%, respectively. The results were similar for residents.
Conclusion: Among pathologists in Turkey, in contrast to current guidelines for CRAs; 1. Intramucosal adenocarcinoma is still a commonly used terminology, 2. High-grade cytological features are over-relied, 3. Insufficient extent of architectural abnormalities is overcalled. We think that strategies to increase the usage of current guidelines in practice should be developed and as agreed by the majority (Question 9), a national polyp guideline seems to be necessary in an attempt to standardize reporting of CRAs in Turkey.

E-PS-06-024
Rectal neuroendocrine tumour G2 presenting as a polyp with hepatic metastases
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Background & objectives: Rectal neuroendocrine tumour (NET) represented 29% of all gastroenteropancreatic NET. The incidence of NET of the rectum has been increasing in the last decades, partly due to improved investigation. They are mostly well-differentiated small tumours with a rather good prognosis.
Methods: We report a case of rectal NET with polypoid presentation showing aggressive clinical behaviour.
Results: A 59-year-old woman with no medical history presented because of pain in the right hypochondrium and loss of weight. Abdominal examination showed hepatomegaly and laboratory test results showed increased liver enzymes. CT showed multiple hepatic lesions. The result of upper endoscopy was normal, whereas colonoscopy revealed an ulcerated sessile rectal polyp measuring 15 mm. Examination

of a rectal biopsy specimen showed submucosal proliferation of uniform cells with positivity for synaptophysin and CD56 in immunostaining. The mitotic count was low and Ki-67 proliferation index was 4%. Percutaneous hepatic biopsy was performed, and microscopic examination showed liver metastasis. The patient received lanreotid because of her symptomatic unresectable hepatic metastases.
Conclusion: Rectal NET are rare, but they are increasing in incidence in the recent years. Despite a relatively indolent behaviour, they are malignant and can metastasize. Most reported risk factors for metastatic disease are tumour size >1cm, muscularis propria invasion, high proliferation index and lymphovascular invasion.

E-PS-06-025
Primary gastrointestinal lymphoma: a Tunisian experience
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Background & objectives: Primary gastrointestinal lymphoma (PGIL) is rare with a heterogeneous presentation and a controversial treatment plan. Our objective was to elucidate the epidemiological, clinical, and pathological features of PGIL and to compare the intestinal and gastric forms in our region.
Methods: We carried out a retrospective descriptive study of PGIL cases, collected in our department of Pathology over 23 years (from 1997 to 2020). The primary nature of the lymphoma was retained in front of an exclusive or predominant digestive site, without peripheral lymph node involvement. The diagnosis was made on the basis of anatomopathological and immunohistochemical criteria.
Results: Our study included 78 cases (52 males and 26 females) with a mean age of 47.5 years. The tumour sites were gastric in 61 (78%), small intestine in 12 (15.4%), and colonic in 2 cases (2.6%). A mixed gastric-intestinal localization was noted in 3 cases (4%). The clinical presentation was dominated by abdominal pain. A high-grade PGIL was noted in 62.5% with a predominantly intestinal location. The B phenotype was noted in 91.8%: It was MALT lymphoma in 63%, followed by large B-cell lymphoma in 24.6%. The T phenotype was noted in 8.2%. It was exclusively located in the intestine and associated with enteropathy (Coeliac disease) in 2 cases.
Conclusion: We conclude that the stomach is the main site of PGILs in our region; that intestinal lymphoma is less common, and mixed gastric-intestinal localization is rare and seems to have a worse prognosis. Gastric lymphomas are often low-grade B lymphomas, potentially curable. However, the majority of intestinal lymphomas are high-grade T phenotype, occurring in younger subjects.

E-PS-06-026
Toxic megacolon caused by leucocytoclastic vasculitis: a case report
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Background & objectives: Leucocytoclastic vasculitis of the colon without other manifestations is extremely rare.
Methods: We report the case of a 52-year-old man, who came to the ER department with abdominal distention and nausea. No signs of rash were observed. Laboratory findings revealed mild anaemia (HGb 11,5g/dL). X-rays showed extended dilation of the colon. Total colectomy was performed.
Results: Histopathological examination revealed perivascular and intravascular neutrophilic infiltration, fibrinoid necrosis, with nuclear dust, of the wall of small vessels of the serosal and muscular layer of the large bowel. Immunohistochemical study with calretinin revealed normal presence of the ganglion cells. Mucosa was normal and submucosa showed oedema. Small bowel had no significant alterations.
Conclusion: Leucocytoclastic vasculitis is commonly associated with Henoch-Schoenlein, systemic lupus erythematosus, drug reactions and connecting tissue disorders. Gastrointestinal involvement applies to patients with polyarteritis nodosa and most commonly affects duodenum and small bowel. In our case isolated leucocytoclastic vasculitis of the colon, without underlying disorder, causing toxic megacolon, is presented.

E-PS-06-027
Simultaneous gastrointestinal neoplasms: Stromal tumour (GIST) combined with carcinoma. Presentation of two cases
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Background & objectives: Simultaneous development of different neoplasms in gastrointestinal system is uncommon. In particular, concurrent development of gastrointestinal stromal tumour and carcinoma is very rare. We present two cases of small intestine GIST's together with gastric and colon adenocarcinoma, respectively.
Methods: Patient A: A 64-year-old male underwent a partial gastrectomy for a gastric tumour. During intraoperative investigation a small jejunum mass was identified.
Patient B: A 82-year-old female underwent a partial small intestine resection for a large tumour measuring 12cm and a left colectomy for a concurrent 3cm colon mass.
Results: Histopathologic findings
Patient A: A cellular, spindle cell, bland looking jejunum neoplasm, 1,2cm with 0-1 mitoses/50HPF was revealed. The gastric tumour was classified as a poorly cohesive adenocarcinoma with signet ring cells and muscularis propria infiltration.
Patient B: The small intestine tumour was a spindle cell neoplasm, quite cellular, storiform patterned with mild pleomorphism and 25-50 mitoses/50HPF. Mucosa ulceration, necrosis and focal peritoneal infiltration were noted.
The colon tumour was a grade II adenocarcinoma, pT2N0.
Immunohistochemically the small intestine neoplasms were positive for: Vimentin, PDGFRA, DOG-1, c-kit and negative for: CKAE1AE3, CD34, SMA, Desmin, HMB-45,Melan-A, S100. Ki67 was 1% and 20% respectively. The findings were compatible with GIST.
Conclusion: GIST's are mesenchymal neoplasms of variable aggressiveness. 20-40% of patients may develop other malignancies synchronous or subsequent, mainly in gastrointestinal system. In that background the majority of GIST's are asymptomatic, incidental findings discovered during the diagnostic-therapeutic approach of the accompanying malignancies. The patients prognosis is defined mainly by the accompanying, often more aggressive neoplasm.

E-PS-06-028
Development of symptomatic Familial Mediterranean Fever (FMF) after kidney transplantation diagnosed through sigmoid colon biopsy: a case report
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Background & objectives: FMF is an autoinflammatory disease with a heterogenous genotype-phenotype correlation. It is characterized by recurrent attacks of fever and serositis. Amyloidosis is a frequent complication in untreated patients which can lead to proteinuria and progress to end stage kidney disease.
Methods: A 64-year-old man of Georgian descent and kidney transplantation was admitted thrice, starting six weeks post-transplantation, with repeating fevers and abdominal pain. His laboratory work-up showed increased serum C-reactive protein and a slight leukocytosis. The last abdominal ultrasound showed a diffusely prominent wall of sigmoid.

Every time he had a spontaneous recovery and was discharged without a definitive diagnosis.
Results: During his last admission, the patient emphasized anamnestically the periodic character of his fevers. We considered colitis, diverticulitis, abscess or lymphoma among clinical differential diagnosis. Abdominal CT-imaging and endoscopic examination showed diverticulosis of sigmoid without inflammation, abscess or mass. The biopsies showed acellular, concentric thickening of the submucosal vessel walls without vasculitis or thrombus formation. Congo red additional immunohistochemical stains confirmed the AA type amyloid deposition. The following genetic analyses showed two heterozygous variants p.Met694Val and p.Glu148Val in the MEFV gene, confirming Familial Mediterranean Fever. 23 months post-transplantation the patient is using colchicine (1 mg/day), has a stable kidney function and has no recurrence of symptoms.
Conclusion: Even if Familial Mediterranean Fever is diagnosed at a late stage, it is important to achieve remission by colchicine treatment to prevent loss of the transplanted kidney due to further amyloid deposition, as well as accumulation of amyloid in other sites such as the gastrointestinal tract and the heart. Colchicine suppresses the inflammatory reaction by interfering with the adhesion and chemotaxis of leukocytes.

E-PS-06-029
A rare case of polypoid gastric metastasis from clear cell renal cell carcinoma
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Background & objectives: Stomach is an exceedingly rare site for metastatic carcinoma, including those originating from the kidney. Signs and symptoms are nonspecific and do not differentiate primary gastric carcinoma from metastatic tumours to the stomach.
Methods: We present the case of a 79-years-old man with a history of clear cell renal cell carcinoma treated with radical nephrectomy. Four years later the patient underwent upper gastrointestinal endoscopic evaluation due to iron deficiency anaemia diagnosed by blood test.
Results: Gastroscopy revealed multiple scattered polypoid lesions in gastric body and fundus, ranging in size from 0,4 cm to 0,7 cm as well as a 2,7 cm polypoid mass that was removed with a polypectomy snare. The tissue samples were sent for histological examination. Fragments of ulcerated neoplasm composed of solid nests of cells with abundant clear cytoplasm and mild to moderate pleomorphic nuclei, with irregular nuclear membrane and occasional prominent nucleoli were microscopically identified. Immunohistochemistry showed tumour cell reactivity for EMA, vimentin, CD10, Cam5.2 and PAX8. CK7, CK20 and CDX2 were negative. The histomorphological and immunophenotypic features were consistent with metastatic clear cell renal cell carcinoma.
Conclusion: Gastric metastasis from renal cell carcinoma can rarely present as polypoid mucosal lesions and may occur several years after nephrectomy. The pathologist must be suspicious enough to include metastatic clear cell carcinoma in the differential diagnosis. Given the abundance of clear cell malignant tumours, obtaining a complete medical history is a prerequisite for a correct diagnosis, just as a proper diagnosis is a prerequisite for a correct treatment.

E-PS-06-030
Vanek's tumour in a child
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Background & objectives: Inflammatory fibroid polyp (IFP), also known as Vanek's tumour, is an uncommon in children that may occur throughout the gastrointestinal tract. We report a case occurring in the ileum and define its main clinic-pathological aspects.
Methods: We presented a rare case of a 13-year-old girl without any medical or surgical history. She had paroxysmal pains progressing for 10 days, initially associated with early postprandial vomiting. The clinical symptoms and CT scan images were consistent with intussusception by a tumour mass. An ilea surgical resection was done.
Results: We received a 20 cm resection specimen of small intestine. We noted a sessile polypoid tumour of 4.5x4 cm, covered focally by an ulcerated mucosa. On microscopy, the tumour was sub mucosal, composed of spindle and stellate stromal cells. The stroma was oedematous containing thin-walled blood vessels and an inflammatory infiltrate mainly eosinophilic. On immunochemical analysis, the spindle cells were negative for CD117, DOG-1, smooth muscle actin, desmin, S100 protein and ALK. The CD34 stain was positive. A diagnosis of IFP (Vanek's polyp) of the ileum was made.
Conclusion: IFP is a rare and benign tumour of the digestive tract. It is seen mainly in adults and very occasionally in children. IFP is frequently revealed in children by intussusception that can be life-threatening, as in the case of our patient. Its diagnosis is evoked on the various morphological aspects on the microscopy and confirmed by the immunochemical study.

E-PS-06-031
intestinal T-cell lymphoma: a report of 7 cases
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Background & objectives: Intestinal T-cell lymphomas (ITCL) are rare with variable clinical and pathological features. WHO classification has been revised recently and classify them into: enteropathy-associated T-cell lymphoma (EATL), monomorphic epitheliotropic Intestinal T-cell Lymphoma(MEITL),ITCL not otherwise specified and Indolent T-cell lymphoproliferative disorder of the GI tract.
Methods: It is a retrospective study including 7 cases of ITCL diagnosed in the Department of Pathology of Farhat Hached and Sahloul University Hospital of Sousse (Tunisia) during 2014-2020. This study included 6 men and a woman.
Results: 4 patients had symptoms of chronic abdominal pain. The other 3 patients underwent emergency operations due to acute perforation or massive haematochezia. The site of lesion involvement was the small bowel in 6 cases and the duodenum in one case. One patient had a history of celiac disease. 7 specimens surgically resected were collected. Grossly, 5 patients had multifocal lesions. On immunohistochemistry, tumour cells were positive for CD3 in all cases, CD5 in 3 cases and negative for CD20 in all cases. 2 of 4 patients with CD56 staining results were positive. One patient was simultaneously CD56+ and granzyme B+ and was diagnosed with intestinal NK/T-cell lymphoma.
Conclusion: ITCL is a rare and aggressive type of extranodal T-cell lymphoma. It can be very challenging to diagnose clinically and particularly on limited endoscopic biopsy samples. Its diagnosis should be correlated to clinical symptoms while the final diagnosis is mainly based on the pathological and immunohistochemical features. An accurate diagnosis selects the proper operative approach that may reduce serious complications and create opportunities for further treatment.

E-PS-06-032
Extramucosal anal canal adenocarcinoma, non-anal gland type, and non-fistula-associated with mucinous appearance: a recently described diagnostic entity
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Background & objectives: Extramucosal anal canal adenocarcinoma, non-anal gland type, and non-fistula-associated has been recently

proposed as a new entity in the WHO classification. Only a few cases of intestinal-type have been reported. We presented a case of such an exceedingly rare malignancy.
Methods: Clinicopathologic features of a case of extramucosal anal canal adenocarcinoma, non-anal gland type, and non-fistula-associated with mucinous appearance were described.
Results: A 71-year-old male experienced painless anal bleeding. The clinical diagnosis was internal haemorrhoids and an anal polyp. Haemorrhoidectomy with excision of an anal polypoid lesion was performed. Poorly differentiated adenocarcinoma embedded in a large amount of extracellular mucin was observed. Most of the cancer cells were centred in the connective tissue. Despite focal ulceration, most of the overlying anal squamous mucosa remained intact. The neoplastic cells showed lower gastrointestinal immunophenotype (CK7-/CK20+/CDX2+/SATB2+). No lymph node metastasis is seen. Computed tomography showed neither intrathoracic nor intraabdominal malignancy. The pathological diagnosis was extramucosal anal canal adenocarcinoma, non-anal gland type, and non-fistula-associated of mucinous-type. The patient had disease-free survival at eight months postoperatively.
Conclusion: We presented a case of extramucosal anal canal adenocarcinoma, non-anal gland type, and non-fistula-associated of mucinous-type. To the best of our knowledge, this was the first reported case of such malignancy of mucinous-type. Recognition of such an uncommon malignancy and excluding its mimics, including secondary anal canal adenocarcinoma, fistula-associated anal canal adenocarcinoma, and mucinous adenocarcinoma arising from primary anal Paget disease, is essential to arrive at the appropriate diagnosis, justify the treatment, and determine the prognosis.

E-PS-06-033
Synchronous and metachronous tumours presentation with gastrointestinal stromal tumours in a reference center in Colombia
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Background & objectives: Gastrointestinal stromal tumours (GISTs) can co-exist with other primary tumours from the gastrointestinal (GI) tract or other extra-GI sites. The aim of this study is to describe patients with synchronous and metachronous GISTs in a reference centre in Bogota, Colombia.
Methods: A case report series of 22 GIST cases with synchronous and metachronous primary tumours were analysed; extracted from a retrospective descriptive study of 207 GIST cases at Hospital Universitario Fundación Santa Fe de Bogotá between 2008 and 2018.
Results: Of the 22 patients, 11 cases had synchronous tumours and 11 metachronous. Mean age at diagnosis were 69 and 68 years old, respectively. 63.4% were male. GIST locations: stomach 68.2% (9 synchronous/6 metachronous), 22.3% small intestine (1 synchronous/4 metachronous), and 9% other. Main histologic subtype was spindle cell (77.3%) and 40.9% were classified as low risk, all CD117/DOG1+. Coexistence tumours included: GI adenocarcinomas (3 synchronous/2 metachronous), pancreatic adenocarcinoma (3 synchronous), 1 synchronous cholangiocarcinoma, 4 metachronous prostatic adenocarcinomas, 2 metachronous papillary thyroid carcinomas, 1 metachronous lymphoma, 1 synchronous multiple myeloma, 2 synchronous neuroendocrine neoplasms (small intestine/peripancreatic) and 1 synchronous gastric-schwannoma. Median size was 1.40 cm (synchronous) vs 12 cm (metachronous) (p=0.0004).
Conclusion: We present cases of sporadic GISTs, which are infrequent tumours. In accordance with results reported in our study and in published literature; the coexistence of GISTs with other primary tumours (synchronous or metachronous) are more common than expected. Synchronous GISTs were mostly located in the stomach (9/11), and low risk (10/11). Metachronous GISTs were mainly classified as high risk (7/11) and mostly located in the small intestine and mesentery. The coexistence of GISTs with other neoplasms should be carefully investigated.

E-PS-06-034
Anal Involvement in patient with pemphigus vulgaris: case report
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Background & objectives: Pemphigus Vulgaris (PV) is a low incidence autoimmune mucocutaneous bullous disease, in which pathogenic antibodies are directed against the keratinocyte cell surface. Although anal involvement is unusual, correlations between its appearence and disease severity have been recently reported.
Methods: A 41-year-old man presented with a one-year history of intense anal pain episodes accompanied with bleeding rectal. He reported recurrent aphthous lesions in the oral mucosa and pharynx as well. He received topical management for anal fissures without symptomatic improvement, he was subsequently scheduled for chemical sphincterotomy with botulinum toxin and fissurectomy, with a clinical diagnosis of probable Crohn's disease.
Results: The excised tissue showed an irregular white anal mucosa with grey areas. Histopathological study of the resection revealed marked epithelial hyperplasia with areas of epithelial erosion, papillomatosis and extensive, multiple intraepidermal suprabasal bullae containing detached keratinocytes and occasional eosinophils. This process is known as acantholysis and follows a disturbance and disruption of the intercellular connections of the epidermis. Additionally, formations of microabscesses in the superficial and middle dermis were identified with significant amounts of lymphoplasmocytic cells, accompanied with areas of acute inflammatory infiltration consisting of eosinophils and polymorphonuclears. This morphology suggests a vegetative variant of PV.
Conclusion: PV lesions can present on the skin or mucosa, although oral lesions are the most common site of initial presentation. Anal canal and perianal skin involvement may appear in extensive disease. Initial misdiagnosis is related to the chronic development and deteriorations of patients with PV. Anal PV is a diagnostic challenge and this case illustrates the importance of a careful evaluation. Limited knowledge of anal PV presentation can incorrectly diagnose lesions as anal fissures or anal Crohn's disease.

E-PS-06-035
Primary sclerosing cholangitis and ulcerative colitis: a case report of malignancy
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Background & objectives: Primary sclerosing cholangitis (PSC) is a major hepatobiliary complication of ulcerative colitis (UC). The concomitance of both pathologies increases the risk of malignancy; however. the etiologic relationship between PSC and UC still remains poorly understood.
Methods: We present a case of a 36-year-old man diagnosed with PSC who underwent liver transplantation due to biliary cirrhosis in 2004. Seven years later, he is diagnosed with a severe and intractable form of UC and submitted to periodic colic biopsies for evaluation of activity and dysplasia, therapeutic adjustment and to rule out cytomegalovirus infection.
Results: In 2018, during a routine biopsy he was diagnosed with invasive adenocarcinoma, with mucin production and signet ring cells. Immunohistochemistry analysis favoured colic origin with CK20 and

CDX2 strongly positive and CK7 focally positive. He underwent total colectomy and the gross evaluation revealed a 10cm ulcerated neoplasm in the caecum, whose histopathological study was in agreement with the biopsy diagnosis, with pT3N2b staging. The molecular study revealed a G12C mutation (p.Gly12Cys), in codon 12 of the KRAS gene. Unfortunately, he died a month later. We cannot discard that the development of this malignant neoplasm and the accelerated tumour growth could have been a main complication of the prolonged immunosuppressive therapy.
Conclusion: UC is the most prevalent form of inflammatory bowel disease, coexisting in 70-80% of patients with PSC. The risk of malignancy is 4x higher in patients with PSC and UC, compared to those with isolated UC. Dysplasia represents the best and most reliable marker of malignancy; however, it can be invisible and difficult to identify. Colonoscopic surveillance with 4 biopsies from every 10 cm of the entire colon and from visible lesions remains the major way to detect early dysplasia.

E-PS-06-036
Structure of the gallbladder wall in calculous cholecystitis on scanning electron microscopy
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Background & objectives: The development of digital technologies allows in-depth study of pathological processes and clearly demonstrate the spatial relationship of various structural elements in tissues. The analysis of the features of the gallbladder was no exception.
Methods: Gallbladder samples were obtained from 1,130 patients operated on for destructive and non-destructive calculous cholecystitis. Part of the gallbladder was examined using a scanning electron microscope. The preparation of samples for the study was carried out according to the standard protocol. The samples were examined using a low-vacuum electron scanning microscope JSM-6010LV (Japan).
Results: The performed studies have shown that in acute destructive calculous cholecystitis, the architectonics of the layers are preserved in most cases. The mucous membrane and submucosal layer of the gallbladder form pronounced folds. The thickness of the submucosal layer increases due to oedema, swelling of connective tissue elements and inflammatory infiltration. The muscle and connective tissue layer are thickened. In non-destructive cholecystitis, the folds of the mucosa are flattened. The muscle layer was sharply thickened due to hypertrophy of muscle fibres and an increase in the percentage of connective tissue in the intermuscular space.
Conclusion: The use of scanning microscopy in the study of the surface of the gallbladder allows you to clearly determine the spatial relationship of the wall layers, to identify changes in the structure of the layers, to identify the localization zone and the prevalence of inflammatory infiltrate and haemorrhage zones.

E-PS-06-037
Synchronous breast carcinoma with carcinoma of the papilla of Vater: report of a rare entity
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Background & objectives: Breast cancer (BC) occurring in man is a rare entity (less than 1% of all male cancers). Ampullary carcinoma (AC) is a rare tumour (0.5% of carcinomas of the gastrointestinal tract). The coexistence of these two tumours is exceptional.
Methods: By the present case, we illustrate a rare situation of synchronous tumour: breast carcinoma with carcinoma of the papilla of Vater in a 41-year-old man.
Results: The patient was diagnosed with invasive carcinoma with no special type of the breast in September 2019. Two months later, he consulted for jaundice. Explorations an ampullary mass measured 20 mm. Pathologic examination of the biopsy specimen concluded to a moderately differentiated adenocarcinoma. The immunohistochemical study for the GATA3 and CK20 antibodies was negative, excluding the hypothesis of breast metastasis. The patient was a candidate for a left mastectomy with a cephalic duodenopancreatectomy. The outcome was good without recurrence or metastasis after a 16-month follow-up.
Conclusion: AC can be sporadic or be part of hereditary syndromes, in these cases, AC is associated with colorectal cancer. Association with BC is not well-illustrated. Some authors suggest that the BRCA2 gene mutation is a common risk factor of these tumours. The frequency of this mutation varies between 4 and 40% for male BC and is about 12,5 % for AC. Further genetic studies will be needed to prove the implication of the BRCA2 gene mutation in this exceptional association.

E-PS-06-038
HER2 positive colorectal cancer: what other markers influence the prognosis?
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Background & objectives: Although HER2 activation is low in colorectal carcinoma (CCR) – approximately 5%– it has been demonstrated that HER2 status is associated with a poor prognosis. We aimed to investigate other prognosis markers that can be used to preview patients' outcome.
Methods: Immunostaining for p53, Ki67, microsatellite instability markers (MSI) and CDX2 was performed on 10 consecutive HER2 positive CRC. Membrane HER2 positivity was scored as 1+/2+/3+. p53 expression was scored as 1+ (5-25%), 2+ (25-75%) or 3+ (>75%). Ki67 was quantified in the same manner as CDX2: the percentage of positive nuclei. MSI analysis was recorded as negative/positive.
Results: All tumours were adenocarcinomas, 90% being moderately differentiated (G2), while only one case was poorly differentiated (G3). Of the 10 cases 60% were HER2 3+, 30% HER2 2+ and 10% HER2 1+. p53 IHC showed 70% of cases 3+, 20% 2+, 10% 1+. High Ki-67 expression (>40%) was observed in all cases. CDX2 was hyperexpressed in each case with over 90% of nuclei stained. MSI, as expected according to the literature, was negative in the majority of cases, with 20% resulting positive. HER2 expression was significantly associated with p53 positivity (p=0.001).
Conclusion: Since HER 2 expression is consecrated to represent a poor prognosis for the patient, it is important to acknowledge all the other factors which may intervene in the process of evaluating the risk, especially those that appear with the highest frequency. High KI67 index and p53 positivity also indicate a poor outcome. CDX2 loss is rare in HER2 positive CRC.

E-PS-06-039
A proposal for modification of Peritoneal Surface Oncology Group International (PSOGI) classification according to Ki-67 proliferation index in pseudomyxoma peritonei (PMP)
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Background & objectives: PMP is classified by PSOGI into three groups: PMP low-grade histology (LG-PMP), PMP high-grade (HG-PMP), and with signet ring cells (SC-PMP). Ki67 proliferation index is a prognostic factor for several tumours. We related its PMP positivity rate to patients' outcomes.

Methods: Prospective study using collected tissue samples from patients with PMP treated in our Unit from 1997 to 2020. The entire cohort was classified according to the new PSOGI LG-PMP, HG-PMP, or SC-PMP groupings and cases with acellular mucin.
In addition, Ki67 proliferation index was determined immunohistochemically in HG-PMP samples.
Results: The 5 years overall survival (OS) were 72% and 22% for Ki67 less or equal to 15% and greater than 15%, respectively.
The HG-PMP group was divided in two subcategories using the Ki67 15% cut-off (PSOGI-Ki67). The multivariate analysis showed as only prognostic factor for overall survival and for disease free survival the PSOGI-Ki67 variable: OS 161+/-14; 128+/-17 y 31+/-8 months for LG-PMP, HG-PMP-Ki67<15% and HG-PMP-Ki67>15%. The mean disease-free survival (DFS) was 138+/-10; 66+/-9 and 19+/-5 months in each group. Mean DFS at 5 years was 100%, 70% and 24%, and mean DFS at 5 years was 90%, 40% y 0%, in each group.
Conclusion: The division of the HG-PMP category into the PSOGI PMP classification according to the Ki67 proliferation index provides two subcategories well defined with significant differences for overall survival and disease-free survival. This new proposal modification must be validated in an international collaborative study.

E-PS-06-040
Unusual presentation of polypoid ileal leiomyosarcoma: a case report
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Background & objectives: We report the case of an 81-year-old woman with severe colic abdominal pain, which underwent emergency surgery after radiological diagnosis of intestinal intussusception. As a result, an uncommon neoplasm in the gastrointestinal tract was discovered.
Methods: We carried out a thorough medical history revision, followed by meticulous macroscopic, microscopic and immunohistochemical study. In addition, a complete literature review was undertaken.
Results: A 15 cm ileocecal resection specimen with a 3.2x2cm ileal pedunculated polypoid lesion was received. The lesion showed a solid, whitish-fibroelastic surface.
Microscopically, the lesion consisted of a disordered proliferation composed by pleomorphic cells, some were spindled-shape, others epithelioid, with marked nuclear atypia, eosinophilic cytoplasm and high mitotic index. The described neoplasm invaded the muscularis propria without affecting serosa. No Necrosis, lymphovascular or perineural tumour invasion was identified. Immunohistochemically, neoplastic cells showed positivity for smooth muscle actin, desmin and caldesmon, while CKAE1 / AE3, S100, CD117, DOG1 and CD34 were negative.
Thus, the final diagnosis was established as pleomorphic leiomyosarcoma with free resection margins.
Conclusion: Leiomyosarcomas are malignant mesenchymal neoplasms derived from smooth muscle cells that rarely develop in the gastrointestinal tract, with the ileum being the most frequent location. Furthermore, the described case showed an infrequent clinical and macroscopic presentation, with intestinal subocclusion that required emergency surgery and resection of the intestinal affected segment. Due to the clinical presentation and the emergency operation, the patient obtained optimal oncological surgery with wide tumour resection and free margins.

E-PS-06-041
Childhood intestinal PTEN hamartomatous polyposis: a case report
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Background & objectives: Gastrointestinal polyps are most frequently sporadic in nature. Some polyps appear as a part of hereditary polyposis syndromes. Hamartomatous polyposis syndromes (HPS) comprise a group of distinct entities. The objective is to analyse epidemiological, clinical and pathological characteristics of HPS.
Methods: A female infant of 2-year-old presented acute bowel intussusception. The patient had the history of bilateral cervical lipoma. Physical examination showed axillary and cervical nodules. Thoraco-abdominal computed tomography revealed small bowel invagination with polypoidal appearance of the intestine. Mediastinal and abdominal lymph nodes were identified. Segmental intestinal resection with left axillary nodules excision was performed.
Results: Macroscopically, the intestine was diffusely involved by sessile polyps measuring 1 to 5 mm. The mesentery comprises hyperplastic lymph nodes. The axillary nodules were with adipose nature. Histologically, polyps were with different histological types. Some polyps were inflammatory composed of enlarged villi with non-dysplastic epithelium and exhibit inflamed axis. Others were hyperplastic polyps composed of serrated hyperplastic crypts. Few polyps were categorized into lymphoid polyps. Mesenteric lymph nodes were hyperplasic. A final diagnosis of hamartomatous polyposis was made. Microscopical examination of axillary nodules confirmed the diagnosis of benign lipoma. Given admixture of polyp histology and the association with lipomatosis and hyperplasic lymph nodes, PTEN hamartoma tumour syndrome was considered.
Conclusion: HPS are rare hereditary cancer syndromes which occur at any age. They include Peutz-Jeghers syndrome, juvenile polyposis syndrome and PTEN hamartoma tumour syndrome (PTHS). PHTS is a highly variable autosomal dominant condition associated with macrocephaly, bowel admixture hamartomatous polyps, lipomatosis, penile freckling and lymphoid tissue hyperplasia. Their diagnosis may rely on clinical and histological criteria but genetic test is the gold standard for HPS

E-PS-06-042
Malignant gastrointestinal neuroectodermal tumour in small intestine presented with perforation in young man; a rare case
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Background & objectives: Malignant Gastrointestinal Neuroectodermal Tumour (MGNT) was a rare tumour of gastrointestinal system. It is an aggressive tumour with a high rate of local recurrence, metastases, and early death from disease.
Methods: A 29 years old male patient admitted to the emergency service with severe abdominal pain. Physical examination, radiological and laboratory findings suggested a perforation is caused by mass 5 cm sized in small intestine. Partial small intestine resection was performed by general surgery department.
Results: We received an intestinal segment measuring 12 cm in length. Intestinal wall showed perforation with extensive exudate. Cut surface showed a mass with extensive necrosis and haemorrhage measuring 5×4.5×4 cm. Tumour was present in the gut wall; overlying mucosa was ulcerated. Microscopically a poorly differentiated malignant tumour showing solid pattern. Tumour cells were having eosinophilic/clear cytoplasm, ovoid nuclei with dispersed chromatin and conspicuous nucleoli. Tumour was mitotically active(5-6/10hpf) and Ki67 proliferation index was 15%. On immunohistochemistry, tumour was positive for vimentin, S100, synaptophysin, CD56, SOX10, cyclin-D1, FLI-1, neurofilament and were negative for panCK, CD117, HMB-45, CD34, SMA, desmin, CD99 and chromogranin. EWSR1 gene rearrangement was determined by the FISH.
Conclusion: We thought that due to the limited literature available on GNET and rarity of this neoplasm documentation of any such case is important. The combined approach utilizing a comprehensive panel of

immunohistochemical markers along with molecular analyses is suggested for identification of this tumour and distinguishing it from its mimickers.

E-PS-06-043

Malignant gastrointestinal neuroectodermal tumour of the ileum: a case report

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Background & objectives: Malignant gastrointestinal neuroectodermal tumour (GNET) is a highly aggressive, recently identified primary gastrointestinal malignant mesenchymal tumour, characterized by epithelioid and/or spindle cells, arranged in various patterns. Its' hallmark is the Ewing sarcoma breakpoint region 1 gene (EWSR1) rearrangement.
Methods: We report a case of an 80-year-old woman, who was admitted with melena, haematochezia and anaemia. The patient underwent capsule endoscopy showing an exophytic bloody lesion on the terminal ileal wall, and a MRI that prompted suspicion of a malignant gastrointestinal stromal tumour (GIST).
Results: A segmentar enterectomy was performed, and the specimen showed a nodular, mass-forming, ulcerated lesion, with 6x5,5x5 cm. Histopathological features included a transmural infiltration by a neoplastic population composed of nests and solid sheets of oval cells, with scant clear cytoplasm, and nuclei had vesicular chromatin with prominent nucleoli. Tumour cells showed immunoreactivity for CD99 (strong and diffuse), and were negative for DOG1. FISH analysis showed split EWSR signal (22q12). Primitive gastrointestinal neuroectodermal tumour was the final diagnosis. The patient remained disease free for 27 months, until she became symptomatic with diarrhoea. CT and PET scan were performed and identified three intra-abdominal metastases.
Conclusion: Malignant gastrointestinal neuroectodermal tumour, although rare, should be suspected in cases of a gastrointestinal tumour displaying epithelioid and/or spindle cells in various patterns. EWSR1 chromosomal rearrangement is recommended to confirm this diagnosis. We report the oldest patient with this tumour arising in the ileum, to our best knowledge. Because of its rarity, the prognostic information of this tumour is limited, no staging criteria are suggested, and treatment response to chemotherapy and targeted therapy remains unknown.

E-PS-06-044

Intestinal tuberculosis mimicking cancer clinically: a case report

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Background & objectives: Tuberculosis is an infectious disease transmitted by air and caused mainly by Mycobacterium tuberculosis. The disease mainly affects the lungs and can affect other organs and tissues in the body. In this case, a form of intestinal tuberculosis will be clinically mimicking cancer.
Methods: Male patient, 49 years old, referred to the Pouso Alegre Hospital/Brazil, due to severe diffuse abdominal pain, greater in the epigastric region, with two months of evolution. After clinical, laboratory, and CT exams, he underwent surgery and, when entering the cavity, a tumour was evidenced in the topography of the cecum affecting the ascending colon and several more lesions in the small intestine.
Results: Samples of intestinal tissues with supposed neoplasia were sent for anatomopathological examination. Having a diagnosis of tuberculosis, involving large and small intestine walls, presenting a chronic granulomatous inflammatory process with central caseous necrosis and positive microscopic examination of acid-alcohol resistant bacillus.
Conclusion: In Brazil and other developing countries, tuberculosis is still a disease in evidence. In this reported case, we affirm the importance of histopathological analysis and diagnosis that will define the correct treatment (in the present case, the clinical approach showed a neoplasm, after the histopathological result, the treatment was completely redirected towards infectious contagious disease.

E-PS-06-045

EBV-positive post-transplant lymphoproliferative disorder: an unusual presentation

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Background & objectives: Post-transplant lymphoproliferative disorder (PTLD) is a rare but serious complication following solid organ transplantation. It manifests in the setting of chronic immunosuppression, and it is often associated with the Epstein Barr Virus. PTLD occurs in only 1-3% of renal transplant recipients.
Methods: we report a case of primary aggressive liver involvement of PTLD in a 29 years female patient 6 years after renal transplant. Renal transplant was followed by immunosuppressive treatment. An 11 cm liver mass was discovered during a routine check-up for the renal transplant and the patient underwent an hepatic segmentectomy with cholestectomy and periportal lymph node dissection.
Results: Gross examination showed the presence of a 10 cm, well-limited and subcapsular mass. Histologically, it is a diffuse lymphomatous proliferation. Tumour cells were large and rounded with scanty eosinophilic cytoplasm and hyperchromatic enlarged nuclei, very often with a prominent nucleolus giving a prominent immunoblastic phenotype. Some cells showed a centroblastic phenotype and others were atypical. On immunohistochemistry, the tumour cells expressed diffusely the anti-CD20 antibody and focally the anti-CD30 antibody. CD5, CD3, ALK and CD15 were negative. Search for EBV infection by means of the anti-LMP1 antibody came back positive. Hybridization "EBER" was positive. The diagnosis retained was that of EBV-positive post-transplant diffuse large B-cell lymphoma of the liver.
Conclusion: PTLD is a serious complication following solid organ transplantation. It occurs in only 1-3% of renal-transplant recipients, in which the gastrointestinal tract represents the most common location. EBV infection is a key contributor in PTLD development. WHO categorizations of PTLD are divided into early lesions, polymorphic, monomorphic, and classical Hodgkin lymphoma type PTLD. Histological examination is the gold standard for PTLD diagnosis. Diagnosis should be considered in any patient presenting with a liver mass following solid organ transplant.

E-PS-06-046

Unusual presentation of gastrointestinal tract vasculitis

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Background & objectives: Involvement of the gastrointestinal tract by vasculitis is rare. It can occur as a solitary organ vasculitis or in the context of a systemic vasculitis. Complications may occur, which may be fatal in the setting of a delayed diagnosis.
Methods: Herein we report a case of 75 years male patient with no medical history who presented with constipation and abdominal pain. Colonoscopy showed the presence of a stenosing tumour of the ascending colon.
Results: A biopsy was performed and did not show tumour tissue. The CT-scan showed the presence of a tumour of the right colon with a perineoplastic abscess, hence the indication for an emergency operation. Right colectomy was performed. On gross examination the right colon was perforated, with a brownish indurated mesocolon. The colonic wall was indurated and the mucosa was ulcerated. Histological examination showed ischemic necrosis of the cecum with perforation as well as the presence of vasculitis of the small and medium vessels with fibrinoid necrosis of the

ileocolic vessels and in the fat of the abdominal wall. Non-necrotizing epithelioid and gigantocellular granulomas were also observed.
Conclusion: Vasculitis involving the gastrointestinal tract is uncommon. It often occurs in young female patients. Inaugural and pseudotumoral presentation as described in our case is unusual but described. Numerous vasculitic disorders may involve the gastrointestinal tract, but, solitary organ vasculitis with no evidence of systemic vasculitis may be almost as common. Involvement of the GI tract may lead to serious complications, including ischemia and perforation. Knowledge of the spectrum of vasculopathies that may affect the gastrointestinal tract is critical for diagnosis.

E-PS-06-047
Colitis cystica profunda with dysplastic features presenting in the right semicolon: a case report
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Background & objectives: Colitis Cystica Profunda is an uncommon non-neoplastic entity. Patients are usually middle-aged males and it is more often encountered in the left semicolon. We hereby present a case of Colitis Cystica Profunda with high-grade dysplastic changes.
Methods: A 53-year-old female patient with history of cystic fibrosis and recently experiencing constipation, came to our Hospital for a scheduled check-up. Colonoscopy showed a firm protruding mass close to the ileocecal valve. A biopsy specimen was obtained which revealed high-grade dysplasia. The patient underwent a right hemicolectomy and the specimen was sent to the Pathology Lab for further evaluation.
Results: The gross examination of the specimen revealed a firm, polypoid, mucosal lesion, with a gelatinous cut-surface, resulting in partial obstruction of the right colon. The microscopic examination showed multiple, well-circumscribed cystic mucosal infoldings, mostly filled with mucin, surrounded by lamina propria and located exclusively in the submucosa, without involvement of the muscularis propria. The misplaced epithelial element often exhibited atypical histology, either of reactive nature or high-grade dysplasia, the latter positive for CK8/18 and p504s. The aforementioned lesion was signed out as colitis cystica profunda with high-grade dysplasia.
Conclusion: Colitis cystica profunda with dysplasia is a rare nosological entity. About 200 cases have been reported in the literature so far. It is most commonly encountered alongside previously diagnosed inflammatory bowel disease and it may be misinterpreted as a malignant lesion both clinically and radiologically. Pathologists should remain alert to the possibility of a possible mucin producing adenocarcinoma. Correlation with the patient's history and the endoscopic and radiologic findings is crucial for the correct pathological diagnosis.

E-PS-06-048
Gastric and colon cancer stages: before and during peak of COVID-19
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Background & objectives: When COVID-19 hit Turkey, most of the elective surgeries were suspended during this time. Our main goal here is to re-evaluate TNM stages of cancer patients undergoing gastrectomy and colectomy before and during the peak of Covid-19.
Methods: The first Covid-19 case was detected in March 2020 in Turkey. Therefore, we evaluated the gastric and colon cancer specimens admitted to our lab in the period of one year prior to and one year following March 2020. We compared the cases, before the Covid-19 pandemic, to the peak of pandemic according their pathologic TNM stage.
Results: This study included 41 gastric cancer and 160 colon cancer patients from the baseline period ;28 gastric cancer, 115 colon cancer patients from the COVID-19 period. Among the gastrectomy specimens before covid, 9 pT1 (21.9%), 5 pT2 (12.1%), 13 pT3 (31.7%) and 14 pT4 (34.1%) were reported. Among the colectomy specimens; 9 were pT1 (5.6%), 10 were pT2(6.2%), 69 were pT3 (43.1%) and 72 were pT4 (45%). During pandemic period, gastric carcinoma stages were distributed as 5 pT1 (18%), 2 pT2(7.1%), 7 pT3 (25%) and 14 pT4 (50%). Also, colectomy specimens during pandemic revealed 4 pT1(3.5%), 8 pT2(7%), 62 pT3(54%), 41 pT4 (35.7%) cases.
Conclusion: During the pandemic, decreased number of gastrectomy and colectomy specimens was observed. The proportion of pT4 gastric carcinoma cases was increased significantly. Besides, distinctive difference in stages of colon cancer patients were absent. Consequently, the adversity to reach health care in pandemic led the gastric cancer patients to be operated at advanced stages. Since pandemic still carries on and admissions to hospitals are fewer than normal, we think that we will encounter with more progressive cancer specimens in the future.

E-PS-06-049
Expression of E6 and E7 oncoproteins in liquid-based anal cytology
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Background & objectives: Anal cancer (AC) have been on the rise for the past 30 years. It was proposed an internal referral flow from the specialized network for people with HIV to assess aspects related to the prevention of AC.
Methods: Volunteers were evaluated by a colorectal surgeon. A anorectal exam was performed and anal swab samples were collected for Liquid-based anal cytology, expression of E6 and E7 oncoproteins and high and low risk human papillomavirus genotyping. When altered cytology was found, a high-resolution anoscopy was performed with biopsy of suspicious areas.
Results: 223 volunteers were evaluated, regardless of gender or age. Positivity for human papilloma virus was 85.6% and genotyping for high-risk subtypes was 44.8%. The expression of E6 and E7 oncoproteins was 57.4%. The anal cytology showed 6.7% of altered samples but none of the biopsies performed during the magnification anoscopy showed dysplastic or neoplastic lesions.
Conclusion: The high positivity of the human papillomavirus in the anal region, highlights the need for prevention programs. However, the number of alterations in cytology was very low and since these are very young patients, it can be suggested that screening programs, locally, can start at a later age.

E-PS-06-050
Emphysematous cholecystitis: case report
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Background & objectives: Emphysematous cholecystitis is a fulminant variety of acute cholecystitis that differs in its pathology and epidemiology from cholecystitis, induced by gallstones. Salient feature of this acute cholecystitis is the presence of gas in the lumen and wall of the gallbladder.
Methods: A rare case of emphysematous cholecystitis, occurring in a 66-year-old female, presenting with septicaemic shock is documented. Grossly, a fully cut open, indurated gallbladder, measuring74x43mm, with a wall thickness of 5 to 8 mm was received. Representative sections were submitted in five blocks. Routine H&E analysis was carried out and the histological features were reported digitally using Aperio Image Scope.

Results: Multiple representative sections from the gallbladder showed classical large bullous emphysematous changes on the surface of the gallbladder, scattered within which acute inflammatory cells and necrotic material in variable proportion were noticed. Similar cystically dilated, gas filled, empty spaces within the muscularis propria were observed. Patchy areas of haemorrhagic congestion were seen in the subserosal coat distinctly. Formation of occasional Rokitansky- Aschoff sinuses with acute necrosis, along with formation of septic emboli within the glands was observed.
Foci of lymphoid aggregates, with presence of hemosiderin- laden macrophages were also seen.
Classical features of necrotizing, emphysematous cholecystitis was confirmed. E coli was isolated from the gallbladder lumen.
Conclusion: Though rare in occurrence, an entity of emphysematous cholecystitis needs to be considered in the acute onset of cholecystitis cases, especially over the age of 50 years. Radiological imaging, as it was done in this case, can help to make a preoperative diagnosis. This is a life-threatening emergency and prompt surgical intervention is required.

E-PS-06-051
Retrorectal adenocarcinoma associated with a tailgut cyst: a case report and literature review
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Background & objectives: Tailgut cyst, also known as retrorectal cystic hamartoma, is a lesion thought to be originated from the embryonic remnants of the tailgut. The last reported incidence was of 0,55% in paediatric population. Non-complete excision leads to recurrence.
Methods: This report presents the case of a 39-year-old woman with a history of a sacrococcygeal cyst that was partially excised in childhood. In September of 2020, a tailgut cyst was excised and diagnosed in our institution. Four months post-surgery, due to persistent back pain, an imagiologic re-evaluation was performed by MRI.
Results: The imagiologic re-evaluation revealed a persistence of the solid portion of the previously described lesion, with the involvement of the anococcygeal raphe, with a major axis of 45mm. An operative excision of this lesion was performed. Microscopically, a proliferation of neoplastic cells with hyperchromatic nuclei was observed, infiltrating the fibrous-connective tissue and forming rare glands. Perineural and lymphovascular invasions were identified. The neoplastic cells were positive for cytokeratin 7, cytokeratin 20, CDX2 and negative for beta-catenin. The diagnosis was of poorly differentiated adenocarcinoma of colorectal versus retro-rectal origin. A fragment of a cystic wall with ciliated epithelium, resembling the previously excised tailgut cyst, was also present.
Conclusion: The history of a previous tailgut cyst associated with a recurrent lesion in the area should increase suspicion for the risk of malignancy. Since the incidence of malignancy is considered to be higher than previously referred in literature, extensive sampling is required. In this case, after analysing the histochemical profile and undergoing an extensive thoraco-abdominopelvic evaluation for a possible primary lesion that held no results, the adenocarcinoma was regarded as a retro-rectal primary entity.

E-PS-06-052
A rare cause of pneumoperitoneum: pneumatosis cystoides intestinalis
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Background & objectives: Pneumatosis cystoides intestinalis is a rare subtype of intestinal pneumatosis that is characterized by gas-filled cavities located in the intestinal mucosa, submucosa and subserosa. It can occur anywhere along the gastrointestinal tract, but the colon is the most common location.
Methods: We report a case of a 90-year-old woman that presented to the emergency department with a 48 hour history of acute diffuse abdominal pain, abdominal distension and vomiting. A computed tomography scan showed free air in the peritoneal cavity (pneumoperitoneum) and multiple air-filled spaces within the wall of a segment of the jejunum along with several diverticula.
Results: The patient was submitted to an emergency laparotomy and due to suspicion of diverticular perforation a segmental bowel resection was performed. Gross specimen of the 20cm long resected segment of the jejunum showed multiple empty cavities expanding the submucosa and the subserosa with a sponge-like appearance. Several jejunal diverticula were found along the intestinal wall, none of them with signs of diverticulitis, perforation or haemorrhage. The histological examination showed multiple empty cavities which were observed predominantly in the submucosa but also in the mucosa, muscularis propria and subserosa. The periphery of these cavities was lined by multinucleated giant cells. The diverticula had no remarkable inflammation and no signs of perforation.
Conclusion: Pneumatosis cystoides intestinalis (PCI) can be divided into primary or idiopathic type and secondary type. Secondary causes of PCI include pulmonary disease, inflammatory bowel disease, connective tissue disorders, iatrogenic procedures, medications and organ transplantation. There are only a few case reports of PCI associated with jejunal diverticulosis and it is hypothesized that the cause of this association could be related with mechanical and bacterial factors.

E-PS-06-053
Secondary tumours of the gastrointestinal tract
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Background & objectives: Secondary tumours of the gastrointestinal tract are rare and may mimic primary tumours at the morphological level. In this study, the distribution of tumours metastasizing to the gastrointestinal system were investigated.
Methods: 39 cases diagnosed with metastasis in the gastrointestinal system in our department between 2010 and 2021 were included in the study. Serosal implants that do not cause mass lesions were excluded from the study.
Results: 23 of the patients were female and 16 were male and their ages ranged from 31-81. The primary focus is the female genital system in ten cases (seven cases of the ovary, two cases of endometrium, one case of endometrial stromal sarcoma), the lung in seven cases, the breast in six cases, the stomach in five cases, the kidney in three cases, the prostate and bladder in two by two. The most common metastasis was located in the colorectal region with 25 cases. This was followed by small intestine metastasis in 12 cases, gastric metastasis in seven cases, appendix metastasis in two, and oesophageal metastasis in one.
Conclusion: The presence of multiple lesions, the absence of tumour growth from the mucosa in resection materials for epithelial tumours, the widespread lymphovascular invasion, the absence of the precursor lesion, the sharpness of the tumour-mucosa transition, as well as the presence of tumour with unexpected morphology for the organ may be diagnostic clues. In such cases, careful anamnesis, endoscopic, radiological findings, evaluation of tumour markers and organ-specific immunohistochemical examination also guides the diagnosis.

E-PS-06-054
Metachronous metastasis of gastric carcinoma to the traverse colon: a case report
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Background & objectives: Advanced gastric cancer is often metastatic to the liver, peritoneum, lungs and bones. On the contrary, gastric metastasis to the colon is quite rare.
We present a rare case of metachronous gastric cancer metastasis to the traverse colon.
Methods: A 57-year-old female with a past medical history of gastric cancer, diffuse type, presented with symptoms of partial bowel obstruction and on CT-imaging was diagnosed with oedema and thickening of the traverse colon wall. The patient underwent a subtotal colectomy. Grossly there was stenosis of the traverse colon lumen and thickening of the wall extending in total length 10cm.
Results: The histological examination revealed whole-thickness invasion of the colonic wall by cancer cells with eccentric nucleus, eosinophilic cytoplasm and occasional signet-ring features. A panel of immunohistochemical markers was used which highlighted the CK7(+), CK20 (-), CDX2(+), GATA3(-), ER(-), PR(-) immunophenotype of the cancer cells. The aforementioned morphological features and immunohistochemical findings, along with the patient's past medical history, established a diagnosis of metachronous gastric cancer metastasis to the colon.
Conclusion: Gastric cancer with synchronous or metachronous metastasis to the GI tract is rare. It is usually associated with diffuse gastric cancer, plastic linitis and peritoneal dissemination. The patients have end-stage disease with poor outcome and short-term survival rate. Differential diagnosis includes other carcinomas that can metastasize to the GI tract, such as lobular breast carcinoma and prostate cancer, so a detailed medical history is paramount for the diagnosis.

E-PS-06-055
Extra-gastrointestinal stromal tumour of the greater omentum (E-GIST) - two cases report
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Background & objectives: E-GISTs are intra-abdominal mesenchymal tumours occurring outside the gastrointestinal tract and comprise less than 5% of GISTs. Great omentum GISTs account for 1% of all E-GISTs. They affect more commonly elderly patients.
Methods: It is very important to recognize E-GISTs given their unknown biological behaviour. We present two cases of E-GIST arising in great omentum, both in males, 67 and 65 years old.
Results: In the first case, the tumour was composed histologically of spindle neoplastic cells with palisading features. There were >5 mitosis/50HPF. In the second case, the neoplastic cells had an epithelioid morphology with <5mitosis/50HPF. In both cases, necrosis was present in <50% of the tumour and no infiltration of the capsule was found. A panel of immunohistochemical markers comprising of Vimentin, CD117, CD34, SMA, Desmin, PDGFRα and DOG1 was used and the findings were consistent with the diagnosis of E-GIST.
Conclusion: It is very important to recognize E-GIST, because there are uncommon and rare intra-abdominal tumours. The therapeutic approach is surgical removal in combination with administration of a tyrosine kinase inhibitor (imatinib mesylate), while chemotherapy and radiotherapy are not effective.

E-PS-06-056
Renal cell carcinoma metastasis in the duodenum - an unusual site
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Background & objectives: Renal cell carcinoma (RCC) metastases to the duodenum are exceedingly rare with less than 30 cases reported in the literature. We report a recent case from our institution, presented with gastrointestinal bleeding.
Methods: A 76-year-old male with NSAID intake and a history of right nephrectomy 9 years earlier for RCC was admitted to the hospital because of episodes of melena. Coloscopy was normal but gastroscopy revealed a 4cm ulcer with dirty base in the duodenum and a biopsy was performed. Sections from the specimen were examined with H+E and immunohistochemistry.
Results: Microscopical examination revealed normal enteric type epithelium on surface with foci of an ulcerated, infiltrative tumour. Tumour cells demonstrated abundant clear cytoplasm and distinct membrane and were mainly arranged in compact nests, showing focally sarcomatoid features. Immunohistochemistry was performed taking into consideration patient's history and tumour cells were positive for Pax8, CAIX, Vimentin, focally for RCC and CD10 and negative for CK7, AE1/AE3, p40, GATA3, S100 and MelanA. Gastrointestinal origin of the tumour was excluded due to negativity for CK20 and CDX2. The morphological aspect and the immunohistochemical profile lead to a diagnosis consistent with metastasis of clear cell renal carcinoma in the duodenum.
Conclusion: RCC behaves unpredictably with a diverse range of clinical manifestations. Small bowel metastases from RCC are rare, the incidence has been described as 2-4%. The duodenum is involved less commonly than the small intestine, yet this possibility must be taken into account in patients with a history of renal cancer regardless of the time after nephrectomy. Clinical correlation and immunohistochemistry are mandatory for establishing a correct diagnosis excluding neoplasms with clear cell morphology arising in or metastatic to this area.

E-PS-06-057
Adenosquamous gastric carcinoma of the pylorus - an elusive entity with peculiar morphology
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Background & objectives: Gastric adenosquamous carcinoma is an exceedingly rare entity, defined as an admixture of glandular and squamous cells, the latter accounting for at least 25% of the tumour. This cancer is particularly aggressive and has a worse outcome than gastric adenocarcinomas.
Methods: The aim of this report is to gain further insight into this rare and aggressive variant of gastric cancer, in order to provide a complete diagnosis and the best therapy strategy. Emphasis is placed on evaluating tumour grade and depth and the amount of squamous component in both the tumour and lymphatic metastasis, possible predictors of survival rates.
Results: We present the case of a 77-year-old man diagnosed with gastric adenosquamous carcinoma of the pyloric region and liver metastasis. On standard examination the tumour exhibits characteristic features of an adenosquamous carcinoma with highly atypical glandular cells and a squamous cell carcinoma component comprising more than 60% of the tumour. The malignant proliferation penetrates the serosa and displays both perineural and lympho-vascular invasion. Five out of twelve lymph nodes present massive tumour invasion, all of which displayed a significant proportion of squamous component.
Conclusion: Gastric adenosquamous carcinoma is associated with a poor prognosis in comparison to typical gastric adenocarcinomas. The mechanism of this remains unclear due to the rarity of this disease. As the squamous component has been linked to advanced stage and resistance to treatment, it is crucial to fully assess its extent in both the tumour and lymphatic and distant metastasis. With a better understanding of gastric adenosquamous carcinomas, future studies can focus on target therapies than will increase survival.

E-PS-06-058
Immunohistochemical phenotype of colorectal carcinoma in patients with KRAS mutation and mismatch repair status
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Background & objectives: Aberrant expression of CK7/CK20/CDx2 is reported in a percentage of colorectal carcinomas (CRC). The objective of this study is to investigate specific morphological and immunohistochemical characteristics of colorectal carcinoma with KRAS mutation status and microsatellite instability.
Methods: A total of 71 patients with CRC and examined KRAS mutation status were included in the investigation. Immunohistochemistry was performed using antibody to CK7, CK20, CDx2, PMS2, MSH6. An automatic immunostainer (Ventana BenchMark GX) was used following the manufacturer' protocols. Fisher's exact test was used for statistical analysis (P value < 0.05).
Results: Immunohistochemical analysis for CK7, CK20, CDx2, PMS2, MSH6 and was performed. Aberrant expression of the typical immunohistochemical profile CK7/CK20/CDx2 was observed in 50% of the cases. Highest sensitivity and specificity was established for CDx2 with 93% of the cases demonstrating positive nuclear expression in the tumour cells. As for the microsatellite status, 20 % of the examined colorectal cancers, showed loss in expression for one or both of the mismatch repair proteins - PMS2 and MSH6, which was associated with loss of the expression for CK20 and CDx2 as well. Downhill correlation was estimated also between CK20 expression and the presence of mutation in the gene for KRAS.
Conclusion: Our results may support the heterogeneity of colorectal carcinoma. Statistically significant correlation was established between the expression of CK20 and CDX2 and MSI- and KRAS mutant colorectal cancers. This may lead to application of immunohistochemical screening panel for selection of patients with colorectal carcinoma for genetic testing. Further studies on larger cohorts correlating different immunohistochemical profiles to molecular subtypes of CRC are needed for better understanding of pathogenesis and behaviour of colorectal carcinoma.

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E-PS-06-059
Multiple primary malignant neoplasms in patients with colon cancer: about 3 cases
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Background & objectives: Although very uncommon, multiple primary malignant neoplasms (MPMN) are becoming an increasingly popular subject in medical literature. Our aim is to describe clinicopathological characteristics of MPMN in patients with colon cancer and to discuss possible physiopathological mechanisms of these associations.
Methods: We report 3 rare cases of MPMN in patients with colon cancer diagnosed in the pathology department of Sfax's university hospital in Tunisia. Clinicopathological data of these three cases as well as the outcome were retrospectively reviewed.
Results: All three patients were females aged respectively 63, 72 and 78 years. All of them had a well differentiated colon adenocarcinoma associated respectively with a papillary adenocarcinoma of the lung, a gastrointestinal stromal tumour (GIST) of the stomach and a hight grade serous cystadenocarcinoma of the ovaries. The first patient developed a metachronous pulmonary cancer, which was discovered during imaging follow-up, after 3 years. The other patients had synchronous tumours. The GIST was detected by computed tomography scan while attempting to stage the patient's colon cancer. The ovarian tumours were discovered incidentally during the surgery of the colon tumour. All patients received appropriate treatment without complications.
Conclusion: The incidence of MMPN has gradually increased. According to the literature, 5% of colon cancer patients have an additional primary cancer. Multiple factors may contribute to the carcinogenesis of MMPN. Genetic factors like defects in DNA mismatch repair may be one of the major causes. Hence, it is important to consider the possibility of a second primary tumour in a patient with a diagnosed colon tumour, and not only consider disease recurrence. In this setting, genome-wide association studies are recommended.

E-PS-06-060
Kaposi Sarcoma localised in gastric mucosa: and a rare case that should be kept in mind!
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Background & objectives: Kaposi sarcoma (KS) is a vascular neoplasm caused by human herpesvirus 8 (HHV8) and it tends to be indolent but may be locally aggressive. Skin is predominant site but may also affect lymph nodes, visceral organs or rarely mucosal tissue.
Methods: A 39-year-old male patient admitted to gastroenterology clinic with mild abdominal pain and nausea. An petechiae and erythematous indurated lesion was detected on corpus mucosa with endoscopic examination. Multiple mucosal biopsies were evaluated in our pathology laboratory.
Results: Histopathologically, revealed a lesion with a diameter of 2 mm composed more extensive, compressed, slit-like vascular channels infiltrating lamina propria of gastric mucosa. There was visible intracellular and extracellular hyaline globules and they stain PAS positive. The endothelial proliferation was monomorphic, there was not significant nuclear atypia or increased mitotic activity. Lesion was shown positive rection with CD31, CD34, HHV8 antibodies. Ki67 proliferation index was 5%. Chronic gastritis and parietal cell hyperplasia was detected in around the lesion. We call the clinician based on these findings and asked for detailed information about patient. We learned that the patient was HIV positive and was diagnosed with dermal KS 2 years ago.
Conclusion: Gastric mucosa biopsies are frequently encountered biopsies in our daily routine work. While evaluate these biopsies we must not overlook lesions with slight signs and extremely rare in this localisation. Before diagnosing vascular-rich areas as inflammation and granulation tissue, we should consider vascular pathologies.

E-PS-06-061
Combined goblet cell adenocarcinoma and low grade appendiceal mucinous neoplasm in the vermiform appendix: a case report
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Background & objectives: We report a rare case of a combined goblet cell adenocarcinoma ("GCA") and low grade appendiceal mucinous neoplasm ("LAMN") arising in the vermiform appendix of 72-year-old female. To our knowledge, only ten other cases have been reported.
Methods: A 72-year-old female presented with severe acute right lower quadrant abdominal pain and underwent laparoscopic appendectomy. The appendix was serially sectioned, revealing a pinpoint lumen and 0.4 cm. thick wall, with a 0.5 cm. distended, mucus-filled area 1 cm. from the line of resection, adjacent to a point of rupture. The entire specimen was submitted for routine processing.
Results: Microscopically, two distinct tumour histotypes were identified. The 10mm. GCA was composed of composed of goblet-like cells in tubules and crypts, accompanied by granular eosinophilic neuroendocrine cells in nests, infiltrating from the submucosa into the muscularis propria. The GCA cells stained positively for chromogranin A and synaptophysin and had a low Ki-67 activity level (2.8%). The 6mm. LAMN was composed of a single layer of low grade mucinous columnar cells forming

cystic spaces filled with basophilic mucin, surrounded by fibrosis, with areas of paucicellular mucin dissecting up to the mesoappendix. The LAMN cells were negative for chromogranin A and synaptophysin. The proximal line of resection was negative for both tumours.
Conclusion: GCAs and LAMNs are among the many appendiceal lesions that may present as acute appendicitis or be incidental findings. Thorough gross and microscopic examination of all appendectomy specimens should be performed to identify these and other appendiceal tumours. The origin and the possible relationship of GCAs and LAMNs is debated. They have different molecular characteristics (Wnt-signaling pathway mutations in GCA, KRAS and GNAS mutations in LAMN) however, some evidence supports a common stem cell origin of both tumours.

E-PS-06-062
Colorectal adenocarcinoma with trophoblastic differentiation: a case report and review of the literature
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Background & objectives: Extragenital nongestational malignancy of trophoblastic tissue is very aggressive and rare. There are only 32 cases of colon choriocarcinoma and trophoblastic differentiation in colorectal neoplasms reported in the literature. We present the only one reported in our Hospital`s archives.
Methods: A 40-year-old woman with long-term inflammatory bowel disease. During her last outbreak, high serum level human chorionic gonadotropin (hCG) (243970 UI/L at diagnosis) was detected. Colonoscopy revealed ileocecal valve stenosis and biopsy was performed. A gynaecological study was requested. Radiological studies showed hepatic lesions.
Results: Ileocecal valve biopsy revealed poorly differentiated adenocarcinoma infiltrating the mucosa, with negative endometrial biopsy and hepatic lesions compatible with choriocarcinoma. Surgical resection (right hemicolectomy) was performed and was diagnosed as poorly differentiated adenocarcinoma with trophoblastic differentiation. Inmunoprofile was concordant: caudal type homeobox-2 (CDX2) +, cytokeratin 20 (CK20) + and hCG +. No microsatellite instability or molecular alterations were detected. The patient is currently undergoing oncological treatment against both tumoral components. Serum hCG levels fall significantly (under 20.000 UI/L) but never reached negative levels. Metastatic hepatic lesions are growing slowly. At this time, the patient has relative clinical stability.
Conclusion: According to the literature about malignant neoplasms with trophoblastic differentiation, the clinical course is being aggressive. Although there is no standardized therapeutic management for these rare tumours, the literature reported the clinical importance of choriocarcinoma targeted regimen for prognosis. Nevertheless, further studies are needed.

E-PS-06-063
Incidental findings of malignant lesions in haemorrhoidectomy specimens: a five-years retrospective study with report of seven cases
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Background & objectives: The objective of this study is to know the incidence of malignant lesions found in haemorrhoidectomy specimens, which were not clinically suspected.
Methods: We carried out five-years retrospective study of haemorrhoidectomy specimens collected of the Mateu Orfila Hospital (Menorca), Spain. All samples coded as "haemorrhoidectomy" and/or "haemorrhoid" between 2015 and 2020, were selected from the Pathology Department database. Clinicopathological and demographic variables were collected from the electronic clinical records.
Results: 320 specimens from 181 men and 139 women, were analysed. The mean age was 44 years (range 20-84 years). Relevant data were identified in 7 specimens (2%), the rest were normal. Incidental findings were: 1.-Anal Intraepithelial Neoplasia (AIN) II-III; 2.-Neuroendocrine Tumour (NET) poorly differentiated; 3.-Adenocarcinoma (AD) well-differentiated (G1) and AIN-II; 4.-AIN-II; 5.-AIN I-II; 6.-Malignant Melanoma (MM); 7.-Squamous Cell Carcinoma (SCC) and AIN-III. The resection margins were positive in two cases, negative in one and could not be determined in four cases. The cases that only presented AIN have followed clinical control; the SCC received QT-RDT, currently with no recurrence. NET and MM cases were treated at another centre.
Conclusion: The haemorrhoids are defined as "symptomatic enlargement, displacement of anal cushions". Its prevalence is estimated at 4.4% (up to 13-20%). The incidental findings of malignant lesions found in the haemorrhoidectomy specimens are rare. In our study the incidence was 2.18%. We consider that the resection edges should be stained whenever possible and include a good representation of the material sent from the haemorrhoidectomy specimens, in order to provide as much pathological information as possible.

E-PS-07 | Digestive Diseases Pathology - Liver/Pancreas E-Posters

E-PS-07-001
A case report of an EBV-positive mucocutaneous ulcer of the Caecum occurring with neuroendocrine tumour. Interesting novel collision tumours
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Background & objectives: EBV-positive mucocutaneous ulcer (EBVMCU) is a rare B-cell lymphoproliferative neoplasm associating mostly with immunosuppression either primary or iatrogenic. EBVMCU was first described by Dojcinov in 2010(1) and first recognized by the WHO classification in 2016 as a distinct clinicopathological entity(2).
Methods: An 89-year-old male presented acutely with clinical features suggestive of intestinal obstruction. Radiological imaging revealed an obstructing caecal neoplasm with possible involvement of the ileal mesentery. A right hemicolectomy was performed. Intraoperatively, there was bowel adhesion, but no perforation seen. The patient was not known to have any past history of immunosuppression or was immunocompromised.
Results: Histology showed a 55mm well-differentiated neuroendocrine caecal tumour (NET), grade 1 (Ki67<1%) (pT4) with multiple tumour deposits, lymphovascular invasion, perineural invasion and nodal metastasis (pN1). In addition, a juxtaposed shallow mucosal ulcer (11mm) was identified with underlying submucosal anaplastic neoplasm comprising polymorphous proliferation of atypical cells with occasional multinucleated and Reed-Sternberg (HRS)-like cells noted. The anaplastic cells were entirely negative for a wide range of epithelial, melanoma and muscle markers but were positive for Vimentin, IRF4, LMP-1, PAX-5, CD30 and CD2. Molecular studies did not reveal gene amplification. The post-operative scan did not reveal systemic lymphadenopathy or hepatosplenomegaly. Given the patient's age, both EBVMCU and the NET were treated conservatively.
Conclusion: EBVMCU is an EBV-driven pathology that may rarely present with intestinal obstruction3.
EBVMCU may represent a diagnostic challenge as it histologically resembles other EBV-related malignant lymphoproliferative disorder4.
This is the first case report of EBVMCU with associated NET which may be a cause of immunosuppression alongside the old age in our case.

Radiopathological correlation and MDT discussion is crucial for optimal evaluation and accurate classification.
EBVMCU on its own has excellent prognosis but in this case, the prognosis will be determined by the NET.

E-PS-07-002
Pancreatic neuroendocrine microadenomatosis in the setting of ampullary ductal adenocarcinoma
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Background & objectives: Pancreatic neuroendocrine microadenoma (PNEMA) is a benign, typically non-functioning, nodular endocrine proliferation, less than 5mm in diameter. Multiple lesions are designated microadenomatosis. It is often discovered incidentally, and it is unknown if may progress to clinically relevant neuroendocrine tumours.
Methods: We present the case of a 58-year-old male, admitted in the Timisoara Clinical County Hospital with obstructive jaundice. He was referred to Surgery Department, where an exploratory laparotomy was performed that identified a tumour comprising the duodenum, the distal choledochus and the head of the pancreas. A cephalic duodenopancreatectomy was performed, the excised biopsy being sent to the Pathology Department.
Results: Macroscopically, an infiltrative tumour was identified with the epicentre in the ampullary area, which affects the ampullary area, the head of the pancreas, the common bile duct, the pancreatic duct, as well as the duodenal wall. Histologically, an ampullary ductal adenocarcinoma of the bilio-pancreatic type was diagnosed. At the level of the remaining pancreatic tissue were observed several nodular neuroendocrine cell proliferations, with diameter of 0.8-1,2mm. They were noncapsulated, with organoid growth, trabecular and pseudoglandular architectural pattern, vascular stroma, and without chronic pancreatitis background. The proliferating cells are intensely positive for synaptophysin, with a Ki67 index less than 1%. Thus, the diagnosis of pancreatic neuroendocrine microadenomatosis was made.
Conclusion: Due to small size, PNEMAs are usually discovered during life in relation to other pancreatic or systemic conditions. There are reported cases in association with MEN1 syndrome, von Hippell Lindau syndrome, pancreatic intraductal papillary mucinous neoplasms, duodenal adenocarcinoma, and ectopic pancreatic tissue. To our knowledge, this is the first case which described the occurrence of neuroendocrine microadenomatosis in combination with ampullary ductal adenocarcinoma.

E-PS-07-003
Primary hepatic marginal zone lymphoma: a case report
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Background & objectives: Extranodal marginal zone lymphoma of the mucosa-associated lymphoid tissue accounts 7-8% of newly diagnosed lymphomas. Other sites of occurrence include lung, salivary gland, ocular adnexa, skin and thyroid. However, lymphoma in the liver as the primary site is extremely rare.
Methods: A 70-year-old male patient was referred for a liver mass on ultrasonography from a medical check up at another hospital. The patient was seronegative for hepatitis B, C and HIV. MRI revealed a low density mass measuring 2.2 cm and an FNB was performed.
Results: Microscopically, nodular and mostly diffuse infiltration of lymphocytes was observed. The lymphocytes were small-to-intermediate size and some of them had centrocyte-like morphology. Lymphoepithelial lesions were present in some bile ducts. Tumour cells express B-cell-associated antigens, such as CD20, CD79a and PanB and are negative for CD3, CD5, CD10, CD23, DBA-44, bcl6, CyclinD1. There are polyclonal for κ and λ light chains. The Ki67 (MIB1) labelling index is 1%. All these results are compatible with a low-grade B-cell lymphoma and especially a marginal zone lymphoma.
Conclusion: Most of the primary hepatic MALT lymphoma cases occur in elderly people and were present with incidentally detected liver masses without specific symptoms. Diagnosis of this condition is important, because the disease is treatable.

E-PS-07-004
Tumoral and peritumoral histopathological analysis in hepatocellular carcinoma after locoregional therapy
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Background & objectives: Radiofrequency ablation (RFA) and transcatheter arterial chemoembolization (TACE) are locoregional therapies (LRT) used to treat hepatocellular carcinoma (HCC). LRT may change tumours phenotype, where histopathological features of apoptosis/proliferation and epithelial-mesenchymal transition (EMT) have been reported.
Methods: Fifteen patients treated with preoperative LRT (TACE n = 12; RFA n = 2; RFA+TACE n = 1) concerning 29 HCCs were studied; 57 cases of HCC surgically treated without LRT were analysed as controls. WHO 2019 histopathological criteria, proliferation/apoptotic biomarkers (Ki67, p53) and mesenchymal biomarkers (alpha-smooth muscle actin (ASMA), vimentin) expression was evaluated in tumour and peritumoral tissues.
Results: Ki67 was relevant in 6 HCCs; 4 cases had peritumoral hepatocytes expressing Ki67 and 3 showed tumoral and peritumoral immunoexpression. Four HCCs expressed p53 and 2 had positive p53 hepatocytes surrounding the tumour; 2 cases displayed both biomarkers. Two cases showed ASMA positive tumour cells and 13 HCCs ASMA positive tumour stroma cells. Peritumoral hepatocytes were ASMA positive in 11 HCCs and 26 displayed ASMA positivity in the extracellular matrix (ECM) surrounding the tumour. Seven HCCs showed vimentin in tumour cells cytoplasm and 13 cases had positive predominant stroma cells. Vimentin in peritumoral hepatocytes of 14 HCCs was concomitant with immunoexpression in the ECM surrounding the tumour of 27 cases.
Conclusion: LRT may have an impact on the proliferative phenotype of HCC and may trigger EMT features, either inducing a higher malignant potential or uncovering the complex heterogeneity of these tumours. An association between LRT, Ki67 and p53 expression in tumour cells and ASMA expression in peritumoral hepatocytes seems relevant. These results need further confirmation as dependent serological markers may acquire relevant role in liquid biopsy.

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E-PS-07-005
Immunohistochemical study of CD34 In chronic viral hepatitis B
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Background & objectives: Vascular lesions associated with chronic viral hepatitis B (CVHB) have been reported as predictors of disease progression.
The aim of the study was to determine the CD34 score in CVHB and its correlation with inflammatory activity and fibrosis stage.
Methods: Study was retrospective on 30 cases of CVHB confirmed by biopsy over 5 years (2013-2018). CD34 score was 1: positive cells ≤ 10%

of sinusoids; 2: positive cells > 10% and ≤ 30% of sinusoids; 3: positive cells > 30% of sinusoids. For activity and fibrosis, the Metavir score was used. In statistical analysis, the significance level was 0.05.
Results: Sinusoidal aberrant expression of CD34 was detected in all cases.
In portal areas, CD34 score 3 was the most frequent score, found mainly in inflammatory activity A2 (14 cases) and in fibrosis stage F2 (8 cases). In central areas, CD34 score 1 was the most frequent score, found mainly in inflammatory activity A2 (12 cases) and in fibrosis stage F1 (9 cases). Analytic study showed that activity and fibrosis were significantly associated with CD34 score in the periportal zones with respectively p=0.018 and 0.01.
Conclusion: Vascular changes observed in chronic hepatitis involve angiogenesis lesions. It is characterized by a modification of the phenotype of endothelial cells inducing sinusoid capillarization. During this process, endothelial cells show aberrant expression endothelial markers such as CD34. In our series, we found a significant association between CD34 score, hepatitis activity and the stage of fibrosis in portal areas. These lesions usually seen in cirrhosis and portal hypertension, occur in CVHB and represent a sign of progression of the disease.

E-PS-07-006
Ciliated forgut cyst of the gallbladder: a case report
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Background & objectives: Ciliated cysts are rare congenital anomalies that develop from the anterior primitive intestine, most commonly identified in segment IV of the liver. Their location in the gallbladder is exceptional rare.
Methods: We report a case of a 54-year-old woman suffering of upper right quadrant pain two years ago. Ultrasound showed a lesion near the fundus of the gallbladder. The patient underwent cholecystectomy via a right subcostal excision. The lesion was also removed.
Results: We received a gallbladder and a separate 5cm cystic lesion. The content of the cyst was a mucoid fluid and there was no communication between the cyst and the gallbladder lumen. Microscopically there was a quite thin fibromuscular wall covered by ciliated pseudostratified epithelium containing some goblet cells. Immunohistochemistry showed that the epithelial lining was ker7 positive, but ker20 and CDX2 negative. A diagnosis of ciliated forgut cyst was established.
Conclusion: Ciliated congenital cyst developing from the foregut is a rare diagnostic entity that should be considered in the differential diagnosis for cystic lesions located infra diaphragmatically in conjunction with liver or gallbladder.

E-PS-07-007
Intrahepatic splenosis on liver cirrhosis
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Background & objectives: Intrahepatic splenosis (IS) is the autotransplantation of splenic tissue in a heterotopic location, after spleen´s surgery or trauma. It is a rare finding located anywhere in the abdominal cavity. We present a case of IS on liver cirrhosis.
Methods: The case of a 64-year-old man with active alcoholism and alcoholic liver disease with oesophageal varices is presented. Splenectomised in 2012 after a traffic accident. In 2021, in the follow-up of cirrhosis, a 20 x 27mm liver lesion in segment V was detected by magnetic resonance imaging (MRI), compatible with hepatocarcinoma. Hepatic resection of the LOE was indicated by segmentectomy.
Results: Macroscopically, splenosis is usually a smooth, shiny, wall-coloured, homogeneous tissue that is difficult to distinguish from an adenoma and, in the case of abundant vascularization, from a hepatic haemangioma. Microscopically, H-E staining revealed sinusoidal structures and lymphoid tissue hyperplasia. A capsule separating the spleen tissue from liver tissue could be clearly detected. Immunohistochemistry staining showed positivity for CD3/CD20, and the expression of the Ki-67 antigen was quite limited. The polyclonal nature of the lymphocytes and the low proliferation activity further confirmed the benign characteristic of the mass.
Conclusion: It is a coincidental finding, but it is important to differentiate it from the ectopic spleen, a more frequent congenital entity with a location close to the splenic hilum, it presents capsule and direct vascularization of some splenic arterial branch, and the differential diagnosis must include focal hepatic lesions with the immunohistochemical battery typical of the most representative tumours.

E-PS-07-008
Primary Hepatic Perivascular Epithelioid Tumour (PEComa): a case report
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Background & objectives: Perivascular Epithelioid Tumours (PEComas) are predominantly present in uterine or gastric tissues. Liver presentations are uncommon and primary hepatic presentations are extremely rare. We reported a primary perivascular epithelioid tumour (PEComa) of the liver with uncertain malignant potential.
Methods: A 31-year-old female patient presented with a one-month history of abdominal pain and bilious emesis. She had a previous diagnosis of hepatic abscess. Abdominal MR reported a lesion, suggestive of hepatic adenoma. The surgical specimen of the hepatectomy had a solid, circumscribed mass, with scarce necrosis, and a larger diameter of 4.5 cm.
Results: Histopathologic studies showed necrosis, epithelioid and spindle cells, moderate nuclear atypia and cells with clear cytoplasms. Infiltrative sinusoidal patterns spread to the parenchyma and resection margins. Mitotic figures were >1x50 HPF. Immunohistochemical studies showed reactivity to CD31-CD34 in endothelium, MelanA, HMB-45, Caldesmon and SMA, and 20% of KI67 expression. Necrosis, mitosis >1x50 HPF, and infiltrative growth, indicates a perivascular epithelioid tumour (PEComa) of the liver with high risk of malignant behaviour. Imaging extension studies were negative for additional neoplastic lesions.
Conclusion: Careful and complete histologic and immunohistochemical study is required due to how unusual the tumour is. The key of the PEComa diagnosis is the co-expression of melanocytic and muscle markers. This diagnosis is usually performed after hepatectomy, the most common management strategy. Because of the uncertain prognosis and behaviour of hepatic PEComas, long term following and valid stratification risk scales are needed. This case highlights the lack of information and studies about diagnosis, management and prognosis of hepatic PEComas.

E-PS-07-009
Solitary fibrous tumour of the pancreas: a rare and sneaky diagnosis
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Background & objectives: Solitary fibrous tumour (SFT), first described as a pleural lesion, may arise at any anatomical location, including the gastrointestinal tract and the pancreato-biliary system. We report a rare case of SFT of the pancreas.

Methods: A 69-year-old man was referred to our tertiary hospital due to a solitary, solid pancreatic mass in the corpus of the pancreas, detected by routine magnetic resonance imaging. He had a prostate adenocarcinoma at the age of 51, treated by radical prostatectomy with lymphadenectomy, radiation and androgen deprivation therapy.
Results: Endoscopic ultrasound-guided fine-needle aspiration biopsy was interpreted as nondiagnostic (Papanicolaou System: Category I). The patient underwent distal pancreatectomy with splenectomy. Grossly, the lesion was whitish, well circumscribed and 3,0x2,4x1,9cm in size. Microscopically, the tumour had an expensive growth pattern and was constituted by uniform, bland, spindle cells arranged in a "patternless pattern" accompanied by the deposition of a hyalinised collagen and prominent vascular network of branching blood vessels. Cellularity was variable. Entrapped pancreatic parenchyma, intimately admixed within the tumour cells, was present. No relevant cytological atypia, necrosis or mitotic figures were identified. Immunohistochemically, the tumour cells showed STAT6, CD34, BCL-2 and CD99 immunoreactivity. The patient is well four months after surgery.
Conclusion: Despite rare, pathologists should considered SFT in the differential diagnoses of mesenchymal tumours detected in the pancreas.

E-PS-07-010
Undifferentiated carcinoma with osteoclastlike giant cells of the pancreas: 2 case reports of a rare tumour
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Background & objectives: Undifferentiated pancreatic carcinoma with osteoclast-like giant cells(UPCOC) is an uncommon pancreatic neoplasm that comprises less than1%of all exocrine pancreatic tumours. It is considered a subtype of ductal adenocarcinoma of the pancreas, in the latest WHO classification. It has a well-defined histogenesis.
Methods: We report two cases of UPCOC diagnosed in the Pathology Department of Farhat Hached Hospital (Sousse, Tunisia). The first patient is a 60years male who presented with a pancreas body mass discovered on imaging. The second one is a 71years female who presented with epigastralgia and a mass involving the stomach wall, the spleen and the tail of the pancreas on imaging.
Results: The first patient underwent distal splenopancreatectomy with recutting of the head of the pancreas and the second had a monobloc removal of the mass, the spleen, the tail of the pancreas and a part of the gastric wall. At gross examination, both masses showed a multiloculated, solid-cystic cut surface with areas of necrotic and haemorrhagic changes. Histological examination showed an undifferentiated proliferation, made of large, rounded, polygonal, elongated, fusiform and giant multinucleated osteoclast like cells. The stroma showed focal bone differentiation in the first case while an associated moderately differentiated ductal adenocarcinoma was seen in the second case. We retained the diagnosis of undifferentiated osteoclastic giant cell carcinoma of the pancreas.
Conclusion: UPCOC is very rare. It often occurs around the sixth decade. Histological study reveals two distinct cell populations. The first one is made of mononuclear, spindle-shaped, atypical cells. The second cell population is made of osteoclastic-like giant cells. Osteoid or cartilaginous formations may be found. The presence of a codon 12 mutation in the KRAS gene suggests that this component derives from pancreatic ductal cells. The treatment is similar to that of classical ductal adenocarcinoma, with which UPCOC shares a poor prognosis.

E-PS-07-011
A case of an IgG4-related disease affecting extrahepatic and intrahepatic bile ducts and the kidney with a concurrent renal cell carcinoma, clinically masquerading as primary cholangiocarcinoma of the biliary tree with renal metastases
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Background & objectives: Immunoglobulin-G4(IgG4) related disease is a systemic fibroinflammatory nosological entity that can affect almost any organ. We hereby present a case of IgG4-related sclerosing cholangitis of the biliary tree and IgG4-related disease of the left kidney with a concurrent clear-cell renal-cell carcinoma(CCRCC).
Methods: A 76-year-old male presented with jaundice. The CT&MRI analysis demonstrated an obstructive 1,7cm lesion of the proximal bile-duct, dilated intrahepatic bile-ducts & multiple tumoral-lesions in segments III,IV and V of the liver along with a well-circumscribed 4cm kidney tumour. These findings were consistent with cholangiocarcinoma of the biliary-tree. A wedge-resection of liver-segment V, left lateral hepatectomy with excision of the common bile duct+cholecystectomy&partial left nephrectomy were performed.
Results: During gross inspection of the liver, multiple firm nodules were recognised. The bile duct & gallbladder wall were thickened & filled with haemorrhagic-necrotic debris. At the left kidney a firm, solid and partially cystic lesion was observed. Microscopic examination of the liver, gallbladder & bile duct showed sclerosing cholangitis, with plexiform fibrosis, obliterative phlebitis & a dense inflammatory infiltrate with an IgG4+/IgG+ plasma-cell ratio of>60%. The intrahepatic nodules had histological features of inflammatory pseudotumors. Similar findings of tubulointerstitial nephritis with dense inflammatory infiltrate & sclerosing stroma were observed in the kidney, with an IgG4+/IgG+ plasma-cell ratio of>70%.The renal inflammatory pseudotumor engulfed a 2,8cm cystic-haemorrhagic lesion that was proven to be a CD10(+)/Vimentin(+)/Ck7(-) grade 1 CCRCC. The case was signed out as IgG4-related disease involving the liver / bile duct / gallbladder & kidney, along with a grade 1 CCRCC.
Conclusion: IgG4-related disease is a clinical entity that has become more common during the last decade due to increased clinical awareness. Its pathophysiology is not clearly understood, though the main theories involve autoimmunity and allergic conditions.
Proper clinical correlation and serological analysis is crucial to the pathologist, especially during intraoperative consultation in order to avoid overdiagnosis. In the absence of clinical information, frozen section analysis was inconclusive in our case.
Reports of renal IgG4-related disease with concurrent renal cell carcinoma are extremely rare in the literature.

E-PS-07-012
Metastasic carcinoid lung tumour in the liver, 26 years of experience
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Background & objectives: Carcinoid tumour (CT) is a rare neuroendocrine epithelial neoplasia that represents less than 1% of lung cancers and rarely metastasizes. The purpose of our work is to provide a series of 13 cases of CT with liver metastases.
Methods: A review of BAG, PAFF and liver biopsies diagnosed in our centre from January 1995 to January 2021 was performed, selecting those with a diagnosis of metastases from pulmonary CT. Some of the clinical, histopathological (study with H-E, presence of necrosis and mitosis count) and immunohistochemical characteristics (Chromogranin, Synaptophysin, CD56, INSM1 and Ki67) are described.
Results: Thirteen patients with CT liver metastases were identified; 7 women (54%), 46% smokers (6 patients), with a mean age of 68 years at diagnosis of metastasis (range 43-81). 69% (9 patients) had stage IV disease at diagnosis. During evolution, 54% (7 cases) presented metastases in other locations (brain 15%, bone-soft tissue 31%, pancreas 8%). In the histological diagnosis, 23% were atypical CT, of which 8% presented necrosis. 85% had <2 mitoses per mm2. All cases showed immunoreactivity for at least two neuroendocrine markers. Ki67 presented a mean of 8% (Range 1-19%), being 46% ≥10%.

Conclusion: The most frequent way of presentation of lung CT was: stage IV, with metastatic liver disease and predominance in non-smoking women over 60 years of age. In almost half of the cases, bone, brain or pancreatic involvement was also observed. The typical CT was the most frequent subtype in our series, observing a Ki67 of between 1 and 19%. 67% of atypical CT were histologically diagnosed by the presence of ≥2 mitoses per mm2.

E-PS-07-014

Case report series of undifferentiated carcinoma with osteoclast-like cells of the pancreas at the Basurto University Hospital over the last fifteen years

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Background & objectives: Undifferentiated carcinoma with osteoclast-like cells of the pancreas has been reported to be less than 1% of pancreas malignancies. Although its histology is typical, due to its rarity, sufficient clinical data is not available and its prognosis remains unclear.
Methods: Systematic research of undifferentiated carcinoma with osteoclast-like giant cells of the pancreas from the Basurto University Hospital database over the last fifteen years. Data regarding cytological diagnostic approach, clinical aspects, and prognosis after surgical resection was collected. Moreover, immunohistochemical profiling of the histiocytic-like and epithelioid cellular components was performed for further characterization.
Results: Two undifferentiated carcinomas with osteoclast-like cells of the pancreas cases were identified in our database from 2006 to 2021, according to diagnostic criteria from World Health Organization (WHO). The most relevant cytological, histological and immunohistochemical profiles were analysed and correlation with previous case reports series described on the literature was performed.
Our analysis demonstrated the impact of a cytological approach by fine-needle aspiration following imaging techniques, in the diagnosis of this neoplasm before surgical procedure.
Conclusion: Undifferentiated carcinoma with osteoclast-like cells of the pancreas is an uncommon malignancy, with few reports on the literature over the last fifteen years, and none in Spain. Due to the lack of data available, there is no consensus on diagnostic procedure, therapeutics and prognosis. We would suggest that a fine-needle aspiration provides accurate information and contributes to a radiologically assisted diagnostic approach.

E-PS-07-015

A 14-year experience in pathological diagnosis of liver tumours using core needle biopsy

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Background & objectives: Core biopsy and histopathological examination are essential for establishing the nature of primary liver tumours, as well as of metastases of unknown origin. This study aimed to investigate the agreement between initial clinical diagnosis and pathological examination of core biopsies.
Methods: We performed a retrospective study on 243 patients examined at the Emergency County Hospital Timisoara, Romania, diagnosed by core biopsy between 2002 and 2016. We examined the percentage of cases for which the pathological examination was diagnostic, the proportion of malignant and benign tumours. To evaluate the agreement between the clinical diagnosis and the pathology report, Cohen's kappa was used.
Results: A definite pathological diagnosis was set for 88% of the cases (82.8% malignant and 17.2% benign tumours), while for the remaining 12%, the result was inconclusive. Primary malignant tumours were identified in 23% of the cases, the rest being metastatic. The origin of the metastases was identified in 54.3% of the cases. A moderate agreement between the clinical diagnosis and pathology report was identified for hepatocellular carcinomas (Cohen's kappa = 0.48) and liver metastases (Cohen's kappa = 0.6).
Conclusion: For the evaluation of liver tumours, core biopsy is a diagnostic tool with moderate agreement between initial clinical diagnosis and pathological report, both for hepatocellular carcinomas and liver metastases.

E-PS-07-016

Synovial sarcoma of the pancreas in a childhood leukaemia survivor

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Background & objectives: Pancreatic synovial sarcoma (SS) is very rare with only one primary and five secondary tumours reported to date. Development of a second malignant neoplasm in survivors of childhood leukaemia is rare (1%) and only 3-5% are sarcomas.
Methods: A 40-year-old man with a history of childhood acute lymphoblastic leukaemia presented with acute abdomen. Imaging showed a ruptured cystic tumour attached to the pancreatic body/tail and no tumours elsewhere. A distal pancreatectomy was performed. Grossly, the tumour was mainly extra pancreatic and cystic (11.5 cm) with inner surface micropapillary projections. A 2.4 cm solid area extended into the resected pancreas.
Results: Histology showed a biphasic malignant neoplasm with a low grade dysplastic papillary epithelial component lining the cystic cavity, and a distinct solid, small cell, poorly differentiated component, with high mitotic activity and Ki67 LI 80%, infiltrating the pancreas. Differential diagnosis included a collision tumour composed of an intraductal papillary mucinous neoplasm and a neuroendocrine carcinoma or extra skeletal Ewing sarcoma/PNET, and a cystic biphasic SS. Immunohistochemistry supported the latter diagnosis (solid area positive for vimentin, TLE1 , BCL2, CD56, rare pankeratin (pan-K) and cyst epithelial lining positive for K20, K7, CDX2,EMA). Fluorescence in situ hybridization (FISH) showed a t(X;18)(p11.2;q11.2) translocation, typical of SS18-SSX1 gene fusion and characteristic of SS.
Conclusion: Biphasic SS diagnosis in unusual locations is extremely difficult when the epithelial and sarcomatous components are not intermingled. Immunohistochemistry with molecular confirmation is essential for accurate diagnosis. The rarity of the SS location in our case supports an extra pancreatic soft tissue neoplasm infiltrating the pancreas rather than a primary pancreatic neoplasm. The known interaction of the SS associated protein SYT with the acute leukaemia associated protein AF10 may underlie the development of these two rare malignancies in the same patient.

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E-PS-08-001

Extramedullary haematopoiesis in an adrenal cortical adenoma: a case report

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Background & objectives: Extramedullary haematopoiesis (EMH) is the expansion and differentiation of hematopoietic stem and progenitor cells outside of the bone marrow. Adrenal location is very rare. We report a case of adrenal cortical adenoma with extramedullary haematopoiesis in patient without haematological disease.
Methods: We presented a 68-year-old woman who had no hematologic abnormality, showing bilateral adrenal incidentaloma discovered incidentally in abdominal CT scan. The two nodules were rounded with well delineated borders, homogeneous and had clear separation from surrounding structures. They were non-functional. However, the right adrenal nodule measured more than 3 cm. So an adrenalectomy was performed.
Results: Grossly, we received an encapsulated nodule measuring 3.7cm. It was extebede by the adrenal which measured 2cm. In cut, the lesion was well circumscribed. It had an homogenous cut surface with yellow colour. Microscopically, the tumour was well defined with an intact capsule and it was made of islands of tumoral cells. These cells had distinct borders and abundant foamy cytoplasm resembling to the normal adrenal fasciculat. Mitoses were exceptional. There were no atypia, no necrosis and no vascular invasion. In the stroma, we found some non-cohesive aggregates of extramedullary haematopoiesis. The diagnosis of adrenal cortical adenoma with EMH was made. The WEISS score was estimated at 0.
Conclusion: The adrenal glands are the seat of a wide variety of diseases. However, EMH in the adrenal is uncommon and it is thought to be a compensatory, physiological mechanism that occurs during altered medullary haematopoiesis like in hemoglobinopathies. In our case the patient do not have any haemoglobinopathies. Many authors suggest the hypothesis that adrenal gland has hematopoietic capacity during the foetal period and EMH may develop from primitive rests in diseased condition, like in our case.

E-PS-08-002
Epidemiological characteristics of thyroid cancer in a Tunisian universitary health care centre
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Background & objectives: Thyroid carcinoma is the most common endocrine malignancy. Its incidence rate has been increasing rapidly around the world without great variability in epidemiopathological characteristics throughout countries.
We aim to study epidemiological and pathological characteristics of TC in our Tunisian population.
Methods: Our study included retrospectively all patients who underwent surgery for TC in Habib Thameur's hospital from 2017 to 2020.
Results: Our sample of 149 patients consisted of 11 men and 130 women (87,2%): a sex-ratio of 0,14, with an age ranging from 17 to 85 years and a median of 46,60 ± 14.1years.
Carcinoma was in the right lobe in 59 cases (39.59%), in the left lobe in 53 cases (35.57%) and bilateral in 37 cases and multifocal in 40 cases.
Papillary carcinoma represented the most frequent histological type and was diagnosed in 133 patients (89%), followed by Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (8 cases), oncocytic carcinoma (6), follicular carcinoma(5),poorly differentiated carcinoma (2 cases) and anaplasic carcinoma(1 case).Lymph node dissection was performed in 71 cases. Node involvement was diagnosed in 26 cases (17,44%).
Conclusion: Our study noted a female predominance, a mean age of 46,60 years and a higher incidence in the third, fourth, and fifth decades of life. Papillary carcinoma was the most common histological subtype. These results are consistent with those of Tunisian, African and world series. Worldwide, the Female/Male ratio for TC incidence varies from 2 to 12 (6,84 in our study) and the most frequent histological subtype is papillary carcinoma in most of the series in the literature.

E-PS-08-003
Poorly differentiated thyroid carcinoma accompanying with follicular variant papillary thyroid carcinoma: a case report
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Background & objectives: Poorly differentiated thyroid carcinoma; is a rare type among thyroid carcinomas and its classification is controversial. Its morphology stand between well-differentiated and undifferentiated carcinomas. It is characterized by the solid/trabecular/insular growth pattern on microscopy and the presence of distant metastases.
Methods: Lytic lesions are detected in lumbar MRI of the 66-year-old patient that presented with leg pain. PET-CT and the histological examination of the lesion confirmed that the primary tumour is of thyroid origin. An isoechoic nodule containing cystic areas is detected in the right thyroid lobe on neck USG. Thyroid fine needle aspiration indicates follicular neoplasia. Total thyroidectomy is performed.
Results: Histological examination of the lytic lesion detected in the iliac canal revealed a follicular patterned tumour compatible with follicular thyroid epithelial cell tumour via immunoexpression of TTF-1, thyroglobulin, vimentin, pancytokeratin and PAX8. PET-CT exhibited malignant thyroid mass. Thyroid fine needle aspiration diagnosed as follicular neoplasia (Bethesda category IV). In the differential diagnosis of the patient, tumours with a dominant follicular pattern with nuclear features of papillary carcinoma were also included. After total thyroidectomy, the patient was diagnosed with poorly differentiated thyroid carcinoma associated with well-differentiated thyroid carcinoma foci of follicular variant papillary thyroid carcinoma.
Conclusion: Distant metastases of thyroid tumours are not always characteristic of the primary tumour. Also, aspiration of poorly differentiated thyroid carcinoma may present as follicular neoplasia. In this case, foci of poorly differentiated thyroid carcinoma with solid/trabecular/insular growth pattern could be recognised by numerous sampling of the solid nodul . Poorly differentiated thyroid carcinoma, can be found with well-differentiated thyroid carcinoma foci in the same tumour, and a detailed examination is required, especially in patients with distant metastasis.

E-PS-08-004
Paediatric paragangliomas: what we should be aware of – about a case
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Background & objectives: Paragangliomas are more frequent in middle-age adults. 30% are hereditary, though almost all of paediatric-onset cases are related to germline mutations. Mostly are found in association with Succinate Dehydrogenase B (SDHB) subunit gene which is related to higher malignization risk.
Methods: We present a case of a 14-year-old male, that was under investigation for intellectual developmental disorder and facial dysmorphism. An array comparative genome hybridization (aCGH) showed a mutation in SDHB gene in 2017. In 2020, following the detection of elevated urinary normetanephrine/noradrenaline, a Ga-DOTA-NOC PET/CT was performed, revealing a lomboaortic expansive solid lesion, with somatostatin receptors overexpression. Tumourectomy was performed.
Results: Grossly, it was a solid, nodular tumour, that measured 4x3,5x2cm with soft consistency and homogeneously tan cut surface with disperse haemorrhagic foci.
Microscopically, it showed a nested and trabecular proliferation of round to oval cells, with abundant granular cytoplasm and chromatin. The immunohistochemical study supported the diagnosis of paraganglioma [chromogranin A+, synaptophysin+, NSE+, CD56+, S100+ (sustentacular cells)].

It was graded according to The Grading System for Adrenal Pheochromocytoma and Paraganglioma (GAPP) as moderately differentiated (score 4) (low cellularity, capsular/vascular invasion present, comedo-type necrosis absent, Ki67 mitotic rate > 3%).
The surgical margin was positive.
Conclusion: Paragangliomas in paediatric population are almost always due to a germline mutation, being the ones in genes coding Succinate Dehydrogenase (SDH) subunits collectively the most common cause of hereditary paraganglioma-pheochromocytoma.
Even in the absence of a family history, genetic testing should be offered for all paediatric patients with paragangliomas and their family.
Patients with SDHB mutation should maintain a lifelong, regular surveillance.

E-PS-08-005
Challenge diagnosis of papillary thyroid carcinoma with cervical adenopathy: lymph-node metastasis or concomitant cervical tuberculous lymphadenitis
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Background & objectives: Papillary carcinoma is by far the most common malignancy of the thyroid and accounts for 65-80%of thyroid cancers. Cervical adenopathy is common, often associated with or even revealing the thyroid nodule. An extemporaneous-examination(EE) of these cervical lymph-nodes is essential to eliminate a metastasis.
Methods: However, the per-operative-discovery of a tuberculous lymphadenitis may lead to a mismanagement of the surgery. The purpose of this study is to discuss the rarity and diagnostic difficulties of the association of cervical lymph-node tuberculosis with metastatic papillary thyroid carcinoma. We report two cases of thyroid nodule associated with cervical adenopathy in two patients of unusual presentation.
Results: First patient was46-year-old woman, operated for a left-lobular-nodule of the thyroid whose EE revealed thyroiditis. In view of the clinic-biological findings, tuberculosis lymphadenitis was suspected and the procedure was completed by a jugulo-carotid-lymphadenectomy. The final histological-examination showed a multifocal papillary thyroid carcinoma with thyroid-granulomatous reaction.11 lymph-nodes received; all were free of metastasis and only one contained necrotizing epithelioid and gigantocellular granulomas. The second patient was 27-years-old with a history of lymph-node tuberculosis, in front of the discovery of a right thyroid nodule associated with a cervical adenopathy. She underwent a cervical adenomectomy which EE confirmed the tuberculous lymphadenitis. A subsequent lobo-isthmectomy revealed on EE a papillary thyroid carcinoma.
Conclusion: The definitive-examination of the lymphadenectomy with the totalization of thyroidectomy concluded to a papillary thyroid carcinoma with 5-metastatic lymph-nodes on the 37-received which are all seats of caseo-follicular lymph-node tuberculosis.
the double cervical localization of a tuberculosis and a metastasis of a papillary thyroid carcinoma remains a rare association and of fortuitous discovery. This association poses a real diagnostic problem for the pathologist, particularly in extemporaneous examination.

E-PS-08-006
Phosphaturic mesenchymal tumour showing a predominant haemangiomatous component
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Background & objectives: Phosphaturic mesenchymal tumours (PMT) are very rare neoplasms associated with paraneoplastic-induced osteomalacia due to renal phosphate wasting. Patients present with muscular weakness, diffuse bone pain, and pathologic fractures. The tumour is usually detected about 5 years after the clinical onset.
Methods: A 40-year-old woman presented with 6-year history of progressive bone pain, muscular hypotonia, and asthenic syndrome. Four years ago magnetic resonance imaging (MRI) showed healed rib fractures and an unconsolidated pubic arch fracture was currently present. She had severe hypophosphatemia and elevated FGF23 serum levels, pleading for oncogenic osteomalacia. A right supraspinatus muscle tumour was detected and was surgically removed.
Results: At the Pathology Department, we received a 5.9X1.8X2.8 cm tumour with ill-defined borders and variegated appearance on cut section. Microscopically, the tumour consisted of monomorphic medium-sized round-to-polygonal or spindle-shaped cells, with a moderate amount of cytoplasm, arranged in large sheets, without necrosis. Cartilage, bone metaplasia, haemorrhagic foci, and dystrophic calcification were present. Mitotic activity was very low. Numerous blood vessels of various calibres, some with thrombus inside were present. Many osteoclast-like giant cells and lymphoplasmacytic infiltrate were also observed. Immunohistochemical stains revealed the mesenchymal origin of the tumour cells and the benign nature of the blood vessels. The postoperative evolution was favourable, with a dramatic improvement in serum phosphorus levels.
Conclusion: Phosphaturic mesenchymal tumour is a distinctive, usually benign neoplasm of bone or soft tissue, associated with paraneoplastic osteomalacia due to increased secretion of FGF23, with complete remission after surgical excision. It affects women more commonly and the diagnosis is delayed for years because of their small size and unpredictable location. Histological diagnosis may be challenging, because of the morphological overlap with other mesenchymal neoplasms. Our case showed a dominant haemangiomatous component. Clinical data and laboratory findings are crucial for diagnosis.

E-PS-08-008
Thyroid pathology as a result of environmental factors?
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Background & objectives: It is well known that the thyroid gland is an organ that is dependent on the ecological situation and reacts to environmental influences. Focal proliferative changes in the tissue of the thyroid gland can directly testify to the ecological tension.
Methods: Thyroid glands were studied in 54 autopsy cases not associated with damage to the genital or endocrine organs. The thyroid gland was dissected into a series of histotopographic sections. The detected pathology was assessed stereomicroscopically in the entire volume of each organ.
Results: Thyroid pathology was found in 51 out of 54 cases (94 ± 3.2%). In 10 cases, the changes were of a diffuse nature: thyroiditis, atrophy and sclerosis of the glands, diffuse-infiltrative cancer. Separate foci of pathological tissue structures were found in 41 thyroid glands (187 non-cancerous and 3 cancerous). Thus, among the asymptomatic pathology of the thyroid glands, focal changes (41 cases out of 51 - 80 ± 5.6%) are much more often diffuse (10 cases).
Conclusion: Thus, the focal proliferative changes occurring in the thyroid gland tissue probably indicate the ecological tension in the region. Under the influence of various goitrogenic factors, adaptive rearrangements appear in the organ, which are manifested in the form of the formation of pathological tissue structures, which undoubtedly requires further in-depth study.

E-PS-08-009
Some histological features in the interpretation of the nodular pathology of the thyroid gland
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Background & objectives: Differential diagnosis of benign and malignant neoplasms of the thyroid gland is still a difficult problem. Especially when the material obtained is scarce, for example, a fine-needle biopsy.
Methods: An analysis of histological specimens was carried out in 2229 cases of surgically removed thyroid glands with nodular pathology. A series of sequential sections helped to represent tissue relationships in the nodules.
Results: Only in a quarter of cases (523 out of 2229, 23%), the nodes were malignant. Large nodules did not have a specific spatial organization. Small nodules (<1 cm) has s spherical growth patterns wish necrotic centre and periphery growth. Benign nodules has a random combination of hyperplasia foci (more often in the centre of the node) each of which is at its own stage of development. In the isolated foci of hyperplasia there are qualitative indications of benign growth, found in other localizations the sectorality of the structure, the transition from proliferating to mature structures.
Conclusion: The spatial organization of tissue structures in the nodes of the thyroid gland must be taken into account when conducting fine-needle biopsies. Fine needle biopsies should be targeted so that changes from the centre to the periphery of a suspicious tissue growth focus can be compared.

E-PS-08-010
Oncocytic variant of papillary thyroid carcinoma; a rare case
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Background & objectives: Oncocytic variant of papillary thyroid carcinoma (PTC), in its pure form and mixed growth of pattern, is extremely rare. Evaluating capsule invasion in these often encapsulated tumours is important. Our aim is to set an example for the approach.
Methods: A 60-year-old man presented an iso-hypoechoic thyroid nodule without thyroid dysfunction but associated with compressive symptoms. Thyroid ultrasound showed a nodule measuring 8 cm in its largest dimension without lymphadenopathy (classified as TI-RADS 3 based on the Thyroid Imaging Reporting and Data System) on the left.
Results: Gross examination revealed an encapsulated 8 x 7 x 5.5 cm, yellow-brown mass that nearly involved the left lobe. The capsule was totally sampled and the lesion was near-totally sampled. Microscopic evaluation showed a lesion of mixed pattern, predominatly follicular/solid areas accompanied by several neoplastic papillae, that is formed of almost purely oncocytic cells with nuclear features of PTC. A meticulous investigation was performed to rule out capsule and/or vascular invasion with serial sections. The diagnosis was “Encapsulated, non-invasive, oncocytic variant of PTC”.
Conclusion: This extremely rare tumour raises some problems. “Oncocytic variant of NIFT-P” (a rather descriptive entity that is not fully defined), and “encapsulated follicular variant PTC” were considered in the differential diagnosis. In the setting of an oncocytic tumour, the neoplastic papillae favour the diagnosis of “Oncocytic variant of PTC”. The existence of mixed pattern of growth raises the possibility of lymph node metastasis, as well as distant metastases despite the apparent absence of vascular invasion. Following-up using TG plasma levels is recommended.

E-PS-08-011
Osteosarcoma metastasis to the thyroid with concomitant multifocal papillary carcinoma. A case report
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Background & objectives: Osteosarcoma metastasis to the thyroid is extremely rare. We report a case of metachronous osteosarcoma metastasis to the thyroid with concomitant presence of papillary thyroid carcinoma.
Methods: A 60-year-old patient with a history of chondroblastic osteosarcoma of the sacrum eight years ago, with metachronous pulmonary and tongue metastases was admitted due to a palpable thyroid mass with pressure effects. Total thyroidectomy was performed. On gross examination, the left lobe was almost entirely replaced by a well-circumscribed, solid, hard, grey-white, 6,2 cm large tumour.
Results: On microscopic examination, the neoplasm showed evidence of a malignant, high grade neoplasm with cartilage and osteoid production. Three foci of papillary thyroid carcinoma surrounded by normal thyroid parenchyma co-existed; the thyroid carcinoma infiltrated two regional lymph nodes. Based on histological findings, our diagnosis was malignant neoplasm consistent with metastasis of the previously diagnosed osteosarcoma, co-existing with multifocal papillary thyroid carcinoma.
Conclusion: The diagnosis of metastatic disease in the thyroid is challenging. Usually, symptoms simulate the clinical presentation of primary thyroid tumours. Imaging studies cannot reliably distinguish between primary thyroid lesions and metastatic disease.

E-PS-08-012
Angiosarcoma is a rare and aggressive tumour of the thyroid. Case report
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Background & objectives: Angiosarcoma(AS) of the thyroid gland is a rare(2-4% of all thyroid neoplasms) but highly malignant tumour with a poor prognosis. Given the importance of the correct histological diagnosis for therapy choice, this is a relevant issue.
Methods: Total thyroidectomy was performed.
Results: There were encapsulated nodes with subtotal necrosis and single papillary-like structures on the periphery. Six lymph nodes had metastases. The neoplastic cells were epithelioid, spindle, or polygonal-shaped with abundant eosinophilic cytoplasm and round, large, nuclei containing prominent nucleoli. The tumours showed high mitotic activity. That's why "papillary thyroid carcinoma with anaplastic" was our first tentative diagnosis. Immunostaining of metastases tissue showed positive staining for pan-cytokeratin, vimentin, CD31, single cells positive for cytokeratin 7, and was negative for CD34, thyroglobulin, TTF-1, PAX-8, and p63. The final pathological diagnosis was angiosarcoma. We detected local recurrence with invasion trachea and bleeding 2 months letter initial surgery. The patient died 6 months after the surgery.
Conclusion: AS may be misdiagnosed as other malignancies, especially anaplastic thyroid carcinoma. Recognizing its clinicopathologic characters and combined application of specific vascular endothelial immunohistochemical markers is important to avoid confusion with other lesions.

E-PS-08-013
Diffuse large B-cell lymphoma primary of the thyroid: case report
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Background & objectives: Primary lymphoma of the thyroid (PLT) is a neoplasm of monomorphic lymphocytes, infiltrating around of the vessels and causing destruction of the follicular structures, accounting for <5% of thyroid malignancies. This is a report of a case of thyroid lymphoma.
Methods: 64-years-old woman, presented an increase in painless cervical volume associated with progressive high dysphagia, significant weight loss and the appearance of painless nodulations on the medial face of the arm and forearm, which ceased spontaneously, before the beginning of the increase in cervical volume, progressing with dyspnoea and nocturnal cough. The patient had hypothyroidism for more than 3 years.

Results: The patient underwent a thyroid biopsy with histopathology showing a neoplasm composed of medium to large lymphoid cells, irregular nuclei, sometimes vesicular and convoluted, sometimes hyperchromatic, with scarce cytoplasm, amidst small and morphologically mature lymphocytes, frequent mitosis and necrosis figures. The immunohistochemical study showed positivity for Bcl6, CD10 and CD20 with 90% Ki67. Based on these findings, a diagnosis of diffuse large B-cell lymphoma of the thyroid was given. Tracheostomy and gastrostomy were performed due to the compressive effects of the tumour, and the patient was referred to haematology.
Conclusion: The diagnosis of primary thyroid lymphoma should be considered when dealing with rapidly growing goitres. Fine needle aspiration is a useful first step in diagnosing thyroid cancers; incisional biopsy for a confirmatory diagnosis with immunohistochemical analysis is often necessary. Compressive symptoms or airway involvement may need surgery as a therapeutic option. The rare occurrence of PTL prevented further studies, prospective and randomized, that would contribute to its diagnosis and treatment.

E-PS-08-014
Multifocal ileal perforation due to massive adrenal amelanotic melanoma metastasis masquerading as adrenocortical carcinoma
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Background & objectives: Adrenal metastases from malignant melanoma have been reported in up to 50% of all metastatic melanoma. Nonetheless, most of them remaining clinically silent and are identified incidentally. The literature reports increased incidence of adrenal metastases in patients receiving immunotherapy.
Methods: We report the case of a 47–year-old male, with clinical history of malignant melanoma, for which he was currently receiving immunotherapy. The patient was admitted in our hospital due to sudden onset of occlusion symptoms. A CT-scan has been performed, revealing a large tumour involving the left adrenal gland, with multifocal invasion of the ileum. The patient underwent surgery.
Results: Two specimens labelled 'left adrenal tumour' and 'ileum' were received in our pathology laboratory. The adrenal tumour measured 21 cm and was composed of high-grade eosinophilic cells with vesicular nuclei and cherry-coloured nucleoli. The cells were arranged in alveolar structures, lacking melanotic pigment. Large areas of necrosis and angioinvasion were noted. The ileal wall was perforated in two places and revealed massive tumoral invasion with similar morphology. The tumour was extending throughout the entire wall, causing mucosal ulceration. The main differential diagnosis was adrenocortical carcinoma. Immunohistochemical studies showed tumour reactivity for S100 and Melanoma cocktail. Synaptophysin, inhibin and AE1/AE3 were negative.
Conclusion: Adrenal metastases of melanoma are rare entities with multifaceted histological aspects. Solely on histological examination, our case featured alveolar and pseudopapillary aspects, with large areas of necrosis, which in the absence of clinical history, would have made the diagnosis extremely challenging. Moreover, to our knowledge, multifocal perforation of the ileum due to adrenal metastasis, has not been previously reported in the literature. This case also strengthens the presumed relationship between immunotherapy and adrenal metastases.

E-PS-08-015
Immunoglobulin G4-related disease associated with Warthin-like papillary thyroid carcinoma: report of a rare entity with a challenging diagnosis
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Background & objectives: Immunoglobulin G4-related disease (IgG4-RD) is a rare fibroinflammatory disease characterized by the presence of dense lymphoplasmacytic infiltration, rich in IgG4-positive plasma cells. Warthin-like papillary thyroid carcinoma (WL-PTC) is a rare variant of papillary carcinoma (PC), occurring predominantly in elderly women.
Methods: We report a case of an incidental discovery of IgG4-RD occurring in a 24-year-old woman who presented with thyroid nodules, cervical lymph nodes and a nodule in the parotid region.
Results: The patient underwent a total thyroidectomie with selective, anterior neck dissection and excision of the parotid lymphadenopathy. On gross examination, thyroid nodules measured 15 and 7 mm and were unencapsulated. Histologically, they showed a papillary architecture with prominent lymphatic stroma at the papillary stalk giving appearance of Warthin's tumour. The lining epithelial cells show typical nuclear features of PC. Histologic examination of the nodule of the parotid showed a dense plasmacytic infiltration including eosinophils with storiform fibrosis and many blood vessels with thick wall and regular endothelium. Immunohistochemistry led to the diagnosis of IgG4-RD confirmed by positive cytoplasmic staining for IgG4.
Conclusion: IgG4-RD is characterized by elevated serum IgG4 concentrations. The diagnosis is based on the association of clinical, serological, and pathological criteria. IgG4-RD can be associated with Riedel, Hashimoto thyroiditis and Graves's disease. The association of IgG4-RD and Hashimoto thyroidis displays an increased prevalence for PC and shows a poor prognosis. To date, only two studies have reported IgG4 positive plasma cells in PC with a background of Hashimoto Thyroiditis.

E-PS-08-016
Dyshormonogenetic goiter with malignant transformation: a rare case
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Background & objectives: Dyshormonogenetic Goiter is an enlargement of the thyroid gland that develops due to hereditary defects in thyroid hormone synthesis. Cases showing malignant transformation are rare in the literature. We aim to analyse the clinicopathological features of this rare entity.
Methods: A 24-year-old male patient applied to our hospital with a swelling in the neck. He had been using thyroid hormone drugs since his childhood. Neck ultrasonography revealed iso-hyperechogenic multiple nodules in both lobes of the thyroid gland. A total thyroidectomy was performed. Gross examination demonstrated multiple nodules measuring from 0.7 to 4,5 cm.
Results: Histologically, the thyroid gland was composed of distinct nodular structures which were separated by thick fibrous bands and including microfollicles or trabecular structures. The follicular epithelial cells had enlarged, vesicular, irregularly contoured nuclei with prominent nucleoli and eosinophilic or clarified cytoplasm. The colloid was decreased through the entire gland. And also, invasive encapsulated follicular variant papillary carcinoma (1.8cm) in the left lobe and papillary microcarcinoma (0.7cm) in the right lobe were identified.
Conclusion: Dyshormonogenesis is the second most common cause of congenital hypothyroidism. Dyshormonogenetic goiter is a characterized by architectural and cellular pleiomorphism which can mimic neoplasia and causes diagnostic difficulties. However, uncommonly, tumours may develop due to chronic TSH stimulation and new genetic changes.

E-PS-08-017
Well-differentiated thyroid tumour of uncertain malignant potential with signet-ring cell morphology: a rare case
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Background & objectives: Signet ring cell adenoma of the thyroid, though rare, is well documented. Our case is the first case in the literature as a well-differentiated thyroid tumour of uncertain malignant potential with signed ring morphology.
Methods: A 39-year-old female patient had a 3.5 cm hypoechogenic heterogeneous nodule in the thyroid left lobe on USG. Fine needle aspiration biopsy was performed from this nodule and it diagnosed as follicular neoplasm (Bethesda category IV). A left thyroidectomy was performed. An encapsulated single nodule 2.5 cm in diameter with colloidal and solid areas was detected in the macroscopic examination.
Results: Histopathological examination revealed an encapsulated nodule with signet-ring cells. Nuclear features of papillary thyroid carcinoma are not seen in these cells. Local capsular irregularities and suspicious invasion signs were detected in serial sections but true capsular invasion could not be proven. Thyroidal origin of these cells was shown with immunohistochemical antibodies (TTF1, Thyroglobulin positivity, CDX2, CEA negativity) and histochemical stains (musicarmin and PAS negativity)
Conclusion: Clear cell changes can be seen in thyroid neoplasms as a result of accumulation of glycogen, lipid, thyroglobulin or mucin in intracytoplasmic vesicles. Rarely, the signet-ring cell morphology can be dominant in follicular lesions. Awareness of this entity is important as it may closely simulate a metastatic mucin-secreting signet ring cell carcinoma. On the other hand, capsular features should be examined detailed because of the invasive follicular lesions can be hide out back of these lesions.

E-PS-08-018
Oncocytic adrenocortical neoplasm of uncertain malignant potential: a case report and review of literature
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Background & objectives: To report a case of an oncocytic adrenocortical neoplasm (OAN), a very rare adrenal tumour with a challenging diagnostic and prognostic assessment.
Methods: A 77-year-old man, without a relevant medical past, performed a computed tomography after a major trauma. The imaging exam revealed a large mass on the left adrenal gland and the patient underwent nephroadrenalectomy. We present a description with laboratory, imaging and pathologic findings.
Results: Hormonal workup was unremarkable. The gross specimen weighed 877g and showed a well-defined and capsulated adrenal mass measuring 141 x 110 x 65mm with tan cut surface with cystic area. Histologically, the tumour was composed of sheets of oncocytic cells with abundant, granular and eosinophilic cytoplasm, and rare mitotic activity. No capsular, venous or sinusoidal invasion was seen.
Conclusion: OANs are very rare tumours in the adrenal cortex and accurate classification is important. The Weiss system cannot be applied to OANs and therefore, diagnostic schemes for OAN have been established, such as the Lin-Weiss-Bisceglia (LWB) system. While the major criteria of malignancy were not met, the large size of this lesion indicates uncertain malignant potential, according to LWB.

E-PS-08-019
An unusual case of medullary thyroid carcinoma mimicking papillary thyroid carcinoma
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Background & objectives: Medullary thyroid carcinoma (MTC) originates in the thyroid parafollicular/C cells and represents 3-4% of the thyroid neoplasms. Present report will be described the difficulty of the diagnosis papillary variant of MTC, without complementary information, and the indispensability of the diagnostic confirmation by immunohistochemistry.
Methods: This case report is about a 67-year-old woman undergoing routine ultrasound and revealed a solid nodule in the right thyroid lobe, hypervascularized with microcalcifications and cystic areas. Fine needle aspiration diagnosis follicular neoplasm, Hürthle cell type with dysplasia. She has subsequently submitted thyroidectomy with the morphological diagnosis of papillary thyroid carcinoma, and the result was requested to be confirmed by immunohistochemistry.
Results: The immunohistochemical examination revealed that it was a papillary variant of medullary carcinoma of the thyroid with the following immunostaining panel: positive chromogranin A and calcitonin in neoplastic cells and positive TTF-1, focally in neoplastic cells. The patient was immediately informed that she would start radioactive iodine treatment without the diagnostic confirmation requested by the pathologist. The conduction for inadequate treatment was interrupted since medullary carcinoma does not capture iodine, the patient was subjected to genetic testing and cancer markers, being free of the disease.
Conclusion: Diagnosis of the papillary variant of Medullary thyroid carcinoma due to its characteristics creates a difficulty in its diagnosis and confusion with papillary carcinoma. The morphological diagnosis without subsidiary clinical information (calcitonin test) can be compromised, and it is essential to perform the immunohistochemical study for the final diagnosis, which is considered the gold standard.

E-PS-08-020
Thyroid cancer – a quick overview: correlations with clinical diagnosis and demographic factors
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Background & objectives: The aim of this study is to determine the prevalence of incidental thyroid cancer in patients who undergo lobectomy or thyroidectomy for different other pathologies, and secondly to evaluate the incidence of thyroid neoplasm based on demographic factors.
Methods: All cases of lobectomy or thyroidectomy examined in our department between January 2018 to December 2020 were analysed retrospectively. The patients were stratified based on clinical diagnosis, age, gender, and resident area. After assessment, a group of 1216 cases of lobectomy or thyroidectomy was identified. Correlation with clinical details couldn't be done because they are not available in most cases.
Results: From all cases, 1076 (88.48%) were sent with clinical diagnosis of goiter, 508 (47.21%) of them turned out to have primary thyroid neoplasm. Among all cases, 62 (5.09%) had clinical diagnosis of thyroiditis, 32 (51.61%) between them had thyroid cancer. The study also analyzes the incidence based on age and gender. Most of the thyroid cancer was in > 41-year age group 494 (85.46%) patients compared with 84 (14.53%) in ≤ 41-year age group. Gender analysis showed that 489 (84.60%) of patients were women and 89 (15.39%) men. In urban areas we noticed a slightly increased incidence of thyroid cancer 328 (56.94%) while in rural areas were 248 (43.05%) cases.
Conclusion: The incidence of thyroid cancer is increasing more and more every year in our region and has a slight tendency to affect younger patients. Considering all the results, a thorough and careful gross examination of each thyroid should be performed, taken into consideration the high probability of diagnosing an incidental thyroid cancer in specimens received as non-neoplastic.

E-PS-08-021
Papillary thyroid carcinoma with mucinous features harbouring ETV6-NTRK3 fusion: expanding the morphologic spectrum of NTRK-rearranged thyroid carcinomas
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Background & objectives: ETV6-NTRK3 translocated PTCs are rare. They are characterized by aggressive clinical behaviour, distinct morphology, and good response to NTRK inhibitors. The presence of mucinous component in this subset of PTCs is a finding that has never been described before.
Methods: We report a 44-year-old female patient, who presented with a progressively enlarging anterior neck swelling of four months duration, accompanied by cervical lymphadenopathy. We describe herein the radiology, cytology and histopathology findings of the neck mass, including immunohistochemical studies as well as molecular analysis by next generation sequencing (Oncomine Focus Assay), utilizing a panel targeting 35 hotspot genes.
Results: Ultrasound showed hypoechoic irregular solid lesion in left thyroid lobe with cervical lymphadenopathy. FNA was consistent with PTC and lymph node metastasis. Histologic examination demonstrated extensive infiltration of left lobe by carcinoma exhibiting dual morphology, partly composed of dilated glands filled with mucin and lined by mucous-secreting cells, while other areas showed conventional PTC. Tumour cells in both components were immunoreactive for pancytokeratin, CK7, CK19, PAX8, TTF1 (less intensity in mucinous component), HBME-1 and galectin 3, but negative for CK20, thyroglobulin, BRAFV600E, synaptophysin, chromogranin, calcitonin, S100, mammaglobin and GCDFP-15. NGS showed fusion between exon 4 of ETV6 gene and exon 14 of NTRK3 gene. Patient was given high dose radioactive iodine therapy. Four months later, imaging studies revealed no evidence of residual tumour.
Conclusion: The presence of locoregionally aggressive PTC that shows distinct morphologic features and negative staining for BRAFV600E, may raise the suspicion of NTRK-rearranged carcinoma. Although rare, they should be correctly identified as they carry an actionable biomarker for targeted therapies. Our case represents the first case of ETV6-NTRK3 translocated PTC that shows extensive mucinous features. This finding expands our knowledge of this subset of PTCs.

E-PS-08-023
Papillary thyroid carcinoma: pathological study of histological variants
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Background & objectives: Papillary carcinoma (PC) is an indolent tumour. The latest WHO classification lists 14 variants of PC with different prognosis. Objective: to determine the frequency of PC variants and describe their main clinical and pathological criteria.
Methods: This is a retrospective study that involved all the variants of thyroid PCs diagnosed between 2017 and2020 in Sousse. Their clinical and pathological parameters were studied.
Results: 18 variants (15.7%) were collected from a total of 114 cases of PC. The variants were distributed as follows: 55% vesicular variant (VPC), 23% diffuse sclerosing variant (DSC), 17% oncocytic variant (OPC) and 5% Whartin-like carcinoma. There were 16 women (88%) and 2 men with an average age of 52y. All the tumours were purely intra-thyroid and presented lymph node metastasis in 66% of cases. They were classified as stage pT1a, pT1b, pT2, pT3a in 38%, 12%, 16% and 34% of cases. The most advanced stages (pT3a) were observed during DSC and VPC. The presence of vascular emboli was noted in 2 cases of DSC (11%).
Conclusion: The most common variant of PC are represented by microcarcinoma and VPC. DSC, high cell PC and column cell PC represent 4.4% of all PCs. These variants are more aggressive, associated with a higher frequency of recurrences, lymph node metastases and resistance to radioiodine. DSC is the only aggressive form noted in our study, representing 17% of PCs against only 6% in the literature. Unlike DSC, OPC, VPC, and Whartin-like carcinoma have the same prognostic impact as the classic variant.

E-PS-08-024
GH-secreting pituitary carcinoma
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Background & objectives: A GH-secreting pituitary carcinoma has symptoms, signs and histological features indistinguishable from benign GH-secreting adenomas. Prognostic markers of aggressive behaviour among these tumours has yet to be resolved.
Methods: We report a case from a series of 397 pitNET. A 57-year-old male with somatotropic pituitary macroadenoma "atypical" according to the WHO classification 2004 (Ki-67>3), with two pituitary relapses without response to Growth hormone antagonists. Ten years later, he consulted for language disorders and memory loss. Imaging tests revealed a single intra-axial occipital lesion approximately 7 cm in diameter.
Results: The microscopic study of the occipital mass showed a neuroendocrine neoplasm with inmunoreactivity similar to the pituitary tumour (strong positivity for synaptophysin, chromogranin, Pit 1 and growth hormone).Ki-67 index was higher than in pituitary adenoma. A molecular study with NGS was negative. Nuclear immunoreactivity for P53 was 15%.
Conclusion: This case corresponds to a pituitary carcinoma originating from an aggressive Pit-NET. There is evidence to suggest that progression from "benign" PITNET to pituitary carcinoma could be due to cumulative changes in molecular pathway abnormalities. Although in our case no molecular alteration was detected, we found a low and weak expression of P53, which could suggest an alteration in the regulation of this protein.

E-PS-08-025
Primary acinic cell carcinoma of the lung metastatic to the thyroid gland and lateral cervical lymph nodes: a case report
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Background & objectives: Primary acinic cell carcinoma (ACC) of the lung is rare, and distant metastases even rarer. We report the case of a 70-year-old male with a history of nodular goiter, who presented to the hospital with hoarseness and difficulty breathing.
Methods: Physical examination revealed a 6x4 cm, multinodular mass within the left thyroid lobe and enlarged lateral cervical lymph nodes. Magnetic resonance imaging with contrast showed an enlarged, multinodular left thyroid lobe with heterogeneous contrast uptake, alongside confluent lateral cervical lymphadenopathies, and bilateral nodular pulmonary lesions. Thyroid neoplasm was suspected, and biopsy of the thyroid and lymph nodes was performed.
Results: Histopathological examination of both thyroid gland and lateral cervical lymphadenopathy revealed a monomorphic tumoral proliferation, arranged in lobules and nests of atypical cells with abundant, clear, and, in some areas, granular, eosinophilic cytoplasm, with eccentric, vesicular nuclei and low mitotic activity. The tumour displayed a fibrous, hyalinized stroma, vascular invasion, occasional psammoma bodies, and small foci of necrosis. Immunohistochemistry showed positivity for CAM 5.2, and TTF1, while thyroglobulin, chromogranin A, ALK, and PD-L1 were negative.
Conclusion: The patient was treated with Carboplatin, Pemetrexed, and Pembrolizumab. The outcome was unfavourable, with numerous treatment and disease-related complications, shortly after followed by death. To our knowledge, this is the first case reported in the English literature of a primary ACC of the lung with metastases to the thyroid gland, and the third case with lymph node metastases.

E-PS-08-026

Adrenocortical oncocytic neoplasm coexisting with a central nervous system tumour based on CT- imaging: a case report

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Background & objectives: Oncocytic neoplasms are commonly discovered in thyroid and kidney resection specimens and oncocytic metaplasia is routine in breast pathology reports, but oncocytic adrenocortical neoplasms (ACON) are very rare.
Methods: We present a case of 50-year-old male who was referred to our hospital for an adrenal gland incidentaloma on CT imaging measuring 79 mm.
The patient has a 20-year medical history of a non-biopsied suprasellar tumour causing obstructive hydrocephalus, treated with a ventricular valve. The preoperative functional workup was negative, and an open adrenal resection was subsequently performed.
Results: Grossly the tumour weighed 220gr, and histologically it showed trabecular and diffuse growth pattern. The tumour cells were large with abundant eosinophilic cytoplasm, centrally placed nucleus and prominent nucleoli. We identified 2mitoses/50HPF and capsular invasion, but no atypical mitoses, necrosis, venous invasion or periadrenal tissue invasion. The neoplastic cells were MelanA(+), Inhibin(+) focally, CKAE1/AE(+) focally, EMA(-), ChromograninA(-), Synaptophysin(+) focally. There was disruption of the reticulin pattern. The tumour was consistent with an adrenocortical neoplasm with a suspected oncocytic nature. Since antimitochondrial antibodies were not available and ACONs are very rare neoplasms, we encouraged a consultation from a referral centre. The tumour was indeed an ACON borderline malignant (Lin-Weiss-Bisceglia criteria).
Conclusion: To the best of our knowledge this is the first recorded case of a patient with coexisting central nervous system tumour and oncocytic adrenocortical tumour. Since ACONs are uncommon, our knowledge of their clinical behaviour relies mostly on small series or isolated case reports and there is no consensus on the follow-up plan or the role of chemotherapy.

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E-PS-09-001

Desert hedgehog gene-related gonadal disgenesis: a rare case report

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Background & objectives: Pure form of gonadal dysgenesis, 46 XY is a form of sex formation disorder characterized by hypoplastic uterus, fallopian tubes and dysgenetic gonads developed from the bipotential gonad into the testicle from 3 to 8 weeks of intrauterine development.
Methods: The patient with complaints of the absence of secondary sexual characteristics and menstruation was examined srutinizely with biochemical analysis, histology, kariotyping and full exome sequencing.
Results: Sexual development corresponded to stage 1 according to Taner. The external genital organs are formed according to the female type. The vagina ends blindly, up to 3.5 cm deep. The uterus is absent in the small pelvis. Hypergonadotropic hypogonadism, hypoestrogenism, low testosterone levels with normal levels of other androgens were noted. Karyotype was 46, XY. Laparoscopy with bilateral removal of the sex glands performed. The gonads on both sides are represented by testicular tissue, the epididymis on the right is of a normal structure. Full exome sequencing demonstrated the mutation in the 2nd exon of the DHH gene (the variant in the homozygous state c.419T> G, p.L140R (513x)).
Conclusion: The above clinical observation demonstrates the importance of multidisciplinary management, morphological and molecular verification of the diagnosis for choosing the correct management tactics for such patients.

E-PS-09-002

Cost-effective immunohistochemical panel for ovarian carcinoma histotype differential diagnostics

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Background & objectives: Morphological features of ovarian carcinoma (OC) histotypes can be ambigous. So additional tissue markers applications should be used to improve diagnostic accuracy. The aim of this study was to develop cost-effective ICH panel for OC differential diagnostics.
Methods: We recruited 87 patients with ovarian carcinomas. 8 monoclonal antibodies were applied for immunohistochemistry (ICH): Ki67, p53, p16, WT1, PAX8, PgR-A and ER. Semiquantative and quantative analyses were used. Chi Automatic Interaction Detection analysis (CHAID) was applied for differential diagnostics.
Results: CHAID helped to hierarchical tree creation with 3 ICH markers (WT1, p53 и PR) for OC histotype detection with overall accuracy 91,7%. High WT1 expression with mutant p53 was highly specific for high-grade serous carcinomas in 97,0%, positive WT1 with wild type p53 was specific for low-grade serous carcinomas in 85,7%. In tumours with negative WT1 expression we used PgR for stratification. It was specific for endometrioid OC in 97% (isolated) and in 100% (with p53 wild type). If PgR was negative clear cell carcinoma was detected with accuracy 75,0%
Conclusion: The developed highly informative IHC panel (WT1, p53, and PR) can be used as a standardized algorithm for determining ovarian carcinoma histotype with 91,7% accuracy. It can improve the detection rate, reduce diagnostic time, facilitate the differential diagnostics and help to choose the optimal treatment option.

E-PS-09-003

A case report of deep aggressive angiomyxoma presenting as a polypoid mass

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Background & objectives: Deep aggressive angiomyxoma is a rare mesenchymal tumour that most commonly arises in the vulvovaginal region, perineum and pelvis of women. The term aggressive emphasizes the often-infiltrative nature of the tumour and its frequent association with local recurrence.
Methods: We report a case of a 43-year-old female, with no significant previous medical history, who presented with a large polypoid mass measuring 8x8cm attached through a stalk to the left labia majora. The lesion grew slowly over 3 years before presentation. There was no pain or associated tenderness.
Results: Following wide local excision of the lesion, the specimen received in our institution was a large pedunculated mass measuring 8.5x7.5x2.5cm. The cut surface had a soft, gelatinous appearance with a tan-grey to pink colour. On histological examination, the lesion was composed of an ill-defined hypocellular proliferation of bland spindle and stellate cells. The background stroma appeared myxoid and contained numerous medium/large sized vessels with thick hyalinised walls. The spindle cells were mostly positive for SMA and focally positive for Desmin and CD34. They also expressed ER and PR. S100 was negative.

The morphological and immunohistochemical features were in keeping with a deep aggressive angiomyxoma.
Conclusion: Despite the nomenclature, the WHO Classification of Tumours of the Female Genital Tract (5th Edition) recognizes that a small subset of these lesions can present as a pedunculated polyp. Deep aggressive angiomyxoma of the vulva needs to be distinguished from benign myxoid tumours with a low risk of local recurrence as well as from malignant myxoid neoplasms. Usually, wide local excision with tumour-free margins and occasionally hormonal manipulation is the treatment of choice.

E-PS-09-004
A rare case of fallopian tube lipoleiomyoma associated with ectopic pregnancy
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Background & objectives: Leiomyomas are the most common benign tumours of the female genital tract and most commonly arise from the uterus. The incidence of fallopian tube leiomyomas is extremely low and there are very few case reports of the lipoleiomyoma variant.
Methods: We report a case of a 33 year old woman, with no significant previous medical history, who presented with perivaginal bleeding and mild abdominal pain. Her last menstrual period was approximately 2 months before presentation. On ultrasound examination, a right tubal ectopic pregnancy was discovered, measuring 35x34x21mm with a chorionic ring and yolk sac. Serum beta-human chorionic gonadotrophin was raised.
Results: The specimen received in our institution was a fallopian tube measuring 65mm in length with a focally dilated portion measuring up to 15mm. On slicing, the lumen contained blood clot and a tan nodule measuring 7x6x4mm. On histological examination, the dilated portion contained chorionic villi along with a small piece of foetal tissue. A placental implantation site was also identified. The tan nodule showed morphological features in keeping with a lipoleiomyoma. Immunohistochemistry (SMA +ve, Desmin +ve, S100 +ve in adipocytes and CK -ve) supports this morphological diagnosis.
Conclusion: Fallopian tube leiomyomas arise from the mesosalpinx or the smooth muscle cells of the blood vessels. They are small and located unilaterally, although there are case reports of tubal leiomyomas as large as 13x9cm. Large leiomyomas can undergo torsion or degeneration. Most cases of tubal leiomyomas are asymptomatic and found incidentally during unrelated surgical procedures or at autopsy. In our case, this incidental lesion which was obstructing the tube lumen might have been the underlying aetiology for the ectopic pregnancy.

E-PS-09-005
Intraepithelial colonization of the uterine tube by a metastatic pancreatic adenocarcinoma simulating a serous tubal intraepithelial carcinoma (STIC)
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Background & objectives: When talking about metastatic tumours of the ovary and uterine tube, the first thing that comes to mind is the Krukenberg tumour. However, metastasis could simulate ovarian and tubal primary epithelial malignancies and pose major diagnostic challenges.
Methods: A 55-year-old female with a left adnexal mass was referred for additional studies. A PET/CT showed a 25 cm hypermetabolic left abdominopelvic mass, a 3 cm mass in the pancreatic tail, and smaller stomach lesions. Cancer Antigen 19-9 levels were 960 U/mL. A total abdominal hysterectomy with left salpingo-oophorectomy was conducted during which multiple peritoneal and omental implants were observed.
Results: Histology showed an adenocarcinoma with focal mucinous differentiation (intestinal-type) extensively involving the ovary, uterine tube, and serosa. A non-mucinous intraepithelial tumour growth pattern was found in the fimbrial and nonfimbriated portions of the tube. Immunohistochemistry showed an abnormal strong diffuse overexpression of p53, diffuse expression of CK7, focal CK20 and CDX-2 expression, and absence of PAX-8 staining, supporting the diagnosis of metastasis, most probably from pancreatic ductal adenocarcinoma.
The intraepithelial pattern of metastasis may not be frequent, but it is of key relevance when it comes to tubal neoplasia since it can be easily mistaken for a STIC. Features like mucinous cytology, involvement of nonfimbriated portions and serosa favour metastasis.
Conclusion: Immunohistochemistry was useful to rule out a STIC and help identify the primary tumour. Lack of PAX-8 expression, along with immunoreactivity for CK7, CK20, and CDX-2 provided support for a nongynecologic origin. The normal endoscopy and the presence of a mass in the tail of the pancreas made this the most probable origin of the tumour. p53 alone is not enough to confirm STIC. An interdisciplinary approach and wise use of immunohistochemistry are essential for a correct diagnosis.

E-PS-09-006
Case report of an ovarian signet ring stromal tumour
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Background & objectives: Ovarian signet ring stromal tumours are exceedingly rare sex cord-stromal neoplasms. We present such a case in a 59-year-old patient admitted for abnormal uterine bleeding. Her gynaecological examination revealed enlargement of the left adnexa due to an ill-defined ovarian mass.
Methods: The ovary was received fresh for an intraoperative consult, measured 3.5/2.5/2.5 cm and had a firm consistency. Its cut surface appeared nodular, homogenous, and grey. The morphology was consistent with an ovarian stromal tumour. Representative sections were submitted for subsequent final diagnosis on formalin-fixed paraffin-embedded tissue. A completion hysterectomy was also performed at the time due to numerous uterine masses.
Results: H&E-stained slides showed a benign stromal proliferation of two cell populations: spindle cells, arranged in vague fascicles, admixed with epithelioid cells featuring a signet ring appearance, with clear cytoplasmic vacuoles peripherally displacing the nucleus. We noticed no atypical mitoses or necrosis. Intratumoral oedema and fibrosis were focally associated. The uterus showed numerous leiomyomas, areas of adenomyosis and extensive endometrial atrophy, explaining the symptoms. The contralateral adnexa displayed no abnormality. Immunohistochemical stains were performed. The mass showed negative AE1/AE3 expression, excluding the possibility of a Krukenberg tumour. Inhibin was positive in a patchy distribution, with variable, moderate-to-strong intensity, consistent with previously reported cases.
Conclusion: Given the characteristic morphology, our final diagnosis was ovarian signet ring stromal tumour. Such benign entities should be included in the differential diagnosis whenever variable amounts of signet ring cells are admixed with bland spindle cells. They should be differentiated from metastases, especially Krukenberg tumours, which are usually bilateral and show strong and diffuse cytokeratin expression. In such cases, clinical history is often helpful. Other stromal tumours might show focal signet ring cell transformation, but only in a patchy fashion.

E-PS-09-007
Carcinosarcoma of the ovary arising from an endometriotic cyst - a case report
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Background & objectives: Endometriosis affects 5-15% of women, 0.5-1% of the cases are complicated by related neoplasm, exceptionally carcinosarcoma. Carcinosarcoma is a malignant tumour composed of epithelial and sarcomatous components. Herein, we report the case of ovarian carcinosarcoma arising from an endometriotic cyst.
Methods: A 55-year-old female patient with a history of hysterectomy due to multiple leyomyomas 17 years ago, was admitted to the hospital because of the pelvic mass and elevated serum CA125. A transvaginal ultrasound revealed 12 cm cystic, partially solid tumour of the left ovary. Surgical resection was followed by standard pathological evaluation and BRCA1/BRCA2 genes mutation testing.
Results: Pathological evaluation revealed biphasic malignant neoplasm of the ovary, within endometriotic cyst, composed of high grade carcinomatous and sarcomatous elements. The carcinomatous component was ambiguous in appearance between endometrioid and serous carcinoma. The sarcomatous component was heterologous with chondrosarcoma differentiation. Immunohistochemically, tumour cells were positive for PAX8, PTEN, CKAE1/AE3, vimentin, patchily for p16, and negative for WT1, beta-catenin, desmin, oestrogen and progesterone receptors. Immunostaining for p53 showed a wild-type pattern. Expression of mismatch repair proteins was retained. CD10 was positive in the stroma of endometriosis. Mutations in BRCA1/BRCA2 genes were not found. Disease was confined to one ovary. Therefore, a final diagnosis of carcinosarcoma derived from endometriotic cyst was rendered.
Conclusion: Neoplasms can develop in endometriosis setting, especially from endometriotic cyst.
Before making the diagnosis of primary ovarian carcinosarcoma, the endometrial origin has to be excluded.
Once the carcinomatous component demonstrates ambiguous morphology as well as endometrioid and/or clear cell rather than serous differentiation, it should raise concern for the possibility of the endometriosis origin. Therefore, diligent tumour sampling and assessment is crucial.
Immunostaining for p53 commonly has mutation-type pattern in both components however wild-type staining pattern can occur.

E-PS-09-008
Androgen receptor (AR) expression in endometrial carcinoma. Correlations with other markers of aggressiveness
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Background & objectives: Endometrial carcinoma (EC) represents an emerging disease with an increasing incidence of aggressive histotypes and advanced stages. We investigated the immunohistochemical expression of the Androgen Receptor (AR) and its correlation with other histological and immunohistochemical markers of prognosis.
Methods: EC hysterectomy specimens were tested with immunohistochemistry (IHC) for Estrogen Receptor (ERα), Progesterone Receptor (PR), AR, Ki67, p53, β-Catenin, E-Cadherin, Bcl-2, CyclineD1, MLH1 , PMS2, MSH2 and MSH6. The IHC expression was evaluated as a percentage of neoplastic cells (%) and dichotomized in high or low expression according to their distribution.
Results: We evaluated 103 Low Grade Endometrioids (LGEC), 15 High Grade Endometrioids (HGEC), 25 Other High Grade Histotypes (OHEC); 111 FIGO I-II, 32 FIGO III-IV. AR showed a variable distribution (Mean:23.8±26.4% Min:0% Max: 95%) with weak positivity (1+) with a significant correlation ($p<0.001$) with ER and PR ($R=0.4$). LGECs showed higher expression of AR than HGEC and OHEC (27.7 Vs 11 Vs 15.6; $p = 0.016$). The AR low cases were G3 (n=28; p=0.001), ER low (n=17; p=0.004) and PR low (n=33; p=0.001). 13 FIGO III-IV cases showed high levels of AR and 3 of these were G3, ER low and PR low.
Conclusion: AR proved to be a promising prognostic marker with a partial correlation with ER and PR levels; its permanence in advanced non-hormone-sensitive cases hypothesize its possible role as a second-line therapeutic target in patients not eligible for chemotherapy.

E-PS-09-009
Adenoid basal carcinoma found incidentally in case with uterine prolapse
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Background & objectives: We detected incidentally adenoid basal carcinoma in the patient with uterine prolapse. We aimed to show that the histopathological examination should be done by the pathologist more carefully in cases where neoplasia is not suspected.
Methods: A 53-year-old postmenopausal woman presented to our clinic with a history of uterine prolapse. The patient had not a cervical mass on pelvic examination and imaging methods. The patient underwent vaginal hysterectomy for uterine prolapse, and ABC was incidentally found in the cervix.
Results: Gross examination of the surgical specimen showed that the ectocervical squamous epithelium was thickened and white in colour. Microscopically, the tumour was composed of multiple small, round-to-oval cells arranged in small nests or cords resembling those of basal cell carcinoma of the skin. There were focally nuclear atypia and pleomorphism. Small, solid cell nests of irregular shape invaded the cervical stroma. Squamous and glandular differentiation were found in the centre of some cell nests. No desmoplastic reaction was observed in the stroma. Tumour cells showed nuclear immunoreactivity for p63 and blocked staining with p16. Focal reaction with CD117, Bcl-2, and Vimentin; negative for ER.
Conclusion: The case was diagnosed as ABC. ABC of the cervix is a rare condition that is considered to be indolent when pure 1. It is essential to distinguish ABC from other kinds of uterine cervix cancer. It is also critical to distinguish between ABC and adenoid cystic carcinoma(ACC). ABC had lower metastatic potential and a favourable prognosis than ACC. Adenoid basal carcinomas (ABCs) are even rarer, but careful histopathological examination is recommended for hysterectomy materials performed due to uterine prolapse.

E-PS-09-010
Endometrioid adenocarcinoma of the ovary with follicular architecture and aberrant thyroglobulin expression: a case report and review of the literature
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Background & objectives: Primary ovarian tumours with follicular pattern(FP) include ovarian endometrioid adenocarcinomas(OEA), sex cord tumours, small cell carcinomas of hypercalcemic type, ovarian carcinoid tumours and monodermal teratomas.
This study is aimed to report a case of OEA with FP and thyroglobulin expression.
Methods: A 76-years-old woman was admitted to our hospital with pelvic pain and weakness. A highly vascularized mass on the right ovary was shown at the ultrasound examination and a partially cystic and solid appearance was observed at the CT scan. Altered laboratory tests were observed and surgery was performed.
Results: A 2 cm-yellowish nodule of the right ovary was observed. At histology, the nodule showed two architectural patterns: a glandular and a

follicular one. The former had the classical aspect of an OEA, whereas the latter was characterized by eosinophilic amorphous material inside cuboidal cells-lined medium and large-sized follicles, resembling thyroid gland architecture. At immunohistochemistry, Cytockeratin 19, Epitheliel Membrane Antigen and Estrogen receptor were strongly positive in both components. Focal expression of CA125, CD99, PAX8, PAX2, Cytokeratin 7, PTEN and Progesteron Receptor was observed. TTF-1, BRAFV600E and HBME-1 were not expressed. On the contrary, the follicles' eosinophilic amorphous material and scattered cells in the glandular component immunoreacted for thyroglobulin.
Conclusion: Numerous primary and metastatic ovarian tumours may show a FP. For the correct diagnosis, a wide set of immunohistochemistry is mandatory and even thyroid markers should be assessed in doubtful cases. In the ovary, thyroglobulin is commonly expressed in struma ovarii. Moreover, its focal expression has already been reported in occasional serous ovarian carcinomas.
To the best of our knowledge, this is the first report of an OEA with concomitant focal FP and thyroglobulin expression.

E-PS-09-011
HLA-E gene polymorphism and its product expression in endometrial cancer Tunisian patients
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Background & objectives: HLA-E has a controversial tumour prognostic value due to the association of either its inhibitory and activating receptor on LT and NK cells.We investigated soluble HLA-E (sHLA-E) expression in endometrial cancer (EC) and analyse its implication as a prognostic marker.
Methods: The quantification of plasmatic sHLA-E was carried out by ELISA in twenty seven EC plasma samples compared to forty five plasma samples collected from healthy donors. Extracted genomic DNA was genotyped for HLA-E alleles using PCR-SSP.
Results: Plasmatic sHLA-E was increased in EC patients compared to controls ($p<0.0001$) with respective mean of 1798 ± 47.96 pg/ml and 2.66 ± 1.93 pg/ml. However, no significant associations were observed between plasmatic sHLA-E and EC clinical and histopathological findings. Also, the polymorphism E* 01: 01/01: 03 of the HLA-E gene does not seem to contribute to the predisposition to endometrial cancer and its spread in our population.
Conclusion: Our data strengthen the implication of sHLA-E molecules in tumour transformation especially in endometrial cancer.

E-PS-09-013
Solitary fibrous tumour of the uterine cervix: a case report and review of the literature
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Background & objectives: Solitary fibrous tumours (SFT) rarely involve the female genital tract, where they can be found more frequently in the vulva. In the cervix, six cases have been described. We report a case of cervical SFT along with a literature review.
Methods: A 48-year-old woman with genital haemorrhage performed MRI which showed an exophytic cervical tumour. Biopsy was initially interpreted as an undifferentiated malignant neoplasm and the patient underwent chemo-radiotherapy without improvement and was sent to our institution. Biopsy material was reviewed and the diagnosis of SFT was rendered. Three months after surgery, she is alive and well.
Results: On biopsy, a mesenchymal neoplasm with cells with indistinct borders with oval nuclei and scant cytoplasm immersed in a collagenous stroma was observed. Neoplastic cells were positive for CD34, CD56, CD99 and STAT6 and negative for cytokeratins, muscle markers, CD10 and ALK. During surgery, a nodular lesion on the vaginal wall attached to the cervix by a pedicle was seen. Total hysterectomy with bilateral adnexectomy and partial vaginectomy were performed. Grossly, a firm 3cm greyish nodule was observed. The neoplasm had hypo and hypercellular areas with hyalinized staghorn-like vessels. No cytological atypia, or necrosis were observed and 1 mitosis/mm2 was counted. A final diagnosis of a low-risk SFT was rendered.
Conclusion: Due to their rarity, the diagnosis of SFT in the cervix can be challenging. Differential diagnosis in this location includes benign and malignant entities such as muscle tumours, endometrial stromal neoplasms, and other mesenchymal neoplasms, such as inflammatory myofibroblastic tumours. Except for one, all cases reported to date have been benign. Awareness of the existence of this neoplasm in rare locations such as the cervix can improve its recognition and thus, enable the correct diagnosis and treatment.

E-PS-09-014
Yolk sac tumour of endometrium: a case report
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Background & objectives: Yolk sac tumour (YST) is a malignant tumour originating from germ cells and mainly arising from the gonads. Extragonadal development is uncommon (5% of cases). We present a rare case of primary endometrial YST.
Methods: A 69-year-old female patient was admitted for postmenopausal vaginal bleeding investigation. Ultrasound examination showed significant thickness of the endometrium with a polypoid appearance and a total hysterectomy with bilateral salpingo-oophorectomy was performed. Six months later a pelvic lympadenectomy was performed due to para-aortic lymph node enlargement.
Results: Histopathological examination revealed a tumour arising from an atrophic endometrial polyp and infiltrating the 2/3 of the myometrium with mixed neoplastic population. The predominant component (accounting for 70%) was a YST, which consisted of polygonal cells with solid and diffuse growth pattern. The rest (30%) was a high-grade clear cell carcinoma. The para-aortic lymph nodes were also infiltrated (90% YST predominance). Immunohistochemical staining regarding the YST cells was positive for Panceratin, CAM5.2, AFP, CEA, HepPar1 (focally), and negative for EMA, CK7, CD15, CD30. The clear cell carcinoma showed positivity for CK7, EMA, p53, p16, WT1. The Ki-67 mitotic index was >80%.
Conclusion: Primary endometrial YST is a very rare malignancy with only 30 cases reported in the literature; recently added in the newest WHO Classification of Female Genital Tumours (5th edition, 2020). The patient age range is 24-87 years. They present either as pure YST tumours or in coexistence with endometrial carcinoma. The histogenesis includes somatic carcinoma differentiation, residual foetal tissue origination and germ cell migration.

E-PS-09-015
Fallopian tube carcinosarcoma. A cohort of 4 cases of a rare entity
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Background & objectives: Carcinosarcoma is a biphasic tumour composed of a high-grade carcinomatous and sarcomatous components. This

is a rare gynaecological malignancy and it is rarely found in the fallopian tube, therefore, not much is known about its biological behaviour.
Methods: We conducted a 20-year-retrospective transversal study (2000-2020) at Coimbra University Hospital, a tertiary hospital in Portugal and reviewed all fallopian tube carcinosarcomas (n=4). Relevant clinical and pathological data was extracted from the hospital database.
Results: The median age at diagnosis was 60,5 years (37-72 years). After a median follow-up of 111.8 months, two of the patients were alive and clinically free of disease; one patient died due to disease progression 33 months after surgery; the remaining patient died of unrelated causes after 137 months. The surviving patients were staged as pT1a and pT1b.
Tumour median size was 13cm (3-20cm). Regarding morphology, the epithelial component was undifferentiated in two, serous in two and endometrioid in one. The sarcomatous component exhibited chondroid differentiation in two, one of them displaying also striated muscle differentiation.
Conclusion: Fallopian tube carcinosarcoma is a rare entity, with a poorly understood biological behaviour, due to its rarity. Early detection and surgical removal may be the keys for a successful treatment.

E-PS-09-016
Mesonephric-like adenocarcinoma of the ovary: a case report
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Background & objectives: Mesonephric-like adenocarcinoma (MNL-AC) is a rare, recently described tumour occurring in the uterine corpus and ovary which exhibits the same morphological and immunohistochemical features with the mesonephric adenocarcinoma of the uterine cervix.
Methods: A 63-year-old woman patient presented with abdominal swelling. The computed tomography(CT) showed a 30× 27 cm multicystic mass on the right ovary. She underwent laparoscopic hysterectomy and bilateral salpingo-oophorectomy, bilateral pelvic lymph node dissection, and omentectomy.
Results: On gross examination, the cut-surface of the ovarian mass contained solid and cystic structures with a yellowish-tan appearance. On histologic examination there was an admixture of various growth patterns with tubular, glandular, papillary, and solid architectures. Tubular and papillary growth patterns were predominant. Intraluminal hyaline-like eosinophilic material was also seen in some tubules. Tumour cells had typically vesicular chromatin, inconspicuous nucleoli, and crowding; mitotic activity was low. By immunohistochemistry, tumour cells stained positive for Pax8, Gata-3, TTF-1 and CD10(luminal staining) whereas stained totally negative with ER, PR and WT-1. p53 exhibited "wild-type" immunoreactivity. Loss of PTEN and ARID1A weren't detected. Mismatch repair proteins were intact. The final diagnosis was mesonephric-like adenocarcinoma of the ovary with a FIGO stage IA.
Conclusion: MNL-ACs are one of the uncommon malignancies of the ovary and the clinical behaviour of these tumours are uncertain. Better understanding of the clinical and pathological features of these tumours avoids misdiagnosis and mistreatment.

E-PS-09-017
KRAS-mutated mesonephric adenocarcinomas of the uterine cervix with MLH-1 methylation, coexisting with uterine low grade endometrioid carcinoma: a rare case report
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Background & objectives: Mesonephric adenocarcinomas (MNAC)are rare, aggressive tumours of the female genital tract often associated with mesonephric remnants/hyperplasia. It is characterized by recurrent KRAS-mutations and lack of PIK3CA/PTEN-alterations. In addition to the KRAS-mutation, we present a case of MNAC of the uterine cervix with methylation of MLH-1.
Methods: A 49-year-old woman patient presented with atypical vaginal bleeding. Pelvic magnetic resonance imaging(MRI) showed a 66 × 48 mm enhancing mass extending to the uterus at the level of the cervix. She underwent laparoscopic hysterectomy and bilateral salpingo-oophorectomy, bilateral pelvic and para-aortic lymph node dissection, and omentectomy. Gross examination showed an infiltrating mass in the cervix, measuring 7x5x4 cm, with extension to the uterine corpus.
Results: Cervical component of the tumour consisted of tubular glands, many with intraglandular villous papillae, lined by one or several layers of columnar cells resembling endometrial glands on histological examination. Immunohistochemically this tumour was diffusely positive with PAX8,GATA3,TTF1 and CD10(luminal staining).p53 exhibited "wild-type" immunoreactivity while oestrogen receptor (ER)and progesterone receptor (PR)were negative. The uterine component of the tumour exhibited low grade endometrioid carcinoma morphology with different immunohistochemical profile.ER and PR were positive in the endometrioid component. Immunohistochemical loss of MLH-1,PMS-2,PTEN and ARID1A were seen in both tumour components. In addition MLH-1 promoter methylation was detected in two components by methylation specific polymerase chain reaction(PCR).Genomic alterations were identified in KRAS p.(G12D) by PCR.
Conclusion: The final diagnosis was mesonephric adenocarcinoma of the uterine cervix coexisting with uterine low grade endometrioid carcinoma with a FIGO stage IBII. Mesonephric adenocarcinomas are one of the rare subtypes of cervical tumours. We described a KRAS-mutated MNAC of the uterine cervix with MLH-1 methylation, coexisting with uterine low grade endometrioid carcinoma. This was the first case of MNAC with MLH-1 methylation as far as we are aware from English literature.

E-PS-09-018
An early stage ovarian carcinosarcoma and its association with primary tubal carcinoma
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Background & objectives: Ovarian carcinosarcoma (OCS) is a rare form of ovarian cancer, the occurrence of carcinosarcoma in association with synchronous tubal carcinoma is uncommon. OCS are usually advanced-stage tumours at the time of diagnosis.
Methods: A 55-year-old postmenopausal patient presented with a pelvic mass. Ultrasonography revealed bilateral ovarian masses, at right 10cm and at left 6cm. Intraoperative consultation of the right unilateral-salpingo-oophorectomy specimen had resulted in a borderline serous tumour that is suspicious of invasion. The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, and partial omentectomy, bilateral pelvic and para-aortic lymph node dissection.
Results: Both ovarian masses were composed of biphasic malignant components. The epithelial component was high-grade serous carcinoma (HGSC) characterized by solid sheets and complex papillary architecture. The mesenchymal component was high-grade pleomorphic and spindle cell sarcoma. Immunohistochemically carcinomatous component was cytokeratinAE1/AE3(+), P53(+), and P16(+); the sarcomatous component was P53(+), P16(+) and Vimentin(+). The right fallopian tube showed an HGSC with an adjacent focus of serous tubal intraepithelial carcinoma (STIC). The right tubal HGSC and adjacent STIC also showed P16 and P53 abnormal expression. The tumour was limited to both ovaries and fallopian tubes with benign peritoneal washing cytology and no sign of lymph node or far organ metastasis (Stage1b:T1bN0M0).
Conclusion: The patient had 6 cycles of chemotherapy using paclitaxel and carboplatin. As OCS is known to have a %15-30 5-year survival rate, our patient is disease-free in her 19-month follow-up. As the fallopian

tube has recently been proposed to be an origin for a majority of pelvic or ovarian HGSC, tubal carcinoma may be the origin for OCS through an epithelial-mesenchymal transition.

E-PS-09-019

Primary uterine angiosarcoma. A case report.

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Background & objectives: Uterine angiosarcoma is a rare and extremely malignant vascular tumour with a poor prognosis. It occurs in perimenopausal and postmenopausal women, with few cases described in the literature. We report a case localized in the uterine corpus.
Methods: We report a case of a 53-year-old woman with an intermittent uterine bleeding for two years without a history of prior pelvic radiation. Magnetic resonance imaging and abdominal computed tomography demonstrated a well defined 26 cm uterine mass localized in the corpus with a depth of myometrial invasion more than 50%. Radical histerectomy with bilateral salpingo-oophorectomy was performed.
Results: Macroscopic examination revealed a uterine cavity filled with a solid tumour measuring 25x20x15 cm. The cut surface was grey with large haemorrhagic and necrotic areas. Microscopic examination showed an extensive infiltration of the myometrium by anastomosing abortive vascular channels and some solid sheets of spindled and epithelioid cells with marked pleomorphism and hyperchromatic nuclei with mitotic figures. Extensive foci of haemorrhagic necrosis were observed and molecular analysis was not possible. Immunohistochemically the tumour cells were diffusely positive for CD31 and FLI1 and focally positive for CD34 and CyclinD1. D2-40, CD10, SMA, desmin, caldesmon, progesterone and oestrogen receptor were negative. The patient was lost to follow up after surgery.
Conclusion: Uterine angiosarcoma is an infrequent tumour derived from vascular endothelial cells. It usually presents in postmenopausal women as rapidly growing uterine mass and can also arise after pelvic radiaton or rarely in a leiomyoma. The diagnosis depends mainly on the histopathological examination and immunohistochemical stains. Breakages at YWHAE, NUTM2A and NUTM2B loci have been detected in some cases of uterine angiosarcoma and may contribute to a better understanding of the pathogenesis.Our case was lost to follow up after surgery.

E-PS-09-020

Clear cell borderline tumour of the ovary. A case report.

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Background & objectives: Ovarian clear cell borderline tumours are extremely rare, comprising less than 1% of borderline ovarian neoplasms. Differential diagnosis with ovarian clear cell carcinoma is critical, requiring an extended sampling in order to rule out this entity.
Methods: A 73-year-old woman with a clinical history of uterine leiomyomas treated with total histerectomy and left salpingo-oophorectomy. The patient presented with acute heart failure and pelvic pain. Computed tomography of the abdomen and pelvis showed a mild bilateral pleural effusion and a 18 cm mass in the right adnexal space. Frozen sections were negative for malignancy.
Results: Gross findings revealed a lobulated circumscribed mass attached to fallopian tube measuring 18x14.5x11 cm with intact capsule. The cut surface was firm and yellowish with fibrous tracts and simple cysts in a honeycomb pattern. Microscopic examination showed a fibrocollagenous background with calcifications and abundant glands in a irregular distribution with single layer epithelium and clear-eosinophilic cytoplasm with dense luminal secretion. The more crowded glandular areas showed hyperchromatic nuclei with moderate atypia and visible nucleoli. Not endometriosis, lymphovascular invasion, stromal desmoplasia or necrosis were found. Immunohistochemically the glandular component was positive for CK7, Napsin-A, racemase, ARID1A and PAX8 and negative for oestrogen and progesterone receptor. KRAS or BRAF mutations were not carried.
Conclusion: Clear cell borderline tumours of the ovary are relatively uncommon. They are frequently associated with ovarian endometriosis as an underlying precursor. Because of the common association with clear cell carcinomas, it is advisable a carefully macroscopic examination and an extensive sampling to rule out this entity. In the present case, we didn´t find criteria for invasion nor transition clear cell carcinoma nor endometriosis after a very extended sampling. The neoplasm showed retention of nuclear immunoreactivity with mismatch proteins.

E-PS-09-022

Recurrent primary Paget's disease of the vulva

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Background & objectives: Vulvar Paget's disease, primary or secondary, is a rare malignancy, with problematic treatment, due to its multi-focal nature and frequent relapses. We report a case of primary vulvar Paget's disease with multiple recurrences and focal, incipient, dermal infiltration.
Methods: A 76 year-old female with a history of pT1N0(sn) [ER(+), PgR(+), HER-2(-)] ductal (NST) breast cancer was admitted to our hospital due to a vulvar lesion. Imaging tests were insignificant. The lesion was surgically abscised. Pathology report showed primary Paget's disease of the vulva. The patient had three recurrences within one year, all treated with local surgical excision.
Results: All four surgically resected specimens were identical under the microscope. Histopathologic examination revealed an intraepidermal, epithelioid neoplasm consisting of small clusters or single cells with moderate nuclear atypia and abundant eosinophilic or amphophilic cytoplasm (pagetoid spread) virtually reaching the lateral borders of the specimens. In one case focal, incipient, dermal infiltration was observed and confirmed immunohistochemically. The neoplastic cells were positive for CK7, EMA, mCEA,GCDFP-15, HER-2(3+), MUC5AC, AR and negative for ER, PgR, S100, HMB-45, p63. The morphological and immunohistochemical findings were compatible with primary Paget's disease of the vulva.
Conclusion: Although Paget's disease of the vulva has been described over 100 years ago still remains a largely confusing, rare disease, difficult to handle and treat. It may be misdiagnosed or belatedly diagnosed. Surgery, traditionally considered standard treatment has been disappointing with positive margins and recurrence rates more than 50%. Moreover wide local resection causes major morbidity and functional defects. Non-surgical treatments like radiotherapy, photodynamic therapy, local chemotherapy and laser ablation are under consideration. Our patient remains under medical attendance.

E-PS-09-023

Morphological basis for predicting recurrent endometrial hyperplasia

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Background & objectives: The endometrium hyperplasia (EH) problem remains current today. Endometrium immunohistochemical features in EH became the basis for predicting the recurrence of EH. Justify prediction of EH without atypia recurrence based on endometrium morphological features.
Methods: The pilot study included 45 women with EH without atypia. On the basis of endometrium Ki-67 and p16INK4a expression patients were divided depending on the EH recurrence risk. At increased EH

recurrence risk (n=15) the therapy corresponded to the developed algorithm. Therapy of patients without increased EH recurrence risk (n=15) and control group patients (n=15) corresponded to the generally accepted.
Results: In the therapy based in the endometrium p16INK4a and Ki-67 expression at 6 months later the endometrium corresponded to the secretion phase middle stage, a statistically significant decrease in the endometrium p16INK4a and Ki-67 expression was recorded, including patients with a high EH recurrence risk. In control group an endometrium p16INK4a and Ki-67 expression was decreased in 66.7% of patients, in 26.7% of women the p16INK4a and Ki-67 expression didn't decrease. In the therapy based in the endometrium p16INK4a and Ki-67 expression at 12 months later endometrium corresponded to the secretion phase middle stage, unlike in control group women, where in 26.7% of patients showed EH without atypia.
Conclusion: The established morphological patterns of the increased EH recurrence risk - a change in the endometrium p16INK4a and Ki-67 expression - made it possible to develop an algorithm for a personalized approach to the patients of reproductive age with EH without atypia. The developed algorithm for the management of EH patients allows reducing the recurrence rate by 37% ((15:11) / (15:15) = 1.37) compared to the EH patients management, generally accepted today.

E-PS-09-024
Primary uterine Ewing sarcoma: case report
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Background & objectives: Ewing sarcoma (ES) is rarely seen in the female genital tract, mostly seen in bone or soft tissue. We aimed to discuss the case diagnosed uterine Ewing sarcoma with histopathological, immunohistochemical and Fluorescent in situ hybridization findings.
Methods: A 46-year-old patient with abdominal and pelvic pain was diagnosed with myoma uteri by physical examination; total abdominal hysterectomy + bilateral salpingo-oophorectomy was performed.
Results: Macroscopic examination, 10x10x8 cm mass located on the posterior wall of the uterus was observed. In the microscopic examination, tumour consisting of monotonous small round cells with narrow cytoplasm separated by a fibrous septa, solid nests, frequent mitotic activity and necrosis was observed. immunohistochemically tumour cells; CD10, CD56 and CD99 positive; H-caldesmon was focal positive, S100, chromogranin, synaptophysin, calretinin, inhibin, keratin, cyclin D1, desmin, LCA and TLE-1 were negative. In order to confirm the diagnosis, t (11; 22) (q24; q12) gene translocation was performed by FISH method and was found to be positive. Based on histopathological, immunohistochemical and FISH data, the case was diagnosed primary uterine Ewing Sarcom.
Conclusion: Ewing sarcoma is an extremely rare malignancy of the female genital tract, mostly seen in children and adolescents. While making the diagnosis, it is important to exclude the entities (such as lymphoma, small cell carcinoma) in the differential diagnosis. The t (11; 22) (q24; q12) found in approximately 85% of the cases was also detected in our case. It is important to support the diagnosis with FISH in cases with suspected Ewing sarcoma with histopathological and immunohistochemical findings.

E-PS-09-025
Concordance of lymph-vascular space invasion in cervical biopsy and resection specimens of squamous cell carcinoma
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Background & objectives: According to European Society of Gynaecological Oncology (ESGO) and European Society of Radiotherapy and Oncology (ESTRO) guidelines the presence of lymph-vascular space invasion (LVSI) in cervical biopsies requires sentinel lymph node examination for stage IA1 and IA2 cervical cancers.
Methods: In this study we aimed to elucidate the relationship between LVSI detected in cervical biopsies and the final histopathologic confirmation of LVSI in hysterectomy specimens for squamous cell carcinoma (SCC) with the goal of preoperatively identifying it. A retrospective pathologic review was performed and thirty-four pathologically confirmed SCC patients who underwent preoperative cervical biopsies and subsequent radical hysterectomies were included.
Results: Presence of LVSI accounted for 2,9% (n=1) of all preoperative cervical biopsies and 41,2% (n=14) of all resection specimens. One cervical biopsy in which the presence of LVSI was detected correlates with the final resection specimen, therefore the positive predictive value is 100.00%. Preoperative cervical biopsy specimens were associated with a poor sensitivity (7,1%; 95%CI: 0.18%-33.87%), and moderate negative predictive value (60,6%; 95%CI: 57.09%-64.02%), for the determination of LVSI in the final resection specimen.
Conclusion: The lack of identification of LVSI in preoperative cervical biopsies does not guarantee that LVSI will be absent in the final hysterectomy specimens. Therefore cervical biopsies lack sufficient negative predictive value for LVSI for SCC seen in hysterectomy specimens.

E-PS-09-026
Case report of somatic malignant transformation of mature ovarian teratoma: a rare, but unfavourable occurrence
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Background & objectives: Malignant somatic transformation of ovarian mature teratomas occurs in only 2% of cases. We aim to present the case of a 69-year-old female admitted for hypogastric pain due to an adnexal mass invading the sigmoid colon and small intestine.
Methods: We received a fresh surgical specimen of 23/18/16 cm, including total hysterectomy with bilateral salpingo-oophorectomy together with sigmoidectomy and partial enterectomy. The specimen revealed a 16/16 cm left adnexal mass, adherent to the digestive segments, with cystic transformation, containing necrotic sebaceous material and hair, along with a yellow-grey solid area in cyst's wall of 10/9/3 cm, suggesting a malignant teratoma.
Results: Histological examination revealed classic components of mature teratoma: keratinized epithelium, sebaceous, sweat and salivary glands, hair follicles, respiratory epithelium, hyaline cartilage and thyroid follicles. The solid area revealed proliferation of atypical squamous cells with areas of keratinization, extensive necrosis, abundant mixed inflammatory infiltrate, lymphovascular and perineural invasion. There was massive carcinomatous infiltration into the muscularis propria of the colon and, respectively, into the submucosa of the small bowel, also showing necrosis and perineural invasion. Colon surgical margins were tumour-free. The contralateral ovary had no abnormality. Immunohistochemistry confirmed squamous phenotype: tumour cells expressed p63 and 34BE12, with lack of p16, CK7 and CK20 expression. At follow-up, the patient developed liver metastasis.
Conclusion: The histopathological and immunohistochemical features were consistent with keratinizing squamous carcinoma G2 arising from mature ovarian teratoma. Although the event is rare, finding a solid necrotic nodule in a large dermoid cyst wall, at postmenopausal age, should raise suspicion for malignancy. Squamous cell carcinoma is the most frequent associated histological subtype. Extra-ovarian spread indicates poor prognosis, therefore studies are required to early identify patients at risk and to evaluate the efficacy of chemotherapy as an adjuvant tool for advanced disease.

E-PS-09-027
A case of undifferentiated carcinoma of the uterus with rhabdoid features resembling SMARCA4-deficient uterine sarcoma
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Background & objectives: Undifferentiated carcinoma of the uterus and SMARCA4-deficient uterine sarcoma may show morphological overlap. SMARCA4-deficient uterine sarcoma is a recently defined neoplasm which has rhabdoid features and loss of expression of SMARCA4.
Methods: A 46-year-old woman presented with vaginal bleeding, abdominal pain and fever. Computed tomography showed a mass located in the uterine corpus that may be compatible with an abscess or hematoma of about 110x80 mm in size. Emergency surgery (total abdominal hysterectomy and bilateral salpingo-oophorectomy) was performed.
Results: In histological examination, the tumour in endometrium showed diffuse infiltration into the myometrium. It was composed of sheets-like arrangement of large atypical epithelioid cells with rhabdoid morphology. Extensive necrosis and lymphovascular invasion observed. Immunohistochemical stains revealed negative staining with pancytokeratin, ER, PR, CD34, desmin, H-caldesmon, and Pax8; focal patchy staining with EMA, S100, SMA and CD10. A wild-type p53 immunostaining obtained. SMARCB1(INI1), SMARCA4(BRG1), MSH2 and MSH6 expressions were retained, although the tumour cells showed loss of expressions of MLH1 and PMS2. The tumour invaded directly cervix uteri and serosa. Also several metastatic nodules were detected in bilateral adnexal tissues. The patient died one month after her surgery.
Conclusion: Final diagnosis was undifferentiated carcinoma of the endometrium with rhabdoid features. It is critical to distinction between undifferentiated carcinoma with rhabdoid features from SMARCA4 uterine sarcoma. Mismatch repair deficiency and intact SMARCA4 expression are useful tools in differentiating between them.

E-PS-09-028
Rare non-epithelial gynaecologic tumours: review of five cases that pose current challenges
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Background & objectives: More than 50% of gynaecological tumours are "rare" (≤6/100,000 women), it refers mostly to non-epithelial subtypes, encompass >30 histological variants and few patients. Hence the difficulty for diagnosis. Our review provides key points with the aim of fighting this ailment.
Methods: Five cases diagnosed in the last 6 years below:
A: 52 y/o. Endocervical polyp recurrence after 2 months. Polypectomy.
B: 62 y/o. Hyperandrogenism without known tumour. Bilateral adnexectomy.
C: 2 y/o. Fever, abdominal pain, CT: 11 cm ovarian tumour, αFP: 20; CEA125: 770. Adnexectomy.
D: 41 y/o. Endometriosis. Hysterectomy and bilateral adnexectomy.
E:19 y/o. Solid ovarian tumour. Oophorectomy.
Results: A: polypoid architecture, normal epithelium, fibromyxoid stroma, mild-atypical spindle cell groups, hyaline cartilage. 11 mitoses/10 CGA. CD10(+), Actin-Myosin(-), Ki67:40%. Adenosarcoma with heterologous hyaline cartilage.
B: yellow ovarian tumour. Polygonal cells, central nuclei with nucleolus, eosinophilic-granular-vacuolated cytoplasm (lipid rich). No Reinke crystals. Inhibin(+), Vimentin(+), Melan-A(+), Calretinin(+), CKAE1-AE3(-), Ki67:3%. Steroid cell tumour.
C: polycystic ovarian tumour. Intracystic papillary- extracystic retiform projections, Sertoli (CK+, Inhibin and EMA-) and Leydig cells (Calretinin+), oedematous stroma (Vimentin+). Sertoli-Leydig Cell Tumour.
D: Fallopian tube incidentaloma. Epithelioid cell cords/nets, monotonous nuclei, eosinophilic cytoplasms. Calretinin(+), Vimentin(+), EMA(-). Wolffian tumour.
E: nodular architecture, no-atypical mixed cell nests, oedematous stroma, dilated vessels. Inhibin(+), Calretinin(+), Melan-A(+), Estrogens/progesterone(+), EMA(-), Ki67:3%. Sclerosing stromal tumour.
Conclusion: - Rare tumours cause >25% of cancer mortality and in all of them a correct pathological diagnosis is important to guide to a correct treatment and a potential better result.
- Mortality rates are high due to the current lack of understanding of the pathophysiology.
- Studies such as molecular testing and circulating tumour-specific biomarkers are promising, but further research will be needed.
- The knowledge of the anatomopathological characteristics of these tumours remains the most reliable for the diagnosis.

E-PS-09-029
Uterine leiomyosarcoma with areas resembling giant cell tumour of soft tissues
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Background & objectives: The presence of osteoclast-like giant cells in uterine leiomyosarcomas is a rare phenomenon. We describe a uterine leiomyosarcoma with areas resembling giant cell tumour of soft tissues. The latter component showed signs of malignancy as well.
Methods: A 55-yr-old postmenopausal woman presented with vaginal bleeding. From D&C material the diagnosis of giant cell tumour with malignant features was given. Pelvic ultrasound showed an intrauterine polypoid mass measuring 60 mm in diameter. Staging CT revealed no distant metastases. The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy and sentinel lymph node dissection.
Results: Grossly an 80 mm large well-defined, polypoid, tan-grey solid mass filled the uterine cavity and infiltrated the myometrium. The cervix, adnexa and sentinel lymph nodes were unremarkable. Histologically the predominant component was a leiomyosarcoma mainly with pleiomorphic morphology. Other parts of the tumour were composed of mononuclear cells intermingling with osteoclast-like giant cells, corresponding to the tumour seen in the D&C material. Here the mononuclear cells showed moderate nuclear atypia and frequent atypical mitotic figures were seen. The giant cell component showed vascular invasion. The two distinct patterns had mainly sharp borders but scattered osteclast-like giant cells were also seen in the leiomyosarcoma areas.
Conclusion: To the best of our knowledge, only a few cases of uterine leiomyosarcoma with giant cell tumour component have been reported so far in the literature. It is uncertain that these tumours are composite tumours with dual differentiation (leiomyosarcoma and giant cell tumour) or simply uterine leiomyosarcomas with the presence of osteoclast-like giant cells.

E-PS-09-030
Vulvar Buschke-Loewenstein tumour: often misdiagnosed
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Background & objectives: Buschke-Löwenstein's tumour (TBL), or giant condyloma acuminata is a rare and poorly defined epithelial tumour. This disease is sexually transmitted by the human papillomavirus. Vulvar localization is rare. We report one case of TBL with cervical, vaginal and vulvar localization.
Methods: We report the case of a 28-year-old patient with a history of type 1 diabetes on insulin discovered 5 months ago following a urinary tract infection. She has been married for 10 months and she is consulting for vulvar lesions.
Results: The clinical examination showed brownish coloured budding and vegetative lesions spread over the vulva, the peri-anal region, the vaginal wall and on the cervix. A cervico uterine smear showed low-grade intraepithelial lesion related to HPV virus. Pathological examination of the biopsies concluded that the tumour was a Buschke-Löwenstein tumour.

The vulvar mucosa was lined with a hyperplastic acanthopapillomatous coating topped by a large ortho and para-keratotic horny layer. Numerous koilocytes are present in the superficial layers. The chorion had a discrete mononuclear inflammatory infiltrate. The patient underwent extensive surgical resection of the tumour and was followed in our outpatient clinic for two years without any signs of tumour recurrence.
Conclusion: Buschke-Löwenstein's tumour is a sexually transmitted pathology whose causal agent is the papillomavirus. This tumour is responsible for mutilating lesions that can affect the functional prognosis of the female and male genital organs, hence the interest of early treatment to avoid giant and disseminated tumours.

E-PS-09-031
Immunohistochemical profile of ovarian cancer microenvironment in young women
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Background & objectives: Ovarian cancer is a major cause of female cancer-related deaths. This study aims to analyse the proportion, density and distribution of T and B lymphocytes and their prognostic significance in young women with borderline and malignant ovarian surface epithelial tumours.
Methods: Clinicopathological and outcome data were collected for 57 women aged ≤50 , diagnosed between 2010 to 2015. Representative tumour sections were stained for CD3 (T cells) and CD20 (B cells) and tumour infiltrating lymphocytes (TILs) scored following the Immuno Oncology Biomarker Group recommendations as stromal, intra-tumoral, aggregates and touching lymphocytes. Data was analysed and correlated to the clinicopathological variables.
Results: The mean age was 38 years and the most common histological type was serous carcinoma (n=21). Risk of malignancy index (RMI) and serum CA125 were significant predictors of ovarian cancer diagnosis (p=0.02). In total, 15/34 cancer patients died of their disease with no deaths in the borderline category. There was significantly greater stromal infiltration of CD3 (p=0.01) and CD20 TILs (p=0.034) and higher intratumoral CD20 in ovarian cancers compared to borderline tumours. The highest CD3 infiltration was in serous carcinoma, exhibiting the highest numbers of CD3 and CD20 aggregates. There was no statistical difference between touching lymphocytes and tumour subtype. There was no significant association between TILs and patient survival.
Conclusion: The count, distribution and density of T & B lymphocytes in ovarian tumours varied by tumour type and invasiveness. Their topographic distribution, however, did not appear to impact on prognosis in young women with ovarian cancer. TILs analysis in an older age group is ongoing to determine its potential prognostic significance.

E-PS-09-032
Malignant Brenner tumour of ovary: a rare case report
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Background & objectives: Most of the Brenner tumours(BTs) are benign, often incidental findings. Malignant Brenner tumours(MBTs) are rare that account for less than 5% of all BTs. Here we report a case with MBT.
Methods: 77-year-old female patient with no relevant medical history presented with abdominal pain and bulk symptoms. Pelvic CT examination revealed a 17cm left pelvic mass with focal calcifications which was consistent with subserosal leiomyoma radiologically. The patient had elevated tumour markers so she underwent total abdominal hysterectomy and salpingo-oophorectomy. Frozen examination performed and resulted as MBT.
Results: Pathologic examination revealed a biphasic proliferation of epithelial cells with areas of solid, well-formed nests, which was compatible with conventional BT morphology, with regions of infiltrative cord-like and single cell growth, which was interpreted as MBT. Benign component accounted for 30% and the malignant component accounted for 70% of the tumour. Cytologically, the tumour showed only mild atypia. Immunohistochemical studies showed p63 and CK7 positivity and mutation type total loss of p53 for both components. Well-formed nests were positive with GATA-3, however invasive areas were negative. The tumour was limited to the right ovary and staged as pT1a. No evidence of lymph node metastasis was found.
Conclusion: On imaging, these tumours demonstrate nonspecific findings. There is no consistent tumour marker for these tumours, but several of them can be high. The primary treatment modality is surgical excision. Due to their rarity, current evidence on the treatment of MBTs are predominantly limited to case studies and small case series. Therefore, the precise role and regimen of adjuvant chemo-radiation therapy for MBT has not been established.

E-PS-09-033
Primary adenocarcinoma of intestinal type of the vulva: an extremely rare neoplasm
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Background & objectives: Primary vulvar adenocarcinoma of the intestinal type is an extremely rare neoplasm with few reported cases in the literature.
Methods: The patient, a 73-year-old woman, presented with a 2-month history of a pruritic, painless vulvar mass. On gynaecological examination, a 3.5cm soft, non-tender grey mass was identified at the labia minora of the vulva and surgical excision was performed.
Results: The histological examination revealed an invasive, moderately differentiated mucinous adenocarcinoma. Immunohistochemically, the tumour cells showed diffuse positive staining for cytokeratin 20, CDX2, CEA whereas CK7 and GCDFP-15, CA125, ER, PR, TTF1, NAPSIN were negative. The final pathologic diagnosis was adenocarcinoma of intestinal type of the vulva. An extensive workup, including chest X-ray, abdominal and pelvic ultrasound, cervical Pap smear and systemic positron emission tomography-computed tomography (PET-CT) did not reveal any other local malignant neoplasm. In addition, both colonoscopy and gastroscopy examination were negative, excluding an adenocarcinoma of the gastrointestinal tract.
Conclusion: Primary adenocarcinoma of the vulva is extremely rare, and its origin remains controversial. There are some reports about the origins of vulvar intestinal-type adenocarcinoma, which suggest that this tumour originates from the cloacal remnants. Adenocarcinoma at this specific anatomical site can originate from sweat glands or present as an adenocarcinoma metastasis, but a true primary adenocarcinoma of the intestinal type is an extremely rare variant at the vulva.

E-PS-09-034
An ovarian somatically derived yolk sac tumour in an 85-year-old woman with aggressive clinical course and resistance to conventional chemotherapy regimens: a case report with reference to the literature
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Background & objectives: Herein, we report a case of a yolk-sac-tumour(YST) in an 85-year-old patient, arising in the setting of bilateral High-grade Serous (HGSC) Ovarian carcinoma and we highlight the aggressive behaviour of these rare neoplasms that are newly-described in the literature.

Methods: Our patient was diagnosed with ovarian HGSC+omental/peritoneal disease(FIGO:IIIC) in 2016,successfully treated with chemotherapy(Cisplatin-Paclitaxel-Carboplatin)with radiological complete regression. She decided against post-treatment cytoreductive surgery. In 2020, she presented with abdominal pain & bilateral adnexal tumours. Hysterectomy & omentectomy were performed. The left ovary was predominantly cystic measuring 9,2cm. Small papillary projections were observed in the inner wall of the cyst. The right adnexa was involved by a solid tumour measuring 13cm, with cystic & haemorrhagic areas.
Results: Morphological and immunohistochemical results for the left ovarian tumour were consistent with High-Grade-Serous cystadenocarcinoma. The right adnexal tumour consisted microscopically of a minor HGSC-component and a major component reminiscent of YST with characteristic Schiller-Duval bodies & typical glandular / papillary / reticular & solid growth patterns. Small foci of mature cartilage and areas of intestinal & hepatoid differentiation were observed.
Immunohistochemically, the neoplastic cells stained positive for aFP, SALL4, CD117, CKAE1-AE3 &also for the "epithelial" markers Ck7&EMA. CDX2 was positive in the intestinal-like areas and TTF-1 showed cytoplasmic positivity in hepatoid areas. S-100 & synaptophysin were positive in poorly-differentiated solid areas, indicative of focal neuroendocrine differentiation. CD30, PLAP were negative. Based on the histological & immunohistochemical results, we diagnosed a "somatically-derived- YST".
The patient was treated postoperatively with cisplatin-etoposide. She died of disease 5 months later.
Conclusion: Our case is in keeping with the theory that YSTs in postmenopausal women derive from pre-existing epithelial neoplasms through a process of neometaplasia / retrodifferentiation. This is evidenced by our patient's clinical history, histology & the immunophenotypic overlap in expression of both epithelial and germ-cell markers. We also highlighted the rapid & fatal progression of the disease upon development of the retrodifferentiated YST component that remained resistant to post-surgical chemotherapy. Therefore, we emphasize the highly malignant potential of this group of neoplasms and the need for more targeted therapies.

E-PS-09-035
Endometriosis of rectum mimicking rectal tumour: case report
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Background & objectives: Endometriosis of ovaries is a well-known entity. Rectal endometriosis, presenting with periodical rectal bleeding is uncommon and always mistaken for an underlying tumour. A case of rectal endometriosis, suspected clinically to be a GIST tumour of rectum is documented.
Methods: A 39-year-old female presented with intermittent rectal bleeding. CT scan revealed a rectal mass with constricted lumen. Resected rectum showed a stricture over the rectum, intramural haemorrhage with a tract measuring 10mm, located at site of stricture. Overlying mucosa showed a polypoidal elevation, measuring 15x15mm. The tract contained altered blood and chocolate coloured material. The adjacent mucosa was nil remarkable.
Results: H&E sections showed a well delineated haemorrhagic sinus tract comprising old haemorrhagic material, with no discernible lining epithelium. Scattered within the muscularis propria and subserosa, a few endometrial glands, occasionally showing cystic dilatation, surrounded by compact endometrial stroma was distinctly noted.
Submucosa showed oedematous thickening without presence of endometrial glands. Overlying mucosa showed a normal configuration and occasional foci of mild hyperaemic congestion.
Resected mesenteric vascular pedicle showed haemorrhagic congestion along with presence of endometrial glands and surrounding endometrial stroma.
No apparent tumour was present.
A diagnosis of rectal endometriosis was confirmed.
Conclusion: Rectal endometriosis can mimic malignancy and can present with on and off bleeding episodes. Long standing cases, as like in the present case can lead to stricture, fibrosis, and formation of sinus tract. This entity should always be included in persistent rectal bleeding, especially in young women. A gynaecological consultation and history of endometriosis is warranted.

E-PS-09-036
Bilateral high-grade serous carcinoma of the fallopian tube with ovarian and uterine involvement – case report
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Background & objectives: We report the case of a 63-year-old woman presenting with abdominal distention and pain, submitted for surgical treatment under clinical suspicion of uterine and left tubal tumour. Total hysterectomy with bilateral adnexectomy was performed.
Methods: On gross examination the uterine cavity was dilated, filled with serosal fluid and the isthmus was obstructed by a polypoid tumour of 2cm. The fallopian tubes were enlarged, up to 11cm with solid appearance and serosal effraction for the left salpinx and with multicystic and papillary tumour of maximum 3cm, for the right one. The ovaries measured up to 1.5/1/1cm.
Results: Histopathological examination revealed bilateral high-grade serous carcinoma of the salpinges, ovaries and uterine body with extensive lymphovascular invasion of both salpinges, ovaries, uterine body, parameters and pelvic omentum (pT2B). Additional small leiomyoma were identified in the uterine wall. The cervix was free of tumour. No lymph nodes were submitted for evaluation. Previous cervical cytology was negative for this patient.
Conclusion: Concomitant involvement of female genital tract organs by serous carcinoma is challenging. Dominant tubal mass with minimal ovarian and uterine disease favours primary salpingeal high-grade serous carcinoma. Finding associated intraepithelial neoplasia or carcinoma for origin placement is desirable but it is low to achieve, particularly in advanced disease. Blockage of fluid drainage from salpingeal tumours caused by proliferated implanted tumoral cells at the internal os is particular for this case.

E-PS-09-037
A case of primary signet ring cell cervical adenocarcinoma
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Background & objectives: Primary signet ring cell carcinoma of the cervix (PSRCCC) is a rare form of mucinous adenocarcinoma of the cervix. PSRCCC is mostly metastatic from gastric, breast, colonic or ovarian carcinomas. To date, there are 24 reported cases of PSRCCC.
Methods: A 45-year-old woman G1P1 was referred to our hospital in the setting of recurrent cervical cancer, status post robotic-assisted total laparoscopic hysterectomy and bilateral salpingo-oophorectomy (RATLH/BSO) in 2019, followed by pelvic radiation and chemotherapy. Recently, she noticed vaginal bleeding, treated by vaginal cauterization/ablation. Biopsy demonstrated recurrent/residual adenocarcinoma. In February 2021 patient underwent total pelvic exenteration.
Results: Preoperative PET CT (January 2021) revealed vaginal mass measuring 36 x 25 mm. Microscopic examination showed cells with eccentric hyperchromatic nuclei and large mucin filled cytoplasmic vacuoles growing in clusters (signet-ring cells). The neoplastic cells were positive for CK7, high molecular keratin (34BE12), monoclonal CEA, p16 (strong and diffuse), and CDX2 (focal weak). The tumour was negative for CK20, CK5/6, p40, synaptophysin and vimentin and showed no PD-L1 expression (CPS < 1). The tumour was positive for HPV 16 genotype. Pelvic wall margins,

distal rectal margin, and 8/21 lymph nodes were positive for carcinoma. The previous biopsies in March 2019 and December 2020 showed similar morphology, immunophenotype and genotype.
Conclusion: PSRCCC is a rare form of mucinous adenocarcinoma of the cervix. It is associated with recurrence and poor outcome. Awareness of this entity is important as it can simulate metastatic signet ring cell carcinoma. Clinical investigations, immunohistological and genetic studies are essential for differential diagnosis and proper classification. It is difficult to clarify the tumour biology of PSRCCC and determine the appropriate therapeutic strategies. In terms of surgery, RATLH is considered superior to abdominal radical hysterectomy.

E-PS-09-038
Expression of programmed death ligand -1 and mismatch repair status in endometrial carcinomas
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Background & objectives: Programmed death ligand -1 (PD-L1) is a co-regulatory molecule which suppresses the local immunity. Mismatch repair (MMR) deficiency has been implicated in the pathogenesis of many malignancies and has been reported to influence response to anti PD-L1 targeted therapy.
Methods: Expression of PD-L1 and MLH1, MSH2, MSH6 and PMS2 was assessed by immunohistochemistry (IHC) on 35 resected cases of endometrial carcinomas (ECs).
Results: Mismatch repair deficiency was noted in 10 cases (28.6% of the cases). PD-L1 expression was noted in 48.6% of the cases (17 cases) in tumour cells and in 65.7% of the cases (23 cases) in the tumour infiltrating lymphocytes (TILs). A statistically significant relation was noted between MMR deficiency and TILs, PD-L1 expression in tumour cells with TILs, and PD-L1 expression in tumour cells and extent of myometrial invasion. No significant relation was seen between MMR status and PD-L1 expression in tumour cells or in TILs.
Conclusion: Approximately one fourth to one third cases of EC showed MMR deficiency. Almost half of the ECs showed PD-L1 expression. However, more studies on a larger sample size are required to study relation between MMR status and PD-L1 expression in ECs.

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E-PS-09-039
Metastases of uterine leiomyosarcoma into the endometrium: a case report
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Background & objectives: The endometrium, as a labile cyclically renewing structure, is rarely considered as an object of tumour metastasis. But sometimes the correct assessment of metastatic lesions of the endometrium is important to determine the type and location of the primary tumour.
Methods: A 39-year-old female patient was presented with acyclic vaginal bleeding. For the past 2 months, she has been taking Gynestril 50 mg per day for leiomyomas. Clinical examination revealed solid tumour nodes in the uterus measuring 5.0, 2.0 and 2.0 cm in diameter. Curettage of the uterine cavity was performed. A total hysterectomy followed. All material samples were examined separately.
Results: On the background of simple glandular hyperplasia with weak signs of secretory transformation histological examination revealed small discrete foci, consisting of polymorphic atypical fusiform cells, with high mitotic index, chaotically arranged. Immunohistochemical staining them was positive for caldesmon, desmin, SMA, ER, PR. Metastases of leiomyosarcoma were suspected. In the tumour nodes, only conventional leiomyomas were found. But taking into account the metastases, repeated examination of serial sections of these benign neoplasms revealed an area with reliable signs of leiomyosarcoma in the largest of them. This was followed by additional examination to detect metastases in other organs and treatment.
Conclusion: This observation is an additional demonstration that morphological analysis of the endometrium can help in the correct assessment of myometrial tumours. We did not find descriptions of leiomyosarcoma metastases in the endometrium in the available literature. The influence of Gynestril on the ability of leomyosarcoma to metastasize remains controversial. For a year after the operation, the woman is under medical supervision and her condition remains stable.

E-PS-09-040
Primary inflammatory myofibroblastic tumour of the uterus: a case report
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Background & objectives: In the uterus, no more than 100 cases of an inflammatory myofibroblastic tumour have been described. The similarity of this rare tumour with other spindle cell neoplasms (leiomyoma, etc.), the uncertainty of its malignant potential causes increased attention to it.
Methods: A 45-year-old female patient was hospitalized with recently appeared acyclic vaginal bleeding. Clinical examination revealed a solid tumour node in the uterine body measuring 5.0 cm in diameter. A total hysterectomy with salpingo-oophorectomy followed. The surgical material was examined, and tissue samples were investigated histologically and immunohistochemically.
Results: Grossly, the well-circumscribed submucosal masses had a white, whorled appearance on cut sections. Microscopic evaluation of the node revealed an unusual structure. It was consisted of spindle cells arranged in whorled anastomosing fascicles embedded within a myxoid stroma and stained paler than leiomyocytes in the adjacent myometrium. Cells with indistinct cytoplasmic borders were often oriented at an angle around elongated thin-walled small vessels. In some areas, the tumour had a storiform pattern and small lymphoplasmacytic infiltrates.
Immunohistochemical staining was positive for Desmin, ALK, ER and negative for SMA, S100, CD10, CD34, EMA, DOG1, HMB45. The proliferative index determined by Ki-67 was up to 5%. Primary inflammatory myofibroblastic tumour was diagnosed.
Conclusion: We would like to report a case of benign inflammatory myofibroblastic tumour without infiltrative growth, cytological atypia, with low proliferative activity as a rare pathology of the uterus. Tumour features such as interlacing bundles of spindled cells, paler colour of cells when stained with hematoxylin and eosin in contrast to the surrounding muscle tissue, small, elongated vessels with fusiform cells around them and variable inflammatory infiltrations are important to suspect this neoplasm, and then to confirm by immunohistochemistry.

E-PS-09-041
Primary endometrial endometrioid adenocarcinoma with signet ring cells: a case report and review of the literature
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Background & objectives: Signet ring cells can be present in endometrial metastatic adenocarcinoma from an extra-genital primary tumour. However, some cases of primary endometrial adenocarcinoma with signet ring cells have been reported. This is among one of the first ten cases reported.
Methods: We report a case of a 76-year-old woman that presented to the emergency department with postmenopausal bleeding. A vaginal ultrasound revealed an endometrial thickness of 9,3mm. The patient underwent abdominal total hysterectomy with bilateral adnexectomy. An intraoperative histologic examination showed an adenocarcinoma

invading more than 50% of the myometrium thickness, therefore justifying peri-aortic and peri-iliac lymph node dissection.
Results: The 70g hysterectomy specimen consisted of uterus and cervix with attached bilateral adnexa. The anterior surface of the endometrium showed a protruding plaque-like neoplasia measuring 3cm in diameter that appeared to infiltrate the outer half of the myometrium wall. Endocervix contained a pedunculated polypoid mass of 1,5cm and was not involved by the tumour. The adnexa were unremarkable. Microscopic evaluation showed an endometrioid endometrial adenocarcinoma with signet ring cells and positive immunohistochemical staining for CK7, ER (focally), PAX-8 and vimentin. An Alcian Blue staining highlighted the mucin content in the signet ring cells. Metastasis were present in two of the twenty-five dissected lymph nodes. The endocervix showed an endocervical polyp.
Conclusion: The identification of signet ring cells in an endometrial adenocarcinoma requires ruling out the more probable hypothesis of a uterine cervix HPV-associated adenocarcinoma, signet ring cell type or of a metastatic tumour, mainly from the ovary, breast or the gastrointestinal tract. The histopathological morphology of endometrioid carcinoma and the immunohistochemical profile of the neoplasia along with the absence of a cervix or extra-genital neoplasia support our diagnosis of this rare entity not yet included in the WHO classification of tumours.

E-PS-09-042
SMARCA4-deficient undifferentiated uterine sarcoma: a case report and review of the literature
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Background & objectives: SMARCA4-deficient undifferentiated uterine sarcoma (SMARCA4-DUS)/malignant rhabdoid tumour of the uterus is a recently described entity that typically affects younger women and is morphologically and genetically related to small cell carcinoma of the ovary, hypercalcaemic type.
Methods: We herein present the case of a 62-year-old woman that presented to the emergency department with a two month history of postmenopausal vaginal bleeding. A transvaginal ultrasound showed multiple myomas and an endometrial thickness of 19 mm. The patient was submitted to an endometrial curettage.
Results: We received an endometrial curettage specimen weighing 4g which consisted of irregularly shaped fragments admixed with blood clots. Histologic examination showed a solid malignant neoplasm composed of diffuse sheets of atypical epithelioid cells with finely vacuolated cytoplasm, large, round and eccentric nucleus and prominent nucleolus with extensive necrosis and high mitotic index. Immunohistochemically, the neoplastic cells were positive for Vimentin, CD34, CD38, SMA (weak), EMA (weak and patchy) and CD138 (weak and patchy) and were negative for cytokeratins, neuroendocrine, melanocytic/nerve sheath, germinative, lymphoid, muscular, vascular and mesothelial markers. The nuclear expression of INI1 and mismatch-repair proteins was preserved, but there was a loss of expression of SMARCA4.
Conclusion: SMARCA4-DUS are typically aggressive tumours with lymphovascular invasion, lymph node metastasis and distant spread. Most of them contain rhabdoid/large cell morphology, but spindle cell and small cell morphology were also described. The inactivation of SMARCA4 is the main oncogenic driver event. The median survival of these patients has been reported to be seven months and they should receive genetic counselling to identify hereditary cancer risk in the family. Our patient passed away eight months after the initial diagnosis.

E-PS-09-043
Uterine arteriovenous malformation: report of a rare entity and review of the literature
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Background & objectives: Uterine arteriovenous malformation (UAVM) is a rare entity. It can be congenital or acquired. Congenital UAVM is developed from a defect during embryologic differentiation leading to abnormal vascular connections. Acquired UAVM occurs secondary to uterine trauma.
Methods: We report a case of UAVM occurring in a 35-year-old woman revealed by menorrhagia and severe anaemia.
Results: Tomography showed a uterine arteriovenous malformation in myometrium and endometrium tissues. A hysterectomy was proposed. The macroscopic study revealed a thick myometrium with a vascular lesion that measured 3 cm. Histologically, the lesion was composed of an admixture of malformed capillaries, arteries, and venules. These structures had variable sizes and were focally dilated and thrombosed. The endothelium lining these vessels showed no abnormalities. The patient was successfully treated with no complications.
Conclusion: UAVM can be asymptomatic or cause irregular uterine bleeding from abnormal connections between artery and vein. Uterine artery embolization is effective in treatment with rare complications. Hysterectomy is a definitive treatment resulting in the resolution of symptoms and allows histological examination. Pathologically, the lesion consists of a network of vessels of different proportions and sizes. The vessels have characteristics of both arteries and veins with prominent fibrous thickening with some elastin as a result of the high intraluminal blood pressure.

E-PS-09-044
Adult granulosa cell tumour of the ovary: a study of 10 cases
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Background & objectives: Adult granulosa cell tumour (AGCT) accounts for 5% of all ovarian cancers. Their histopathologic features are nonspecific. The objective of this study was to evaluate clinicopathological features and evolutionary characteristics of AGCT.
Methods: This is a retrospective study of ten cases of AGCT of the ovary, collected in the pathology department of the M. Slim Hospital over a period of 16 years (2002 to 2017). Evolutionary data were collected from medical records of the gynaecology department of the same hospital.
Results: The average age of our patients was 58 years. Pelvic ultrasound allowed objectifying the ovary tumours in 8 cases and CT scans in 2 cases. All tumours were unilateral and confined to the ovary, without rupture. Seven patients were treated with unilateral adnexectomy and 3 with a hysterectomy and bilateral adnexectomy. Eight tumours were encapsulated with a smooth lobulated surface. Seven tumours were solid and 3 solid and cystic. Tumour size varied between 8,5 and 25 cm. The histopathological study allowed us to make the diagnosis in 6 cases. In 4 cases, an immunohistochemistry study was made. No recurrence was noted with a median follow up of 5 years.
Conclusion: Although the course of AGCT of the ovary is often indolent, an unpredictable disease course with recurrence rates up to 50%. Then, an attentive examination of tumour specimens must be done, evaluating prognostic factors as the stage, nuclear atypia, and tumour size.

E-PS-09-045
Crohn's disease of the vulva: a case report
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Background & objectives: Various body sites can be affected by extraintestinal Crohn's disease (CD), but vulva involvement is a rare condition. Vulvar lesions are commonly "metastatic" in that they show typical CD granulomatous inflammation but are not adjacent to the GI involvement.

Methods: A 43-year-old woman with a past medical history of ankylosing spondylitis and left hemicolectomy due to large bowel CD presented to the gynaecology clinic with hardness and oedema in the right vulva. All haematological, biochemical and immunological findings were within normal range. Tumour markers, viral markers and Mantoux test were negative. A biopsy of the right labia majora was obtained.
Results: Histopathological examination revealed the presence of a chronic inflammation with formation of noncaseating granuloma and presence of multinucleated giant cells.
On the basis of the clinical, laboratory and endoscopic data, and the exclusion of other granulomatous and infectious diseases, the diagnosis of "metastatic" CD of the vulva was established.
Conclusion: Vulvar CD has been documented in females 8 to 74-year-old patients, mostly premenopausal. Most of the cases presented at least 6 months after the initiation of GI symptoms, but also on rare occasions during or even prior to the onset of inflammatory bowel disease.
Since the differential diagnosis of vulvar CD includes all infectious and non-infectious diseases with noncaseating granulomas, clinicopathological correlation including a detailed medical history and a physical examination is crucial for the confirmation of the diagnosis.

E-PS-09-046
Vulvar sarcomatoid squamous cell carcinoma: a rare variant in an unsual location
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Background & objectives: While sarcomatoid squamous cell carcinoma is a well-documented variant, most commonly of the larynx, only few cases have been reported in the lower female genital tract.
We present an unusual case of sarcomatoid squamous cell carcinoma of the vulva.
Methods: A 77-year-old patient presented to the gynaecology department with an aggravated vulvar mass arising from the right labia minora and eventually underwent a radical vulvectomy with bilateral inguinal lymph node dissection and bilateral pelvic lymph node sampling.
Gross pathology revealed an ulcerated exophytic tumour arising in the right labia minora measuring 4.5 cm.
Results: The histopathologic examination revealed a polypoid tumour with biphasic growth pattern. In the superficial portion, the tumour consisted of infiltrating keratinizing squamous cell carcinoma of intermediate differentiation, whereas in the deeper portion the neoplasm gradually transitioned into spindle cell sarcoma-like areas. Increased mitotic activity and atypical mitoses, were noted. The immunohistochemical analysis with the special markers CKAE1-AE3, CK5/6, EMA, p63, Vimentin, S100, Desmin, SMA and CD34, revealed the following immunophenotype of the malignant spindle cell population: CKAE1-AE3(+), p63(+), Vimentin(+), SMA(+) focally, CK5/6(-), EMA(-), Desmin(-), CD34(-), consistent with sarcomatoid differentiation. All lymph nodes were free of metastases.
The aforementioned features of the tumour established the diagnosis of sarcomatoid squamous cell carcinoma.
Conclusion: To date, only 19 cases of vulvar sarcomatoid squamous cell carcinoma have been reported.
Most recorded patients were elderly with a rapidly enlarging polypoid mass. The tumours are often locally advanced at the time of diagnosis with rapid recurrence, progression and usually associated with a poor outcome. However, a few patients with early-stage disease have a very long survival rate highlighting the importance of timely diagnosis and complete excision of the tumour.

E-PS-09-047
Intravascular leiomyomatosis of the uterus: presentation of two cases
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Background & objectives: Intravascular leiomyomatosis (IVL) is a rare tumour characterized by intravascular growth of benign smooth muscle cells with a propensity to extent to the pelvic/broad ligament veins, the inferior vena cava and even heart and pulmonary vessels.
Methods: Two patients, 48 and 49 years old, presented to the gynaecology clinic with menometrorrhagia. A gynaecological ultrasound revealed tumours with benign mesenchymal features measuring 9cm at the right parametrium and14cm at the uterus wall respectively. Patients underwent hysterectomy and bilateral salpingo-oophorectomy. The frozen section of the parametrium tumour was compatible with a benign mesenchymal tumour.
Results: On gross examination of the first patient's hysterectomy with bilateral salpingo-oophorectomy specimen, the parametrium tumour had a worm-like configuration, which implied an intravascular spread from the uterus wall vessels to the parametrium vessels. At the gross sectioning of the second hysterectomy specimen, we detected three solid, white, rubbery intramuscular nodules measuring up to 14cm. Microscopic and immunohistochemical examination confirmed on both occasions that the tumours were leiomyomas arising from a large vessel wall.
Conclusion: Even though IVL is a benign slow-growing tumour, it can have morbid results, when it extends into the heart causing mechanical obstruction. Thorough work-up can raise the suspicion of IVL prior to surgery, especially when located at the broad ligament or pelvic veins, in which case the treatment of choice is total hysterectomy rather than tumour enucleation. Initial pathological diagnosis of uterus/pelvic IVL is valuable for implementing appropriate follow-up and treatment as well as prospective diagnosis of recurrence.

E-PS-09-048
Mesonephric-like adenocarcinoma arising in presacral teratoma of a patient with Currarino syndrome
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Background & objectives: Currarino syndrome is a rare congenital syndrome characterised by anorectal malformations, sacral anomalies and presacral teratoma. Rarely, somatic type malignancies may arise in the latter. However, mesonephric-like adenocarcinoma has not been described yet in this context.
Methods: A 39-year-old woman with radiological findings corresponding to Currarino syndrome underwent surgery with removal of presacral teratoma at the age of 5 years. Thirty-four years later, the patient underwent spinal surgery due to worsening of local neurological symptomatology. A mass, 15 mm in diameter, was removed from the sacral area. A comprehensive assessment (immunohistochemistry, NGS) of the sample was performed.
Results: The archival slides of the original presacral mass showed structures of teratoma with multiple PAX8+/WT1+/GATA3-/SALL4- mesonephric structures including abortive glomeruli and tubules. The mass removed during the second surgery consisted of a well demarcated tubular and microfollicular carcinoma composed of uniform, slightly atypical cuboidal cells with high mitotic rate (19/10 HPFs). Tumour cells coexpressed cytokeratin 7, PAX8, GATA3 and TTF1, while other markers were negative (thyreoglobulin, SALL4, RCC, HNF1beta, cytokeratin 20, neuroendocrine markers). Next generation sequencing of the tumour did not detect any KRAS mutations. No other tumour was identified during subsequent PET-CT and detailed radiological work-up of the patient.

Conclusion: The morphology and immunoprofile of the tumour corresponded to mesonephric-like adenocarcinoma, a rare entity arising in female genital tract and associated with activating KRAS mutations. Although adenocarcinomas or neuroendocrine tumours have been seen in presacral teratoma in Currarino syndrome, mesonephric-like adenocarcinoma has not been described yet. The primary origin in teratoma is further supported by the presence of multiple mesonephric structures in the tissue of the original teratoma and the lack of any tumour elsewhere after the radiological work-up.

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E-PS-09-049

Desmoplastic small round cell tumour - case report

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Background & objectives: Desmoplastic small round cell tumours (DSCRCT) are highly aggressive mesenchymal neoplasms, frequently involving the serosal surfaces of the abdominal cavity in young males. They are unique among round blue cell tumours family in terms of histological, immunohistochemical, and karyotypic traits.
Methods: A 19-year-old female presented with ongoing abdominal pain and distension. CT scan showed bilateral expansive abdominal and pelvic solid masses replacing the ovaries and numerous disseminated peritoneal nodules of various dimensions. A smaller pararectal mass was also identified. Following excisional surgery, representative sections were submitted for histological examination on formalin-fixed paraffin-embedded tissue. Routine and immunohistochemical stains were performed.
Results: Histology revealed a proliferation of small, round to oval cells, some markedly atypic, arranged in a lobular or solid configuration, with a hypocellular fibrotic stromal reaction. Focal nuclear palisading, rosettes, cystic and microcystic spaces were present, as well as areas of central necrosis. Immunohistochemically the neoplastic cells expressed EMA, Synaptophysin, NST, CD56, Vimentin, and AE1/AE3 in isolated cells. Some areas of the tumour expressed Inhibin. The cells were negative for CK7, WT1, TTF1, and CDX2. Three potential differential diagnosis were taken into consideration: DSCRT, small cell carcinoma of the ovary, hypercalcaemic type, and adult-type granulosa cell tumour. Desmin stain showed a paranuclear-dot pattern of expression, suggestive for a DSRCT.
Conclusion: FISH analysis detected EWSR1 gene rearrangements in 74,3% of the cells leading to the final diagnostic of DSCRT. Variations in cell aspect, architectural patterns, stromal component, and immunoreactivity can occur, leading to diagnostic challenges. DSCRT must be differentiated from entities like PNET, rhabdomyosarcoma, neuroblastoma, neuroendocrine carcinoma, mesothelioma, lymphoma, etc. Medical professionals must be aware of these potential pitfalls and carefully integrate the clinical, imagining, and pathological information. Molecular biology studies are mandatory for an accurate diagnostic.

E-PS-09-050

Well-differentiated gastric-type adenocarcinoma of the endocervix - two mirror images of the same entity

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Background & objectives: Gastric type adenocarcinoma of the endocervix (GAS) is a rare, non-HPV-related neoplasm showing gastric differentiation and following an aggressive course. We report two cases of well-differentiated GAS emphasizing the main pathological features.
Methods: A 75-year-old female, who previously had a total hysterectomy with bilateral adnexectomy for a benign lesion. She presented 5 years later with vaginal bleeding. CT scan showed an iodophile mass replacing the vaginal cuff, invading the urinary bladder and the perirectal fat. The second case, a 60-year-old female with similar symptoms, came to our laboratory for a second opinion.
Results: Both patients underwent biopsy. We performed and analysed routine and immunohistochemical stains. The HE slides showed a glandular infiltrative proliferation, with variable-sized, slightly angulated tubular structures, encompassed by a desmoplastic stromal reaction. The neoplastic cells showed clear to pale eosinophilic cytoplasm, basal nuclei with few conspicuous eosinophilic nucleoli, and focal atypia. In one case the morphology resembled normal endocervical glands, without the usual bluish hint of the mucinous cytoplasm. Immunohistochemically, the neoplastic cells showed positivity for MUC5, CK7, CEA, PAX8. P53 showed a mutation-type pattern. ER, PR, p16, CK 20, CDX2 were negative. Based on morphological and immunohistochemical features, our diagnostic was well-differentiated gastric-type adenocarcinoma of the endocervix, HPV-independent.
Conclusion: GAS is characterized by deceptively bland features making the diagnostic very difficult on small samples like biopsies, conizations. The pathologist needs to be aware of this rare entity and differentiate it from both benign and malignant entities: LEGH, endocervicosis, endocervical tunnel clusters, usual type and clear cell adenocarcinoma, as well as metastases to the cervix. Scrutiny of subtle histologic findings, correlated with the immunoprofile and integrated into the clinical history of the patient, when available, lead to an accurate diagnostic.

E-PS-09-051

Mesonephric-like adenocarcinoma of the ovary; case report

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Background & objectives: Mesonephric-like adenocarcinoma (MLA) has been newly described in the ovary. There are 11 cases of MLA of the ovary in the literature. This is the first case of MLA coexistent with the endometrioid adenocarcinoma (EA) of the ovary.
Methods: A 63-year-old woman had postmenopausal bleeding. Magnetic resonance imaging revealed a malignant mass in the left ovary. It was sent for intraoperative consultation which was 12x11x8 cm in size, with a cystic, dirty yellow, haemorrhagic and solid areas on the cut surface. The result was reported as "primary malignant epithelial tumour of the ovary".
Results: Histologically the tumour had two epithelial components. The first component was EA. The other component consisted of tubulopapillary structures lined by cells with scanty clear cytoplasm, nuclear crowding, moderate atypia, vesicular nuclei, prominent nucleoli. Histochemically PAS and d-PAS did not show any cytoplasmic staining, but PAS (+) accumulation was detected in the lumen of the tubules. Tumour cells were diffuse positive with cytokeratin7, PAX8, GATA3, TTF1, CD10 (luminal) but focal positive with calretinin and p53. Napsin A was positive only in isolated cells. ER, PR, WT1 were negative. This component was diagnosed as MLA. As a result, our case was evaluated as MLA coexistent with EA.
Conclusion: Although MLA has different histomorphological appearances, it's a tumour that should be kept in mind in the differential diagnosis when evaluating a tumour with different histologic findings in the ovary.

E-PS-09-052

Combined adenocarcinoma and undifferentiated ca of the cervix and endometrium, posing differential diagnosis between dedifferentiated endometrial carcinoma and adenosquamous carcinoma with basaloid features

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Background & objectives: Dedifferentiated carcinoma is composed of an undifferentiated carcinoma and a juxta-opposed differentiated component. Squamous differentiation is a well-recognized feature of endometrial carcinomas. Basaloid squamous carcinoma is characterized by small basaloid cells with often abrupt transition to squamous epithelium and comedonecrosis.
Methods: A 76-year-old woman presented with postmenopausal bleeding of 3-months duration. D&C was diagnostic of endometrial endometrioid Ca, grade II. She underwent total abdominal hysterectomy with bilateral oophorectomy and pelvic lymphadenectomy.
Results: In the cervix there was a circumscribed tumour of 1,9X1,7cm, with central necrosis. The endometrial cavity was filled by a partly polypoid tumour of 3,7X2X3cm, without obvious connection with the cervical tumour. Both tumours were deeply invasive with similar histological features. Tumours were consisting of two juxta-opposed elements, one more superficial well differentiated adenocarcinoma and one more deeply-seated solid, extensively necrotic, monomorphic undifferentiated carcinoma with basaloid features and peripheral palisading. There was extensive squamous differentiation of the endometrial adenocarcinoma and abrupt interphase between the two elements in the endometrium, imparting a biphasic appearance. Scarce abrupt foci of mature squamous epithelium inside the undifferentiated component were recognized, as well as LVIs.
Conclusion: Morphologic and immunohistochemical findings were consistent with endometrial adenocarcinoma of dedifferentiated/undifferentiated type (diffuse positivity in KerAE1/AE3, EMA). Nevertheless, the morphological appearances of the undifferentiated component including the scarce abrupt microscopic foci of mature squamous epithelium, peripheral palisading and geographic necrosis were reminiscent of basaloid squamous cell carcinoma, therefore consistent with adenosquamous carcinoma of the basaloid type. There is no matching case report in the literature, nor included in the latest, 5th edition of the WHO Classification of Female Genital Tumours.

E-PS-09-053
Primary large cell neuroendocrine carcinoma of the endometrium. An exceedingly rare case
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Background & objectives: Large cell neuroendocrine carcinoma of the endometrium is very rare, often mistaken for poorly differentiated carcinoma. Diagnosis is based on the presence of polygonal cells with prominent nucleoli, a NE growth and the expression of at least one NE marker.
Methods: A 71-year-old woman was admitted in our hospital with the diagnosis of 'serous' carcinoma of the endometrium in D&C. MRI revealed an endometrial mass of approximately 3cm, with possible obstruction of the cervical os. There were no enlarged lymph nodes or elevated serous tumour markers. She underwent TAH @ BSO, omentectomy and pelvic and para-aortic lymph node dissection.
Results: The endometrial cavity was dilated and filled by a haemorrhagic, friable polypoid mass of 5,5X4X2cm, which was protruding through the cervical os. Histologically, the tumour was a high grade, undifferentiated carcinoma, consisting of large, dyscohesive, pleomorphic cells with moderate eosinophilic cytoplasm and enlarged markedly pleomorphic nuclei with prominent nucleoli. There were few rosette-like formations, brisk mitotic activity, extensive necrosis and haemorrhage. There was superficial infiltration of the myometrium and extension to the endocervix, LVIs and residual atrophic polyp. The tumour cells were diffusely positive in the three NE markers (synaptophysin, chromogranin, CD56). Omentum and lymph nodes were free of tumour. The final diagnosis was LCNEC of the endometrium, FIGO II.
Conclusion: LCNECs of the endometrium are rare, present mostly in the 6-7th decades, with vaginal bleeding, are bulky tumours and tumours confined to polyps and most likely under-reported. They are characterized by geographic necrosis and typically strong diffuse cytoplasmic positivity for NE markers. The later distinguish them from undifferentiated carcinomas that exhibit focal NE staining. Their recognition may have an impact on treatment of these patients. Although LCNEC has an aggressive behaviour, 28% of the patients survive at least 5 years.

E-PS-09-054
Bilateral carcinosarcomas of the ovary: report of two cases with review of the literature
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Background & objectives: Ovarian carcinosarcomas, also called malignant mixed Mullerian tumours (MMMT) are rare variant of ovarian tumours, with few cases reported in the literature. Our aim is to investigate clinicopathological aspects and prognosis of theses exceptional mixed Mullerian tumours.
Methods: We report two cases of bilateral ovarian carcinosarcoma, who were operated on at the department of Obstetrics and Gynaecology and diagnosed in the department of Pathology of Habib Bourguiba University hospital of Sfax, Tunisia. Clinical features, pathological aspects, treatment and outcome were herein described.
Results: The two female patients were aged respectively 45-year-old and 61-year-old. They both presented with clinically suspect pelvic masses. The first patient underwent hysterectomy, bilateral adnexectomy, and lymphadenectomy. The second patient had bilateral adnexectomy with omentectomy. Macroscopically, the patients had bilateral ovarian involvement with solido-cystic tumours. Histologically, the tumour's first patient was composed of an endometriod grade 1 adenocarcinoma (80%) admixed with an undifferentiated sarcoma with liposarcomatous features (20%). The tumour was classified pT1c2N0. The tumour's second patient was composed of a high-grade serous adenocarcinoma (70%) admixed with a stromal sarcoma with rhabdomyosarcoma features (30%). The tumour was classified pT3cNx. Eight months after the diagnosis the second patient died.
Conclusion: MMMT are very rare accounting for less than 1% of all ovarian tumours. They are very aggressive tumours that are usually diagnosed at an older age compared to women with epithelial ovarian cancer. These tumours contain both sarcomatous and carcinomatous components. The poor prognosis associated with this rare disease, emphasizes the need for collaborative prospective studies targeted to better understand the molecular changes of theses malignant tumours, and the need to design new therapeutic regimens to improve patient's survival.

E-PS-09-055
Microscopical and proteomics features of carcinosarcoma-minireview and report of nine cases
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Background & objectives: Uterine carcinosarcoma is an aggressive biphasic tumour, comprising less than 5% of gynaecological carcinomas, the mean age being 65. The aim of this study is to analyse the heterogeneity of the microscopic and proteomics characteristics of this special tumour category.
Methods: We report nine cases diagnosed in the last five years in our hospital. After the microscopical examination, the immunohistochemical tests were mandatory to support the diagnoses. All data were analysed depending on demographic characteristics, hormonal status

(premenopausal, postmenopausal), as well as diagnostic features, including a panel of seven immunohistochemical biomarkers (Ki-67, p53, SMA, Desmin, Vimentin, AE1/AE3, Cyclin D1).
Results: The age at diagnosis varied between 47 and 87 years old (mean 63 years old), most patients being postmenopausal. Regarding the epithelial component, 77.8% was represented by pure endometrioid carcinoma. In most cases, the presence only of the homologous component was observed, represented mainly by fibrosarcoma, while the heterologous component was given by chondrosarcoma in all cases. Most cases were diagnosed in stage II with lympho-vascular invasion in four cases and no perineural invasion. Immunohistochemical results proved the diagnoses for all cases and highlighted the mutational pattern of p53 biomarker (two cases with overexpression and null-type pattern of staining for the others).
Conclusion: Our study points out the decreasing age at the time of diagnosis and the uniqueness of this type of gynaecological tumour governed by the heterogeneity of morpho-pathological features. Their aggressivity is determined not only by the variety of epithelial and mesenchymal component, but also by the presence of genetic mutations. The p53 gene, which is involved in cell survival, is frequently mutated and is associated with a poor prognosis. A prompt and correct diagnosis is crucial for improving overall survival.

E-PS-09-056
Vulvar and cervical diseases in patient with immunosuppression - a case report
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Background & objectives: Human papillomavirus(HPV)infection of the genital tract causes changes in the vulva, vagina and cervix. Local and general immunity are the defense factors against HPV. People with weakened immune systems are at higher risk of the pathogenic effect of the virus.
Methods: A 25-year-old woman with systemic lupus erythematosus (SLE) treated by immunosuppressive therapy had control gynaecological examination and she need treatment of vulvar condyloma. Colposcopy showed suspected cervical dysplasia. Excision of vulvar lesions was performed.
Results: Pathohistological analysis of vulvar tissue showed more diagnosis on different tissue samples of vulvar region: condyloma accuminatum, moluscum contagiosum and vulvar intraepithelial neoplasia grade 3. The cervical lesions corresponded like High-grade SIL. P16 an Ki-67 was intensely positive in all layers of the cervical epithelium.
Conclusion: HPV infection also causes malignant transformations of vulvar and cervical tissue in cooperation with cofactors, such as decrease immunity, local and general. Local immunity also is decreased if there is a competitive non-HPV infection. If there are no adequate clinical controls, premalignant and malignant changes may be prevented. The gynaecological examination and HPV typing is required at regular intervals, especially in persons with immunosuppression.

E-PS-09-057
Mature ovarian teratoma degenerates into squamous cell carcinoma in a young woman: a case report and review of the literature
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Background & objectives: Ovarian teratoma is a pathology of the young women. Its malignant transformation is rare. The aim of this observation is to report a case of mature degenerated ovarian teratoma in a young woman and to study its clinicopathological features.
Methods: Reporting the case of a 34-years-old patient presented with a pelvic mass. On ultrasound examination, it was a mass of the right ovary with double cystic fatty components. The blood tumour markers (CEA and CA-125) were normal. The therapeutic decision was an anexectomy with pathological examination.
Results: At the gross examination, the cut surface of the tumour reveals a solido-cystic appearance, and cavities filled with fatty material. The solid part was firm whitish. Histologically, this latter was formed by invasive nests and sheets of squamous epithelial cells, which are in connection with superficial atypical squamous-type epithelium. There were conspicuous central keratinization. Tumour cells were large, with abundant eosinophilic cytoplasm, very atypical nuclei and numerous mitoses. The tumour infiltrated massively the adjacent ovarian stroma. There were no vascular or perineural invasion. The thin cystic wall was made of fatty and fibrous connective tissue with hair follicles, smooth muscle, and some thyroid vesicles. These teratomatous structures were mature.
Conclusion: Malignant transformation of mature ovarian teratoma is a rare event, occur especially in postmenopausal women. Its occurrence in young patient, as our case is exceptional. The most common tumour component to undergo malignant transformation is squamous epithelium (80% of cases), with formation of a typical squamous cell carcinoma. It can be suspected in view of the association of risk factors and radiological criteria, but the definitive diagnosis is based on the anatomopathological study.

E-PS-10 | Haematopathology E-Posters

E-PS-10-001
CD31 (PECAM1) immunohistochemical stain on megakaryocytes in myelodysplastic syndromes
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Background & objectives: Myelodysplastic syndromes (MDS) are clonal disorders of pluripotent stem cells characterized by ineffective haematopoiesis with dysplasia of myeloid lineage and cytopenia.
In this series we evaluated usefulness of CD31 immunoreactivity to detect dysmegakaryocyts and micromegakaryocyts in MDs.
Methods: we realized a morphological study based on comparison between histology (H&E) and immunohistochemistry (IHC) using specific primary antibody against CD31 (PECAM1)
Both techniques was performed on formalin-fixed paraffin embedded bone marrow (BM) core biopsy sections from 10 patients (8 with MDS and 2 with normal BM).
Number, morphology and distribution of megakaryocytes were reported for each biopsy.
Results: Normal BM biopsys: in sections stained with H&E, megakaryocytes are singly scattered or grouped in loose clusters, they are not found in a paratrabecular location.
On average 7cells / space have been detected.
In IHC, megakaryocytes CD31 positive are slightly more frequents (15 cells/ space).
BM with MDs: Megakaryocytes are usually increased in number and clusters in a paratrabecular location are seen, they are often dysplasic with hypolobated nuclei, micromegakaryocytes can be observed.
The mean number is (15cells/Space).
Immunohistochemical staining for CD31 detected dysplastic megakaryocytes of aberrant localization grouped in clusters and micromekaryocyts. (25 cells/space)
Conclusion: The diagnosis of myelodyplastic syndrome requires a set of clinical arguments and biological data.
Anti-CD31 in our own experience has proved to be highly sensitive for megakaryocytes normal and dysplastic.
CD31+ megakaryocytes in bone marrow (BM) are a nonspecific finding observed under normal conditions should not be interpreted as hyperplasia, however it may be useful as a diagnostic tool in the detection of dysplastic megakaryocytes particularly micromegakaryocytes that can be difficult to seen in usual coloration.

E-PS-10-002

Crystal-storing histiocytosis in bone marrow: a case report

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Background & objectives: Crystal-storing histiocytosis (CSH) is a rare lesion resulting from intra-lysosomal accumulation of immunoglobulins. It is associated with lymphoproliferative disorder, particularly myeloma. We present a case of CSH discovered in a bone marrow biopsy of a patient who had myeloma.
Methods: We report the case of a 57-year-old man who had myeloma and whose bone marrow biopsy was analysed in the department of pathology of the university hospital of Monastir.
Results: A 57-year-old man consulted for back pain since 6 months. Biological assessments showed an advanced renal failure with proteinuria and a hypogammaglobulinemia. Myeloma was diagnosed in this patient. The histological examination of BM biopsy showed sheets of polygonal cells with abundant eosinophilic cytoplasm. Needle-shaped, refractile crystals were confined to the cytoplasm. These cells were strongly positive for CD68 confirming the diagnosis of crystal storing histiocytosis.
Conclusion: CSH is a rare disorder characterized by accumulation of crystal-laden non neoplastic histiocytes. This phenomenon could easily be misdiagnosed as a granulomatous reaction or a storage disorder. Recognizing its clinicopathologic characteristics is essential, as its presence is highly associated with an underlying lymphoproliferative disorder and especially plasma cell myeloma.

E-PS-10-003

Kikuchi–Fujimoto disease: analysis of 6 cases and literature review

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Background & objectives: Kikuchi–Fujimoto Disease (KFD) or histiocytic necrotizing lymphadenitis is known to be a benign condition, which usually affects female. A viral aetiology is advanced but not yet proven. We assessed the clinical and pathological characteristics of KFD with literature review.
Methods: This study included 6 KFD collected over 12 years (2008-2019) in the department of pathology of the university hospital of Monastir. A Lymph node biopsy was performed in three cases and lymphadenectomy was performed in other cases.
Results: Patient's ages ranged from 11 to 34 years with an average age of 22 years. Most patients were female (sex ratio = 5/1). Cervical lymphadenomegaly (6 cases), fever (6 cases) and joint pain (4 cases) were the most frequent symptoms. Diagnosis is confirmed by lymph node histology which revealed paracortical foci of necrosis with abundant karyorrhectic debris and a histiocytic infiltrate associated with plasmacytoid monocytes and lymphocytes without neutrophils or follicular hyperplasia. In 2 cases Hodgkin's lymphoma has been suspected, absence of Reed–Sternberg cells and the lack of the characteristic background cell population had excluded this possibility.
Conclusion: KFD is an uncommon, self-limited, and perhaps underdiagnosed process with an excellent prognosis. Distinguishing KFD from malignant systemic disorders may even be difficult for pathologists using histological examination techniques and requires close cooperation between clinician and the pathologist. In order to minimize the risk of misdiagnosis and to minimize potentially harmful and unnecessary treatments.

E-PS-10-004

Incidental discovery of a Hodgkin's lymphoma: a report of 2 cases

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Background & objectives: It is common for lymph nodes to harbour unexpected findings of indolent and non-life-threatening pathologies revealed by pathological examination. However, aggressive malignancies such as Hodgkin's lymphoma might also be an incidental discovery especially when shadowed by another aggressive primary tumour.
Methods: Through reporting 2 cases of a concomitant primary malignancy and a Hodgkin lymphoma we aim to remind of the possibility of such incidental encounters where aggressive neoplasms are clinically occulted by other pathologies,
Results: Our first case is a 51-year-old female complaining of cervical lymph-node swelling. Imaging also found a nodule of the thyroid. A thyroidectomy and biopsies of the lymphadenopathies were performed. Histologically, the lymph-node biopsy revealed a sclerosing nodular classical Hodgkin's lymphoma CD30(+)/CD15(+). The thyroid harboured a classical variant of papillary carcinoma metastatic to 5/8 lymph-nodes, 3 of which were also infiltrated by the lymphoma. The 2nd case is a 42-year-old male suffering from an occupational-exposure-induced lichen. Examination revealed a suspicious fast-growing ulceration of the ankle and a 3cm inguinal adenopathy. Both were removed. Pathological examination found an infiltrating well-differentiated squamous-cell carcinoma. Unexpectedly the lymph-node was infiltrated by a classical Hodgkin's lymphoma CD30(+)/CD15(+).
Conclusion: While a metastatic lymph node is the most likely diagnosis when a primary tumour is already suspected, one should bear in mind that incidental discoveries of lymphomas are rare but documented occurrences increasing in incidence due to a better healthcare approach.

E-PS-10-005

Indeterminate cell histiocytosis: clinical significance of the histopathological diagnosis

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Background & objectives: Indeterminate cell histiocytosis/tumour (iCH) is an exceedingly rare and poorly understood disorder characterized by the infiltration of CD1a+, CD207/langerin- mononuclear cells in different tissues. We hereby describe 2 cases of iCH to emphasize the clinical heterogeneity of this condition.
Methods: Case 1: female new-born presenting with 8 macular-nodular erythematous itchy lesions, widespread on her skin diagnosed with iCH. 2 years later the lesions are slowly regressing. Case 2: 65 years old woman with a history of non-Hodgkin Lymphoma in remission. She presented with a generalized, necrotizing, and confluent papular cutaneous eruption diagnosed as iCH. She was lost at follow-up.
Results: In both patients, the cutaneous infiltrates showed a proliferation of CD1a+, CD207/langerin- mononuclear cells leading to a diagnosis of iCH. However, they were cytologically different. Case one presented with a monomorphous dermal proliferation of medium-sized cells with round nuclei and a moderate amount of eosinophilic cytoplasm with mild epidermotropism. On the other side, case 2 showed a highly pleomorphic infiltrate made of medium to large-sized cells with one to multiple, often atypical nuclei and abundant eosinophilic cytosol. In addition, these cells displayed epidermotropism with destruction of the epidermis above the lesion. Moreover, the Ki67 index was 15% in case 1 while it reached 50% in case 2.
Conclusion: After 30 years from its description, it is clear that iCH represents a clinically heterogeneous group of conditions ranging from self-healing to life-threatening conditions possibly associating with haematological and epithelial tumours, especially among adult patients. Although there are no defined prognostic criteria, cell atypia and proliferation may correlate

with the aggressiveness of the clinical course. As for other histiocytoses, a diagnosis of iCH must prompt a multidisciplinary evaluation of patients to rule out multisystem involvement and neoplastic associations.

E-PS-10-006

Mixed histiocytosis: a new intricate chapter in the universe of histiocytoses, the pathologist must know

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Background & objectives: Mixed histiocytosis is defined as the synchronous or metachronous occurrence of lesions with Langerhans-cell histiocytosis (LCH) and/or non-LCH (NLCH) morphological and immunohistochemical features in a single patient. This condition is the best representation of the plasticity of the neoplastic histiocyte.
Methods: We reviewed the worldwide literature on mixed histiocytosis, as well as our cases, providing evidence on the need to distinguish between the different clinical and histopathological forms of mixed LCH and NLCH. We hereby propose a clinical classification for mixed histiocytosis and present examples of each subcategory from our cohort of histiocytosis patients.
Results: Our analysis of the literature revealed three clinically, histopathologically, and prognostically distinctive groups of mixed histiocytosis patients. The larger group of patients included mostly young adults displaying a BRAF-mutated multisystem histiocytosis involving bone and skin with a clinical-pathological phenotype in-between LCH and Erdheim-Chester disease. 15% of them died of disease after a median of 7 months. The second group included chemotherapy-treated children with BRAF-mutated single-system bone LCH, relapsing with cutaneous juvenile xanthogranulomas. The third group included patients with nodal, cutaneous or bony single lesions, featuring both LCH and NLCH infiltrates, often represented by Distombes-Rosai-Dorfman disease. BRAF-mutated cases accounted for 33% of patients.
Conclusion: Mixed histiocytosis is a complex group of localized or multisystem conditions, whose diagnosis needs a multidisciplinary approach. Our proposed subclassification allow to distinguish patients with different clinical burdens, therapy needs, and prognosis and supports the concept of a pERK-driven clonal disorder with protean clinical manifestations. Moreover, from a pathogenetic point of view, mixed histiocytosis may be a source of information on the mechanisms of cell maturation, microenvironmental and immunological shifts, as well as of cellular response to therapy in histiocytosis.

E-PS-10-007

Reticulohistiocytosis-like cutaneous eruption in a patient with polymyalgia rheumatica, and JAK2-mutated chronic myelomonocytic leukaemia

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Background & objectives: Cutaneous eruptions featuring histiocytosis-like infiltrates may be observed in patients with chronic and acute myeloid neoplasms and may correlate with worse prognosis and reduced overall survival.
Methods: An 82 years-old Caucasian man was diagnosed with a JAK2-mutated chronic myelomonocytic leukaemia type-0, with low-risk CPSS and without need of any specific treatment. Two years after diagnosis he developed innumerable, confluent, erythematous-brownish macules over the trunk and proximal limbs.
Results: A skin biopsy revealed a dermal infiltrate of large epithelioid, scalloped and spindled-shaped, mostly mononucleated cells with prominent nucleoli and abundant granular, glassy eosinophilic cytoplasm. These cells were positive for CD163, CD68R, CD14, partially positive for CD33 and Cyclin-D1, negative for CD1a, CD34, CD117, MPO, TCL1, pan-B and pan-T cell markers and had a low proliferative index (<2%). The results were consistent with a non-Langerhans cell histiocytosis, which, despite the unusual morphology, could be included in the spectrum of reticulohistiocytosis.
Conclusion: Reticulohistiocytosis is a heterogeneous group of histiocytoses characterized by large CD163+, CD1a- cells with abundant glassy eosinophilic cytoplasm, accumulating in the skin and other organs. A subset of cases specifically associates with myeloid neoplasms, and a clonal relationship was demonstrated once. Nevertheless, reticulohistiocytosis is morphologically and phenotypically different from other cutaneous manifestations in course of haematological neoplasms (e.g. leukaemia cutis, Sweet syndrome). Despite the limited number of patients reported, it should be considered in the differential diagnosis of these patients.

E-PS-10-008

Plasmacytoid dendritic cell blast neoplasm: report of two clinical cases

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Background & objectives: Blactic plasmacytoid dendritic cell neoplasm (BPDCN) is an aggressive haematological neoplasm characterized by a diffuse monomorphous blast cell infiltrate, classified by the WHO as a distinct entity. Our purpose is to describe the clinic-pathological features found in two clinical cases.
Methods: Dermatological and haematological data were extracted from computerized medical records of two patients diagnosed between January 2018 and December 2020. In addition, the histological sections of both hematoxylin-eosin and immunohistochemistry of the corresponding biopsies were examined.
Results: The two cases were males aged 84 and 77 respectively. Both had scattered indurated skin lesions (head, trunk, extremities), with no other accompanying symptoms. In addition to the skin biopsy, medulogram, flow cytometry and bone marrow biopsy were performed. The skin punch showed a diffuse dermal infiltrate of medium-sized plasmacytoid cells. Cell proliferation in skin, bone marrow and cytometry expressed CD123, CD43, CD4 and CD56 among other markers. Cytogenetic analysis identified alterations in chromosomes 8 and 12, and c-MYC rearrangement by FISH. These findings led to a definitive diagnosis of BPDCN. The first patient died 8 months after diagnosis. The second patient is currently undergoing chemotherapy.
Conclusion: BPDCN seems to show a higher incidence in males from the 6th decade of life onwards. The appearance of scattered indurated skin nodules is the clinical finding that, together with the biopsy of these lesions, helps to make a diagnosis. Bone marrow involvement is observed as the disease progresses. Positivity of neoplastic cells for CD123, CD4 and CD56, and rearrangement of the c-MYC gene (8q24) are characteristic.

E-PS-10-009

MYD88 mutation in amyloid light-chain amyloidosis without B cell neoplasm

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Background & objectives: Amyloid light-chain (AL) amyloidosis is associated to lymphoproliferative processes with plasmacytic differentiation. However, in many patients it is possible to deepen into the nature of

the underlying process through a careful analysis of the associated lymphoid infiltrate.
Methods: We report a case of a male patient with multiple episodes of severe pericardial effusions and an M component (IgM) in the proteinogram, who underwent a pericardial biopsy.
Results: The histological study showed extensive pericardial amyloid deposits positive for light kappa chains by direct immunofluorescence techniques. Protein AA and Transthyretin were negative. Focally, discrete lymphoid infiltrates of irregular distribution were observed with no tumour mass. Restriction for light kappa chains was demonstrated by in situ hybridization. MYD88 showed c.794T>C:p.L265P mutation. A bone marrow biopsy was performed, which did not show significant microscopic findings. However, its molecular study found the same MYD88 mutation.
The case was diagnosed as AL amyloidosis associated with monoclonal gammopathy of uncertain significance without evidence of lymphoma.
Conclusion: This MYD88 mutation is associated with several B neoplasms. It is detectable in more than 90% of patients with Waldenström macroglobulinemia and lymphoplasmacytic lymphoma.
The immunohistochemical and molecular characterization of the lymphoid tissue associated with primary amyloidosis allows a more complete typing of the underlying cellular process that can be useful in the follow-up of the patients.

E-PS-10-010
Monotypic versus monoclonal: atypical marginal zone hyperplasia – a case report of a rare reactive condition
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Background & objectives: Atypical marginal zone hyperplasia (AMZH) of mucosa associated lymphoid tissue is a reactive condition occurring in childhood that histologically and immunophenotypically resembles extra nodal marginal zone lymphoma of mucosa-associated lymphoid tissue but lacks clonal immunoglobulin gene rearrangements.
Methods: We present a case of an 11-year-old female with no previous history of disease, with progressive enlargement of two cervical lymph nodes, with no other symptoms. A fine needle aspiration detected a lambda monotypic B-cell population by flow cytometry. One of the nodes was excised for morphologic, molecular and genetic studies.
Results: The lymph node was fragmented and showed partial alteration of the architecture; residual follicles (RF) with hyperplastic germinal centres and some follicles containing "moth-eaten" germinal centres (MEGC) and expanded marginal zones (MZ)The expanded MZ contained predominantly small, medium and scattered large B-cells expressing CD20, BCL6 (weak), IgM and negative for CD10, IgD, BCL2, MUM1, CD3 CD5 and EBER The RF and MEGC contained BCL2-CD10+, BCL6+, large B-cells. Both the MZ and RF centres showed marked lambda predominance. Clonal rearrangements for the immunoglobulin genes IgH and IgK were not detected.
These appearances are consistent with a polyclonal but monotypic lambda proliferation, consistent with atypical follicular and marginal zone hyperplasia.
Conclusion: This is a rare entity and most published cases are extra nodal. In the lymph node, similarity with paediatric nodal marginal zone lymphoma is a potential source of error. Understanding the difference between monotypic and monoclonal is crucial in the differential diagnosis.
There is an association in the literature between Haemophilus influenza and AMZH in nodes of head and neck region, but this correlation was not possible to establish in our case.

E-PS-10-011
Morphological and immunohistochemical features of a case of multifocal histiocytic sarcoma
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Background & objectives: Histiocytic sarcoma(HS) is an extremely rare malignant neoplasm of mature, non-Langerhans histiocytes. HS is sporadic or clonally related to a separate hematologic malignancy, appears mostly in extranodal locations(skin, soft tissue, lung, central nervous system) and can be unifocal or multifocal.
Methods: A 68-year-old female with CT-scan showing a 5cm tumour next to the upper pole of the left kidney; a 4cm mass on the left parietal pleura with osteolysis of the 7th rib; osteolytic lesions of left ilium, left acetabulum and vertebral body(L4-L5) with invasion in the soft tissue and left posterior root of the spinal cord(L4-L5); with lumbar adenopathy.
Results: A resection of the mass from the vertebral body(L4-L5) was performed for decompression and diagnostic purpose. Tissue was fixed in formalin, processed, embedded in paraffin, examined on H&E and ancillary immunohistochemical stains.
Microscopic examination revealed an infiltrative malignant proliferation of medium-large cells, with marked cytologic and nuclear pleomorphism, large hyperchromatic nuclei, with prominent nucleoli, numerous multinucleated giant cells, with focal spindle cell morphology, brisk mitotic activity and extensive necrosis. Immunohistochemical stains showed strongly and diffusely positive vimentin, CD4, CD14, CD45, CD68 and CD163, focal and weak staining for S100 and negative CD3, CD20, CD21, CD23, CD30, CD38, Langerin, AE1/AE3, MelanA, synaptophysin, GATA3, inhibin, calretinin, with a Ki67 index of 40%.
Conclusion: HS is a rare histiocytic neoplasm with a vast differential diagnosis including other histiocytic/dendritic cell neoplasms, myeloid neoplasms, lymphomas, melanoma, and carcinoma. Morphological features together with an extensive panel of immunohistochemical markers are the key for accurate classification.

E-PS-10-012
A clinicopathological analysis and diagnostic approach of a rare case of primary non-Hodgkin epitheliotropic T-cell lymphoma in the small intestine
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Background & objectives: Monomorphic epitheliotropic intestinal T-cell lymphoma, formerly known as enteropathy-associated T-cell lymphoma, is a rare, aggressively peripheral extranodal T-cell lymphoma, infrequent in native European and Caucasian populations. The study presents the clinicopathological features and diagnostic approach of this rare entity of lymphoma.
Methods: A 69-year-old male patient presenting with an abdominal mass, intestinal transit disorders and weight loss. The abdominal computed tomography scan revealed features suggestive of malignancy. Following the clinical and imagistic investigations, surgical resection of small intestine with other areas of involvement have been performed. Further to the histopathological examination, an immunohistochemical testing was mandatory, by using the monoclonal antibodies.
Results: Histopathologic evaluation of the tumour revealed a proliferation of medium- to high-sized monomorphic lymphocytes, with vesicular nuclei, proeminent nucleoli and a moderate amount of clear to pale eosinophilic cytoplasm, with an association of infrequent Reed-Sternberg-like cells. Immunohistochemical assessment of the aforementioned tumour using CD3, CD8, CD5, CD20 and CD30 confirmed the T cell proliferation line and the monomorphic epitheliotropic intestinal T-cell lymphoma diagnosis.
Conclusion: In the present case, a final diagnosis was not possible without the aid of immunohistochemical tests and due to its poor prognosis, it needs to be distinguished from inflammatory bowel diseases and less aggressive T-cell lymphomas. Otherwise, early diagnosis of

monomorphic epitheliotropic intestinal T-cell lymphoma diagnosis is essential for timely management.

E-PS-10-013

Even lymphomas don't always read the Blue Book

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Background & objectives: A peculiar case of an 84-year-old woman with sudden acute abdominal pain and no medical records. The clinical suspect was an acute abdomen and the CT scan showed a possible perforation of the intestine; no specific cause was identified.
Methods: All surgical specimens underwent formalin-fixation, paraffin-embedding and hematoxylin-eosin (H&E) staining. Immunohistochemical stains were routinely performed in an automatic stainer, with the following primary antibodies: CD20, CD3, CD5, CD23, Bcl2, Bcl6, CyclinD1, Mib1 (ki-67), CD4, CD8, CD56, TIA1 and EBER.
Results: Urgent small bowel resection was required. Macroscopically, a tear was observed in the intestinal wall, which was slightly thickened, and multiple nodules were present in the perivisceral tissue. Microscopically, the intestinal wall was effaced by a monotonous diffuse proliferation of small to medium size lymphoid cells with round regular nuclei, finely dispersed chromatin, inconspicuous nucleoli and a rim of pale perinuclear cytoplasm. The adjoining mucosa showed normal villous architecture; however, there was a remarkable increase of intraepithelial lymphocytes. Immunohistochemistry revealed the following profile: CD20-, CD3+, CD5-, CD23-, CD4-, CD8+, CD56+, TIA1+. Ki67 labelling index was 65-70%. EBER was negative.
The diagnosis of monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL) was formulated.
Conclusion: Intestinal B-cell lymphomas are more frequent compared to T-cell, of which the WHO lists 4 entities (EATL, T/NK nasal type, PTCL-NOS, and MEITL). Although EATL was the first option, due to its frequency in Europe and epidemiological features of our patient (sex and age), the absence of celiac disease and the histological findings were against this. This case is peculiar, being exceedingly rare at our latitude, and we want to share it to encourage our colleagues to expect the unexpected.

E-PS-10-014

Composite lymphoma in the orbit: a case report

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Background & objectives: Two distinct simultaneous lymphomas, in the same anatomical location are rare, defined as a composite lymphoma. We report a case of a 83-year-old male presenting with exophthalmos and diminished vision for one year, without relevant oncological history nor immunosuppression.
Methods: An orbital mass biopsy identified two different lymphomas. Flow cytometry, immunohistochemistry and molecular genetics were needed to distinguish them. Peripheral blood analysis had normal CBC, LDH and Albumin, slightly elevated ß2-microglobulin (3,75 mg/L); elevated Kappa (28.7 mg/L), normal Lambda (22.1 mg/L) with a normal ratio Kappa/Lambda (1/3) and an elevated IgM (839 mg/dL) and normal IgG, IgA.
Results: On histological examination, a CD5+ small B cell lymphoma was diagnosed as a MALT lymphoma and at the periphery, a monotypic plasma cell proliferation was identified. The MALT Lymphoma was IgM, kappa and the plasma cell component was IgA, lambda by IHC.
Ig gene rearrangement analysis of the whole sample is in accordance with two different neoplastic populations: 1) IGHV3-74/IGHD1-26/IGHJ4 (productive) + IGHD-IGHJ and IGKV2-28/IGKJ2 (productive) + IGKV2-29/KDE; 2) IGHV4-59/IGHD7-27/IGHJ4 (productive) + IGHD-IGHJ and IGKV2-29/IGKJ5 (unproductive) + Intron-KDE. The patient started a treatment using CP-R [cyclophosphamide + prednisone + rituximab] with clinical improvement of the proptosis but died before ending the chemotherapy.
Conclusion: Although plasma cell differentiation is common in MALT lymphoma, the same light chain is shared by all cells. Identifying two different monotypic light chains in separate areas suggests a composite lymphoma, here confirmed by the presence of two distinct receptor gene rearrangement patterns. The diagnosis of a second clone as Lymphoplasmocytic Lymphoma, usually associated with Waldström Macroglobulinemia, might lead to a different therapy, depending on the staging of the patient.

E-PS-10-015

Haematopoiesis extramedullary: uncommon case of giant adrenal incidentaloma mimicking tumour mass

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Background & objectives: Haematopoiesis extramedullary is a proliferation of the hematopoietic cells outside of the bone marrow , in the adrenal is rare with fewer than 10 cases reported, and is finding as well as giant mass mimicking tumour lesion is extremely rare.
Methods: We report the case of a 38-year-old woman who had been known to have β-thalassemia and presented to the hospital for the biological evaluation, and abdominal pain. She benefited from an X-ray showed a giant right adrenal mass, solid, with high uptake, with contrast enhancement and splenomegaly. Consequently, the differential diagnosis included a malignant adrenal tumour. Therefore, the patient underwent right adrenalectomy.
Results: Gross examination revealed a well-circumscribed brownish mass measuring 13 cm in maximum dimension, with a haemorrhagic, reddish brown cut surface. A rim of normal looking adrenal tissue was noted at the periphery. Histology revealed the mass to be composed of mature hemopoietic elements, with a predominance of erythroid series. A few megakaryocytes were also noted.
Conclusion: The diagnosis of extramedullary haematopoiesis must be considered in any patient with hematologic disorders and thoracic or abdominal mass. An unnecessary procedure could be avoided.

E-PS-10-016

An unusual presentation of blastic plasmacytoid dendritic cell neoplasm with bone marrow and skin involvement

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Background & objectives: Blastic plasmacytoid dendritic cell neoplasm comprises <1% of haematologic malignancies, characterized by an aggressive clonal proliferation of immature plasmacytoid dendritic cells (PDC). Most patients, usually elderly men, present with cutaneous lesions, with subsequent extension to bone marrow and peripheral blood.
Methods: A 70-year-old man was admitted for skin lesions increasing in number and dimension over the last 6 months. Clinical examination revealed multiple violaceous, non-erythematous maculopapular cutaneous lesions located on the trunk. The complete blood count indicated mild leukopenia (3.87×10^9/L) and thrombocytopenia (131×10^9/L). Abdominal sonography revealed mild hepatosplenomegaly. Skin and bone marrow biopsies were also performed.
Results: Peripheral blood smears examination showed 20% polymorphous population of intermediate-sized lymphoid cells, with PDC immunophenotype on flow-cytometry (weak CD45, CD56+, CD123+, HLA− DR+, CD4+) and lack of expression of lymphoid and myeloid markers. The skin biopsy disclosed a diffuse non-epidermotropic proliferation of monomorphous medium-sized neoplastic cells with immature morphology (irregular nuclear contour, multiple inconspicuous nucleoli and scant cytoplasm). BMB showed a 17-18% interstitial infiltration of neoplastic cells featuring the same histopathological aspects as described in the

skin. IHC performed on both skin and bone marrow biopsies also demonstrated a PDC profile of neoplastic cells (CD56+, CD123+, TdT+, CD68+).
Conclusion: As an uncommon condition, the diagnosis of BPDCN is challenging and requires a step-by-step approach using a large panel of antibodies, since neoplastic cells can resemble lymphoblasts or small immunoblasts. Despite the apparently indolent clinical presentation, the course is aggressive. Disseminated lesions, as well as bone marrow extension, usually develop progressively towards the terminal stage of the disease. However, in our case, the patient presented with cutaneous lesions and simultaneous involvement of bone marrow and peripheral blood.

E-PS-10-017
In situ follicular neoplasia arising in a cervical branchial cleft cyst – morphological diagnosis with serious implications
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Background & objectives: A branchial cleft cyst is a benign lesion commonly presents as a unilateral neck swelling. Detection of incidental malignancy is very uncommon with malignant lymphoma being an exceedingly rare finding.
Methods: The patient was evaluated using preoperative ultrasound, CT and MRI neck scans and fine-needle aspiration cytology (FNAC). The excision biopsy was submitted for histological examination followed by immunohistochemistry (CD20, CD3, CD10, CD21, CD23, bcl-2, bcl-6, and Ki67) according to the standard protocols.
Results: A 53-year-old man with unremarkable past medical history presented with a painful right neck lump. CT-scan revealed a 35mm right cervical cyst with no cervical, axillary, mediastinal, or hilar lymphadenopathy. The cyst and an adjacent lymph node were excised. Histologically, the cyst was lined by stratified keratinising squamous epithelium encased by dense lymphoid tissue with prominent secondary follicles. The lymph node architecture was preserved with follicular hyperplasia. Some germinal centres in the cyst wall and the lymph node were effaced by tightly packed CD20+/CD10+/bcl-2+ centrocytes. These findings were reported as synchronous nodal and extranodal in situ follicular neoplasia (ISFN) affecting a branchial cleft cyst and locoregional lymph node.
Conclusion: ISFN is a WHO entity. It can be suspected on morphological assessment and confirmed by immunohistochemistry both in nodal and extra-nodal sites.
ISFN should prompt studies to exclude overt lymphoma in other sites, as reportedly, half of ISFN cases are associated with concurrent or previous overt follicular lymphoma. Only a small number of cases progress to overt lymphoma.
We are not aware of previous reports on the involvement of branchial cleft cyst lymphoid tissue by ISFN.

E-PS-10-018
Bone marrow involvement by primary oxalosis: a rare case report
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Background & objectives: Primary hyperoxaluria is a rare genetic abnormality, characterized by excess of endogenous oxalate production with a deposition of calcium oxalate crystals in several tissues mainly in kidneys, myocardium, spleen, soft tissues. However, bone marrow localization is very rarely observed.
Methods: We report the case of a 37-years-old man with chronic renal failure on haemodialysis since 2017. His medical history revealed primary hyperoxaluria. Since the patient was a candidate for combined hepato renal transplant, an osteomedullary biopsy was performed to evaluate the extension of oxalate deposits.
Results: Histological examination showed the presence of extensive calcium oxalate crystals deposits surrounded by foreign body giant cell reaction. Stromal fibrosis, poor residual haematopoiesis and thickened bony traeculae were also observed. The polarized light revealed intense pale green birefringence of these deposits. Bone marrow involvement was then confirmed.
Conclusion: Primary hyperoxaluria is a congenital metabolic abnormality caused by mutation of the AGXT gene (alanine glyoxylate aminotransferase). The clinical symptomatology is diverse, secondary to calcium oxalate deposits in the various tissues. The bone marrow localization is very rare and the diagnosis relies on the presence of specific oxalate needle-like crystals on histological study. Moreover, the diagnosis of this disease is often late, which makes its prognosis mediocre and difficult to manage.

E-PS-10-019
A strange renal colic: stones with surprise
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Background & objectives: Erdheim-Chester disease (ECD) is a rare clonal non-Langerhans histiocytosis, characterized by heterogeneous clinical presentations and molecular features. Therefore, diagnosis and appropriate treatment are often delayed. Retroperitoneum and bone metaphysis e.g. are critical sites that can harbour numerous diseases including ECD.
Methods: A 48-years old man with a history of renal colic episodes, complained 2-week-long colic lower back pain. Uro-TC demonstrated ureteral stones and a retroperitoneal mass causing bilateral hydronephrosis, necessitating JJ-catheterization. Biopsy revealed a foamy and multinucleated histiocytes proliferation CD163+, CD68R/PGM1+, CD14+, Factor XIII+/-, Cyclin-D1-/+, S100p-, CD1a-. We hypothesized ECD, indicating the necessity of further diagnostic exams, for confirmation and management.
Results: CT and PET total body revealed mammary chain, interaortocaval and iliac lymphadenopathies, a pulmonary nodule and a mass between pericardium and ascending aorta, but no bone lesions. Brain RM was unremarkable and no signs of diabetes insipidus were observed. Complete blood count, VES, CRP and ACE were normal. Tumoral markers were negative. Sequencing analysis for BRAFV600E and NRAS mutation were negative, while ac.35G>A (p.Gly12Asp) mutation on KRAS exon 2 was found. Following ECD diagnosis confirmation, the patient started INFalfa2b therapy.
Conclusion: ECD is rare, heterogeneous and insidious. Molecular advances and new drug development significantly decreased morbidity. However, diagnostic delay is still frequent, especially in absence of typical presentation, as many different neoplastic disorders such as lymphomas, sarcomas and non-neoplastic conditions, (e.g. retroperitoneal fibrosis, IgG4-related disease) should be ruled out. ECD diagnosis and management require a multidisciplinary approach and histopathological and molecular analysis are an essential part of the diagnostic process and a therapeutic guide.

E-PS-10-020
Plasma cell myeloma, JAK2 positive myeloproliferative neoplasm and NK/T cell lymphoma nasal type: a peculiar case of haematological comorbidities
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Background & objectives: Coexistence of myeloid and lymphoid neoplasm in the same patient is rare, often following cytoreductive therapy; this combination might suggest the existence of a common precursor.
Methods: A 72-years male patient affected by JAK2+ myeloproliferative neoplasm (MPN) treated with hydroxyurea for thrombocytosis and IgG/K multiple myeloma (MM), complained nasal obstruction. Septum biopsy showed an infiltrate of medium-sized cells with convoluted nuclei, and a T-cell/NK phenotype: CD2+, CD3+ (cytoplasmic), CD56+, Granzyme+ and Perforin+, EBER+. An extranodal NK/T cell lymphoma nasal-type was diagnosed.
Results: At the best of our knowledge, association between MPN, MM and NK/T lymphomas has not been reported previously in literature. Both myeloid and lymphoid malignancies originate from hematopoietic cells, in whom one or more genetic events, some of which known, cause a deregulated proliferation. It has also been reported that acute leukaemias, displaying a mixed phenotype, can undergo a lineage switch, sporadically. It might be postulated that a common stem cell could be reprogrammed from lymphoid to myeloid lineage or vice versa, in a setting including immune defects and/or chronic infections.
Conclusion: Comparing known mutations in lymphomas and myeloproliferative diseases, we hypothesized a common event involving JAK-STAT pathway. Intrinsic characteristics, such as immune status, combined with external agents (e.g. EBV), might have created a favourable setting. Whole Exome and Transcriptomic studies on similar cases of concomitant hematologic neoplasms could be useful to better clarify the biological relationships between the various lineage components, bringing to light putative common mutagenic events that might link these different cellular lines.

E-PS-10-021
Bone marrow histopathological features in HHV8+ HIV- Multicentric Castleman disease: a case report
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Background & objectives: Multicentric Castleman disease (MCD) is a lymphoproliferative disorder classified according to its etiological drivers. Bone marrow (BM) involvement is rare and the limited literature data mostly focused on HHV8+HIV+MCD cases. We describe the BM findings in an HHV8+HIV- MCD patient.
Methods: A 75-year-old man presented with multiple lymph nodes enlargement, and signs of multi-organ failure. Laboratory analysis revealed pancytopenia and elevated C-reactive protein. The IL6 level was 67,76 pg/ml. Serologic test for HHV8 was positive whereas HIV test was negative. Clinically a lymphoproliferative disorder was suspected, and patient underwent lymphadenectomy and BM biopsies.
Results: The lymph node histology revealed many regressed germinal centres with scattered HHV8/LANA1 positive cells, mostly in the perifollicular area, as well as numerous interfollicular polytypic plasma cells. A diagnosis of HHV8+ MCD with mixed histopathology was made. The BM histology showed a slight hypercellularity, an interstitial and perivascular infiltrate of polytypic plasma cells (30% of BM cellularity), and small lymphocytes (10% of BM cellularity), either T (CD3+) or B (CD20+); HHV8/LANA1 positivity was confined mostly on B lymphocytes. The CD68R immunostaining evidentiated numerous positive histiocytes with hemophagocytosis. On such findings, a diagnosis of BM involvement by MCD was made. The patient died of disease shortly afterwards.
Conclusion: BM changes in MCD HHV8+/HIV+ patients predominantly consist of reactive plasmacytosis ascribed to increased IL6 levels coupled with the presence of lymphoid follicles exhibiting the typical changes of Castleman disease; in addition, scattered HHV8/LANA1+ cells and increased amount of histiocytes with sporadic hemophagocytosis can be found. BM histologic features in our case of MCD HHV8+ but HIV- overlapped with the reported one in similar but HIV positive cases, thus suggesting that these changes might develop independently from the HIV-status.

E-PS-10-022
Marginal zone lymphoma in a one-year-old child and B-cell acute lymphoblastic leukaemia following lymphoma remission: Louis-Bar syndrome presented with lymphoma and leukaemia. A rare case report
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Background & objectives: Marginal zone lymphomas are present rarely in children and young adults as either primary nodal or extranodal disease.
Methods: A 1-year -old girl patient without a known disease presented with neck swelling and fever. She received antibiotic treatment one week but were not decrease of symptoms. On physical examination, multiple lymph nodes were palpated in both parotid and cervical chains. On abdominal examination revealed hepatomegaly. Excisional biopsy was performed from the masses in the right submandibular region and sent to pathology.
Results: Microscopically, lymphoid infiltration of medium sized cells which partly eliminated the structure of the salivary gland was observed. Immunohistochemically, lymphoid cells were stained diffuse positive with CD20 and pax-5. Diffuse expression with cd43 and bcl-2 was seen in these cells. Germinal centre markers such as CD10,Bcl-6 and MUM-1 were negative. Ki67 proliferation index was 40%. With these findings, the case was evaluated as Marginal zone lymphoma(MZL). Chemotherapy was applied for MZL. Approximately 6 months after the patient was in remission, hepatosplenomegaly and thrombocytopenia were detected during the routine control. A diagnosis of acute lymphoblastic leukaemia was made by examining the peripheral smear, bone marrow aspiration smear and bone marrow biopsy. Ataxia telangiectasia gene mutation was found in the genetic testing of the patient.
Conclusion: Here, we aimed to present a one-year-old patient with ataxia telangiectasia gene mutation who presented with the diagnosis of marginal zone lymphoma and then acute lymphoblastic leukaemia in the light of the literature.

E-PS-10-023
Angioimmunoblastic T-cell lymphoma: the many-faced lymphoma - analysis of 9 cases
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Background & objectives: Angioimmunoblastic T-cell lymphoma (AITL) is a subtype of mature peripheral T-cell lymphoma(PTCL). The WHO classification recently acknowledged its complexity with the addition of other AITL-like subsets. AITL resides under the umbrella of nodal T-cell lymphomas with follicular T helper(TFH) phenotype.
Methods: It is a retrospective study including 9 cases of AITL diagnosed by lymph node biopsy in the Department of Pathology of Farhat Hached and Sahloul University Hospital of Sousse (Tunisia) during 2014-2020. This study included 5 men and 4 women. The mean age was 49 years ranged between 23 and 71. Most patients presented with generalized lymphadenopathy and hepatosplenomegaly.
Results: Histologically, the lymph nodes showed partial or total effacement of the normal architecture by a polymorphic lymphoid infiltrate including neoplastic T-cells and various chronic inflammatory. A perivascular proliferation of follicular dendritic cells(FDC) and a vascular proliferation were present. The differential diagnosis included atypical

reactive processes, Hodgkin's disease, B-cell lymphomas and other PTCL. On immunohistochemistry, the neoplastic T cells expressed CD3 in all cases, CD5 in 6 cases, CD2 and CD7 in 4 cases. They were positive for CD4 in 7 cases. A smaller CD8+ population was present in 2 cases. They expressed TFH markers: BCL6 in 3 cases and CD10 in 6 cases. 5 cases expressed CD23 showing FDC proliferation.
Conclusion: AITL is a neoplasm of mature TFH cells which occurs mostly in the middle-aged and elderly. Lymph node biopsy is needed to confirm this diagnosis which may be difficult especially in the early phase although the well described histologic features. Unlike many other lymphomas, no specific phenotypic or molecular markers have been identified so far to assist the diagnosis that often leads to delayed or wrong histologic diagnosis, denying the patient the chance of early treatment.

E-PS-10-024
Intranodal palisaded myofibroblastoma in a middle-aged adult: a case report of a rare lymph node-based benign neoplasia and review of the literature
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Background & objectives: Intranodal palisaded myofibroblastoma is a benign neoplasia of ill-defined pathogenesis based in the lymph node. It occurs predominantly in the inguinal region in adults aged between 45 and 55-years old.
Methods: We report the case of a 57-year-old male with a history of right inguinal adenomegaly measuring 23x18mm, without other enlarged lymph nodes in the regional chains. The patient was submitted to lymph node excision. We received a 2g and 20x15x10mm lymph node, already sectioned by the largest axis, with smooth external surface. The cut surface was multinodular, elastic and yellowish whitish.
Results: The histological analysis revealed a well-defined lesion, separated from the surrounding lymph node parenchyma by a thin pseudocapsule, with moderate to high cellularity and consisting of spindle cells organized in short fascicles, in swirls and which often displayed palisaded nuclei. The cytoplasm was scarce, slightly eosinophilic and fibrillar, and the nuclei hyperchromatic and elongated. The fusiform cells had frequent paranuclear hyaline globules and, sometimes, peri-nuclear vacuoles. In 50 high-power fields we identified 4 mitoses. The lesion had areas of collagenous and hyalinized matrix. The neoplastic cells were immunoreactive for β-catenin, SMA, Cyclin D1, Calponin, CD99 and Desmin; and negative for EMA, CAM5.2, CD34, S100 protein, Podoplanin, SOX-10 and STAT6 expression.
Conclusion: This case illustrates the main immunophenotypical features of this extremely rare benign neoplasia based in the lymph node, which is generally cured by local excision. Local recurrence is rare and, consequently, it has an excellent prognosis.

E-PS-10-025
Angioimmunoblastic lymphoma in the setting of chronic lymphocytic leukaemia/small lymphocytic lymphoma mimicking a Richter syndrome: is there a possible role of EBV or Ibrutinib-Venetoclax treatment?
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Background & objectives: Chronic Lymphocytic Leukaemia/Small Lymphocytic Lymphoma (CLL/SLL) may transform into a clinically aggressive lymphoma called Richter syndrome. The majority of transformation are to Diffuse Large B-Cell Lymphoma, while Angioimmunoblastic T-cell lymphoma (AITL) is a rare variant of Richter syndrome recently described.
Methods: We present a 60-year-old male diagnosed 7 years ago (2014) of CLL with RAI stage 0, Binet-A. He remained stable without treatment until 2017, he developed lymphadenopathy and splenomegaly and started treatment with Ibrutinib+Venetoclax, with good response and minimal residual disease in blood (0.18%). In January 2020, he presented with worsening general condition, pancytopenia, and high EBV-viral load.
Results: In 2014, IGHV-mutated CLL del(13q) was diagnosed by flow cytometry (CD19;CD5;CD23;CD20;kappa). There was ZAP70<20%, CD38<30% without TP53 mutation. In January 2020 after respiratory infection, relapsed with pancytopenia, EBV was positive (20.515 copies/ml) and worsening of CT scan. After received valaciclovir, he switched to ibrutinib alone due to remained pancytopenia.
In November 2020, increasing EBV and worsening the PET-CT scan a lymph node biopsy showed effacement of lymph node architecture due to diffuse large atypical T lymphocytes (CD2+;CD3+;CD5+;CD4+;CD10+;BCL6+;PD1+;ICOS+), expansion of follicular dendritic cells (CD21+), high endothelial venules and isolated regressed follicles consistent with pattern III AITL. We also observed isolated B-cells CD30+ and EBER-ISH+. A BM biopsy revealed focal micronodular infiltration.
Conclusion: Regarding to the literature, CLL/SLL cases transformed into T-cell lymphomas are rare and specially include PTCL, NOS and ALCL. Recently, Trimech et al. described 2 cases with composite AITL and CLL/SLL and one case with same evolution as our case. In our patient, del(13q) was the CLL prognostic factor identified, was only treated with Ibrutinib and Venetoclax and we only observed EBV reactivation in the clinical evolution so EBV or treatment might be involved in the pathogenesis of AITL.

E-PS-10-026
Kaposi's sarcoma and nodular lymphocyte predominant Hodgkin lymphoma presentation in the same lymph node: a rare case report
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Background & objectives: Coexistence of Kaposi's sarcoma with Classical Hodgkin Lymphoma in the same lymph node is frequently encountered, but its association with Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL) is extremely rare, only 4 cases have been reported in the literature.
Methods: A 40-year-old male presented with fever and night sweats for about a month had a lymph node in the right axillary region on physical examination. Numerous lymphadenopathies were observed in the bilateral jugular area, posterior cervical triangle, right axillary area and left inguinal areas with USG. No history of other disease was seen. Right axillary lymph node was excised.
Results: Histopathological examination revealed fascicles of spindle-shaped cells arranged between cleft-like vascular spaces filled with red blood cells. Additionally, Hodgkin-like cells with bilobed large nuclei, some in the form of popcorn, were seen in a nodular infiltration pattern that disrupted the lymph node architecture. Hodgkin-like cells were positive for CD20, CD45, OCT2, BOB1 and negative for CD30, CD15. The lymphocytes around these large cells were found to be positive in the rosette forming pattern with PD1 staining. Spindle cells were positive for CD34, CD31, HHV8. EBER ISH result was negative. The patient was diagnosed as NLPHL concomitant with HHV8 positive Kaposi sarcoma without immunosuppression. Serology for HIV infection was also negative.
Conclusion: It is rare for NLPHL to be seen synchronously with KS in the same lymph node. Absence of HIV/ Immunodeficiency is also very rare entity in terms of occurrence with Kaposi's sarcoma infiltration in the primary lymph node without skin involvement. The case is important because of its rarity and different clinical presentation.

E-PS-10-027
Low-grade B-cell lymphoma with IRF4 gene rearrangement: a case report
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Background & objectives: A case of low-grade B-cell lymphoma with IRF4 rearrangement presenting as a thigh mass. Although rearrangements involving the IRF4 gene have been described in myeloma and large B-cell lymphomas, few reported cases of low-grade B-cell lymphoma harbouring this translocation exist.
Methods: This case displayed both a follicular and diffuse growth pattern suggestive of follicular lymphoma, was composed predominantly of centrocytoid cells, and lacked prolymphocytes or the large cell morphology typically seen in large B-cell lymphoma with IRF4 rearrangement. There was no evidence of a translocation involving the BCL2 gene. Diffuse MUM1 positivity by immunohistochemistry prompted FISH testing.
Results: This case displayed both a follicular and diffuse growth pattern suggestive of follicular lymphoma, was composed predominantly of centrocytoid cells, and lacked prolymphocytes or the large cell morphology typically seen in large B-cell lymphoma with IRF4 rearrangement. There was no evidence of a translocation involving the BCL2 gene. Diffuse MUM1 positivity by immunohistochemistry prompted FISH testing. With this case we expand the spectrum of lymphomas harbouring the IRF4 gene rearrangement and emphasise the importance of integrating morphology with molecular and cytogenetic findings.
Conclusion: This case displayed both a follicular and diffuse growth pattern suggestive of follicular lymphoma, was composed predominantly of centrocytoid cells, and lacked prolymphocytes or large cell morphology seen in large B-cell lymphoma with IRF4 rearrangement. There was no evidence of a translocation involving the BCL2 gene. Diffuse MUM1 positivity by immunohistochemistry prompted FISH testing. With this case we expand the spectrum of lymphomas harbouring the IRF4 gene rearrangement and emphasise the importance of integrating morphology with molecular and cytogenetic findings.

E-PS-10-028
Primary Non-Hodgkin lymphoma of bone of the femur and humerus: a case report and review of the literature
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Background & objectives: Lymphoma of bone is a rare neoplasm composed of malignant lymphoid cells, producing a tumefactive lesion within bone. We report a 13-year-old male who presented with progressively increasing swellings at the right shoulder and right mid-thigh for three months.
Methods: Radiological images revealed lytic destructive lesions associated with soft tissue masses in both sites and a pathological fracture on the right humerus. The patient had no significant medical history. Histological, immunohistochemical tests (CD20, CD45 positivity) but negative with CD99 and Cytokeratin 20; and FISH assessment of biopsies from the lesions confirmed the diagnosis of primary non-Hodgkin lymphoma of bone.
Results: Unfortunately, due to COVID-19 outbreak, the patient was unable to follow-up treatment and died shortly after establishment of the diagnosis. Delay in diagnosis and treatment is of serious concern when it comes to improve the prognosis of patients with this disease.
Conclusion: Primary bone lymphoma especially in African paediatric population is rare. Delay in diagnosis and treatment as it was the case in our patient is of concern when it comes to improve the prognosis of patients with this disease. Clinicians should have a suspicion of index for unusual cases and thus vigorously work-up including proper and timely diagnosis for optimal patient care.

E-PS-10-029
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) with extensive IgG4 plasmacytic differentiation of the submaxillary gland: case report
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Background & objectives: We report a case of extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) with extensive IgG4 plasmacytic differentiation. This entity may be misdiagnosed as an IgG4-related disease. Our aim is to report a case affecting a salivary gland.
Methods: A 68-year-old man presented a 3 cm cervical tumour in his left submaxillary region of days of evolution. There were no supra or infradiaphragmatic lymphadenopathy in computed tomography scan. High serum IgG4 levels were detected in the analysis. Cervical FNA was reported as: images suggestive of reactive pattern lymphadenopathy. After two months without size reduction, the tumour was biopsied.
Results: The histological study showed a monomorphic lymphoid infiltrate of small and irregular lymphocytes with a dendritic expansion. The lymphocytes had a B cell phenotype (CD79a and CD20) with MNDA and BCL2 coexpression. There were numerous Kappa-restricted plasma cells, and the IgG4/IgG ratio was >80%. IgH rearrangement was clonal for FR1, FR2 and FR3. MALT lymphomas accounts for 7% of all B lymphomas. The most common site is the stomach, but they may be seen in ocular appendages, skin or salivary glands. 30% of them present plasmacytic differentiation, that has no prognostic implication. MALT lymphomas with extensive IgG4 plasmacytic differentiation has been described in skin, ocular adnexa, meninges and renal hilium.
Conclusion: In a patient with a major salivary gland infiltrated by an IgG4 plasmacytoid infiltrate, a MALT lymphoma with IgG4 plasmacytic differentiation should be ruled out based on clinical data, histology and IgH rearrangement so that they are not misdiagnosed as an IgG4-related disease. These entities share some locations such as major salivary glands and high serum IgG4 levels may be seen in both entities. IgG4-related disease presents storiform fibrosis and obliterative phlebitis but no clonal IgH rearrangement or mass formation.

E-PS-10-030
Incidental finding of high grade plasmablastic neoplasm in a 76-years-old patient with rectal adenocarcinoma. Case report of a double primary malignancy
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Background & objectives: Double primary malignancies are increasing in incidence, due to early detection of tumours. We describe a case report of an incidental finding of high grade plasmablastic neoplasm in 76-years-old patient who underwent surgery for rectum cancer.
Methods: A 76-years-old patient with a prior diagnosis of rectal adenocarcinoma underwent surgery. We received part of left large bowel (rectosigmoid) measuring 15,5 cm in length. There was an adenocarcinoma, NOS, low grade 3,8cm in greatest dimension. We found 15 lymph nodes in the rectal fat ranging in diameter from 0,2 to 0,7 cm. The pathologic stage was pT3N0.
Results: One lymph node, measuring 0,2cm in greatest diameter was infiltrated by a relatively monomorphic population of lymphoid cells. There was also extranodal extension. The cells were medium to large and had morphological plasmacytic differentiation. We performed an extensive immunohistochemical assay. The neoplastic cells were positive for LCA, CD79a, CD138 and had clonal expression of κ light chains. The lymphoid markers CD20, PanB, CD3, CD5, CD23, CyclinD1, Bcl-6, Bcl-2, CD30, CD56 were negative. The proliferation index (MIB-1) was 90-95%. EBER assay was negative or inconclusive in our laboratory. Thus, the final diagnosis was between high grade plasmablastic neoplasm. The differential diagnosis was between plasmablastic lymphoma and plasmablastic multiple myeloma.
Conclusion: The patient underwent bone marrow trephine biopsy which was negative. She underwent chemotherapy and is free of disease 1 year

later. This case of double malignancy underscores the importance of lymph node sampling in surgical specimens. We should always remember that it is imperative for a pathologist to be always on alert for other coexistent nosologic entities besides the clinically indicated ones.

E-PS-10-031

Myeloid sarcoma of the cranial vault in a small child: if we don´t think about it, we won´t diagnose it

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Background & objectives: Megakaryoblastic Acute Myeloid Leukaemia with t(1;22) accounts for less than 1% of AML; it is more frequent in girls younger than 6 months without Down syndrome and usually starts with hepatosplenomegaly and cytopenias. The debut as myeloid sarcoma is exceptional.
Methods: A 1 year and 1 month old girl arrives at our centre from another hospital with two lesions in the cranial vault diagnosed as small blue cell neoplasm with normal karyotype and a pending NGS study. At our centre she was found to have cytopenias and splenomegaly so a bone marrow biopsy was performed.
Results: The bone marrow was found to be 70% infiltrated by small blue cells with the rest of the hematopoietic series remaining between them without dysplasia and with moderate increase of reticulin fibrosis. An extensive immunohistochemical panel was performed and the only positive marker was vimentin. A few days later, the NGS study in bone marrow and cranial vault revealed a fusion between the RMB15-MKL1 genes, so immunohistochemistry for CD61 was performed and was positive.
The aspirates were dry (no cellularity due to fibrosis) and there were less than 4% of megacarioblasts in the blood smear, response to induction was evaluated with three bone marrow biopsies with absence of tumour infiltration.
Conclusion: Megakaryoblastic AML M7 is a diagnostic challenge given its rarity and broad differential diagnosis. Ruling out Down syndrome and mutational genetic study is important for prognosis. In cases of fusion between RMB15-MKL1 genes, intensive treatment gives a favourable prognosis to these patients.

E-PS-10-032

Synchronous bone marrow infiltration by splenic marginal zone lymphoma (SMZL) and high-grade lymphoma with intermediate features between nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) and T-cell/histiocyte-rich large B-cell lymphoma (TCHRLBCL)

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Background & objectives: Diagnosing bone marrow (BM) infiltration by synchronous lymphomas is challenging. We describe a case of synchronous SMZL and large B-cell lymphoma reminiscent of NLPHL/TCHRLBCL, first suspected in a BM biopsy. Synchronous or metachronous SMZL-NLPHL/TCHRLBCL were not reported so far.
Methods: Herein we report a case of a 64-year-old woman (unremarkable previous medical record) presenting with asthenia, weight loss and generalized lymphadenopathy. Workup revealed lymphocytosis, bicytopenia and massive splenomegaly. Flow-cytometry of peripheral blood disclosed a monotypical small B-cell population with a non-specific immunophenotype. A BM biopsy was performed. A lymph node was later excised to clarify the final diagnosis.
Results: BM histomorphology disclosed two distinct patterns of lymphoid infiltration: a)Intrasinusoidal/interstitial, comprising small B-cells (CD20+/IgD+/CD11c-/AnnexinA1-/BCL6-/CD10-/CD5-/CyclinD1-) consistent with SMZL; b)Macronodular, comprising scattered large B cells (CD20+/CD19+/CD30+/EBER-/IgD-/EMA-) within a background of small T-cells (CD3+/PD1+/CD57+) and epithelioid histiocytes. This unusual combination prompted lymph node excision. Histomorphology showed capsular thickening with septae delineating nodulariform compartments and architectural effacement by a serpiginous lymphoid proliferation. This included scattered and clusters of large B-cells with centroblastic and rare "popcorn" morphology (CD20+/CD19+/CD30+/EBER-/MUM+/BCL6-/CD10-/IgD-/EMA-), a T-cell/histiocyte-rich background (CD3+/CD4+/PD1+/ICOS+ and CD3+/CD8+), dispersed IgD+ small B-cells and disrupted follicular dendritic cell meshworks. PD1-rosettes around large B-cells were seen focally. These features resembled both NLPHL and TCHRLBCL but did not allow classification as either.
Conclusion: When diagnosing BM infiltration by spleen-based small B-cell lymphomas (e.g. SMZL), unusual clinical (e.g. generalized lymphadenopathy) and/or morphologic features (e.g. macronodular pattern) warrant consideration of a rare scenario of synchronous lymphoma, as illustrated by this case, a previously unknown association. This case also highlights that, by current WHO classification criteria, there is a morphologic grey-zone between NLPHL and TCHRLBCL (reflecting a biologic continuum?). We suggest a provisional entity to accommodate these cases and better study their biologic relationship with NLPHL/TCHRLBCL.

E-PS-10-033

A clinical case of acute myeloid leukaemia in a child with ependymoma of the cerebellum and IV ventricle of the brain

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Background & objectives: Acute myeloid leukaemia (AML) in patients could be a long-term effect of antitumor therapy. Cytostatics damage DNA and cause unbalanced translocations and deletions of the arm of 5 and / or 7 chromosomes.
Methods: A case presented of an 11-year-old patient with AML, which developing 3 years after combination therapy. Histological, cytogenetic, immunological studies of bone marrow trepanobiopatate, analysis of clinical and laboratory findings.
Results: A suboccipital craniotomy, microsurgical removal of a tumour of the cerebellum and IV ventricle was performed in 2014. Conclusion of the pathological examination: ependymoma with increased proliferative activity, Grade II. From 2015 to 2017, 25 courses of chimiotherapy (temozolomide+etoposide) were carried out, since 2017 radiotherapy after the 2nd and 3rd relapses, in 2018 radiosurgical treatment for the frontal, temporal, parietal regions, the cerebellopontine angle and the region of the 4th ventricle. In 2019, in bone marrow punctate: a population of anaplastic blast cells with pronounced cytoplasmic clasmatosis was identified. FISH study revealed monosomy 7 in 95% of nuclei. The immunophenotype of the blast population corresponded to acute myeloid leukaemia, with co-expression of CD7, CD56.
Conclusion: The causes of AML in this patient could be excessive doses of radiotherapy during treatment, high doses of chemotherapy drugs and a large number of chemotherapy courses. Treatment-associated leukaemias have a medical and social problem, as they are refractory to treatment and are associated with poor survival, which implies the importance of choosing an adequate treatment strategy for patients with cancer.

E-PS-10-034

Diffuse large B-cell lymphoma in a patient with common variable immunodeficiency

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Background & objectives: Common variable immunodeficiency (CVID) is the most frequent humoral immunity disorder with the onset in the 3rd-5th decade of life. Patients with CVID have a high relative risk (30 up to 400x) of developing different lymphoproliferation, mainly B-cell lymphomas.
Methods: We present a 41-year-old female with CVID who has remained in 6 years observation in our hospital because of autoimmune haemolytic anaemia and mild hepatosplenomegaly. In 2019 due to localized lymphadenopathy, the histological and flow cytometric assessment of inguinal lymph node (LN) was performed without conclusive results and confirmed TCR clonality.
Results: In 2020 the patient was hospitalized because of generalized lymphadenopathy with significant splenomegaly and fever. The cervical LN excisional biopsy and trephine biopsy were performed. Histopathological evaluation of the LN revealed a diffuse proliferation of medium-large-sized lymphocytes with following immunophenotype: CD20(+),Pax5(+),CD10(-),Bcl6(-/+),MUM1(+),FOXP1(+),Bcl2(+),IgM(+),c-myc(-),CD5(-),CyclinD1(-),Tdt(-),CD34(-),CD43(-),CD123(-),CD138(-),CD30(+)single cells,CD23(-),ALK1(-),Ki67-80%. The trephine biopsy examination demonstrated hypercellular bone marrow (BM) with nodular, paratrabecular infiltration of medium-large-sized atypical cells expressing CD20, Pax5 and MUM1. The PET imaging showed metabolic active proliferation in multiple LN both sides of diaphragm, spleen and BM. The patient was treated with R-CHOP regimen for six courses.
Conclusion: The diffuse large B-cell lymphoma (DLBCL), NOS, non-GCB type with 50% of BM involvement was diagnosed. The clinical course of this patient emphasizes the variable nature of lymphoproliferative lesions arising in patients with CVID and underscores an individualized approach to pathologic interpretation and diagnostic intervention. Patients with CVID have increased susceptibility toward developing lymphoma and should stay under close observation.

E-PS-10-035
Primary follicular lymphoma of the femur – challenging diagnosis in different histopathological diagnostic techniques.
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Background & objectives: Primary non-Hodgkin lymphomas of bone (PBL) are uncommon, mainly including large B-cell lymphomas (>80%). Follicular Lymphoma (FL) is an indolent nodal disease of adults above 60. Bone localization is usually reported as the progression of nodal cases.
Methods: We present a 23-year-old male with a tumour localized in the proximal epiphysis of the left femur, metabolically active infiltration starting below the neck and extending downwards about 60 mm with visible discrete sclerotization below the neck and minor lytic changes; discontinuity of the border lamina of the lesser trochanter (SUV max 10.7) and infiltration of soft tissues was seen.
Results: For the diagnosis, the intraoperative examination followed by flow-cytometry (FMC) and postoperative material evaluation was performed. The infiltration with centrocytes and centroblasts was seen presenting immunophenotype: CD20(+),Pax5(+),LMO2(+),BCL2(+/-)weaker,BCL6(+),CD10(-),FOXP1(-),CD5(-),MUM1(-),TdT(-),Ki67(+) in 90% of cells. In FMC compared to the nodal FL, the case was characterized by lack of CD10 and monoclonal-light-chain, low expression of CD81 and BCL2, with CD54 and CD49d aberrant manifestation. PET imaging revealed metastatic lesions in the liver and spleen; the final staging was CSIVA and low-risk FLIPI1/2 and PRIMA. The patient underwent 8xRCVP followed by 2 years of rituximab maintenance with complete metabolic remission. The patient remains free of disease in 30 months of follow-up.
Conclusion: In conclusion, primary FL of bone is the casuistic phenomenon of unclear prognosis. The presented case is unique because of the primary localization and young age of the patient. The differential diagnosis with primary/metastatic bone tumours by the intraoperative examination supported with FMC was essential to avoid over-therapy by surgical treatment. In the presented case, after immunochemotherapy, spectacular remission was seen with more than a 2-years follow-up.

E-PS-10-036
Erdheim-Chester disease: report of a challenging case through multidisciplinary collaboration
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Background & objectives: Erdheim-Chester disease (ECD) is a rare clonal non-Langerhans cell histiocytosis, recognized as a neoplasm in 2016. Less than 1000 cases have been reported. Herein, we report a case of ECD diagnosed after repeat biopsies emphasizing the histologic differences between them.
Methods: A 58-year-old male was admitted to the hospital due to slightly elevated temperature, presenting frequently during the past two years. PET/CT and MRI were performed, revealing infiltration of perirenal tissue, which was biopsied and sent to our pathology department. The patient had undergone biopsy twice before and the corresponding slides were retrieved from our archives and reviewed.
Results: Histological sections revealed among collagen fibres, a few histiocytes with abundant foamy (xanthomatous) cytoplasm and small nuclei, either single or in small clusters. Multinucleated histiocytes were identified rarely. Immunohistochemically, these cells were positive for CD68, fascin and cyclinD1 and negative for S100, CD1a, ALK and tryptase. Molecular analysis revealed BRAFV600E mutation. Upon correlating pathological with clinical and radiological features (hairy kidney appearance), the findings were consistent with ECD. Instead, the reviewed slides showed dense lymphoplasmacytic infiltrate, predominantly plasmacytic, in a background of storiform fibrosis, with scarce or few foamy histiocytes, resembling mostly IgG4-related disease. However, there was no increase in number of IgG4+ plasma cells or an abnormal IgG4+/IgG+ ratio.
Conclusion: ECD usually presents with non-specific clinical and histopathologic findings, posing diagnostic challenges. Perirenal tissue fibrosis along with chronic inflammation may lead to overlook foamy histiocytic cells, if they are few. When perirenal biopsy specimens present histopathologic features of non-specific inflammatory response or IgG4-related disease, ECD should be included in the differential diagnosis and repeat biopsy may be of merit. A multidisciplinary approach is required for the diagnosis and treatment of ECD.

E-PS-10-037
An incidental diagnosis: a rare entity of primary uterine cervical lymphoma concurrent with endometrial adenocarcinoma
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Background & objectives: Primary lymphomas of the female genital tract (FGT) are rare and account for 0.18% of extra nodal lymphomas. Coexistence of primary lymphoma and primary epithelial tumour in the FGT is extremely rare. Unlike systemic lymphomas, there are no B symptoms.
Methods: A 53-year-old woman presented with vaginal bleeding. The patient was operated with a pre-diagnosis of endometrial malignancy. Endometrioid type endometrial adenocarcinoma was seen in the hysterectomy material. Also, far from this malignancy, in the uterine cervical stroma, atypic lymphocytic infiltration was observed. It has been proven by immunohistochemical studies that it has B cell immunophenotype and high ki67 proliferation index.

Results: Macroscopically, a well-circumscribed, soft and brownish area limited to the cervical submucosa, with 7 mm in diameter was identified. Histopathological examination revealed atypic lymphocytic infiltration in the cervical wall. Diffuse immunostaining for B cell markers, high proliferation rate, angioinvasion and monoclonality for immunoglobulin heavy chain on FISH study of the infiltration directed us to call the lesion as an early onset of B cell Non-Hodgkin lymphoma without lymph node involvement. Further radiological studies revealed also no other nodal disease. The patient was accepted as primary uterine cervical lymphoma concurrent with endometrial adenocarcinoma.
Conclusion: Cervical lymphomas typically produce bulky lesions just below the intact surface epithelium. Primary cervical lymphomas are usually localized and have a favourable prognosis than secondary ones. Due to their rarity, lymphomas are often not considered in a female genital tract and can be misdiagnosed as inflammatory reactive processes. Therefore, even a small lymphoid infiltration containing atypical cells should be evaluated closely and immunohistochemical methods should be used. Awareness and histology are essential for the correct diagnosis of this curable malignancy.

E-PS-10-038
Marginal zone B-cell lymphoma of the renal pelvis: an unexpected find in nephroureterectomy specimen
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Background & objectives: To report on a case of Marginal Zone B-cell lymphoma of the Renal Pelvis and update the literature concerning this topic.
Methods: A 72-year-old woman diagnosed with urothelial carcinoma of the bladder (pT1) 4 years ago by TUR and subsequently treated with BCG. On TC and NMR, an expansive solid lesion was observed in the renal sinus, with effacement of its edges and fat of the left renal hilum. Surgery was performed for the presumed diagnosis of upper urinary tract tumour.
Results: In the left-nephroureterectomy specimen, a mass of brownish-coloration and firm-consistency of 5.3 x 4 cm was observed occupying the renal pelvis, in continuity with the adipose tissue of the renal sinus as seen in the serial-sections. Histologically showed a vaguely nodular growth lymphoid neoplasm, consisting of small regular cells with few blasts, some small atrophic centres. Immunohistochemically, was positive for CD20, CD79a, BCL2, IgD. Ki67 low. Negative for CyclinD1, CD5, CD23, CD10, BCL6, GCET1, SOX11, CD3, CD138. Low-grade small B-cell non-Hodgkin lymphoma, compatible with Marginal Zone Lymphoma was diagnosed. The patient has not received chemotherapy and remains alive and well with no evidence of recurrence on careful follow-up 3 months-postoperatively.
Conclusion: Marginal Zone B-cell lymphoma of the upper urinary tract is an extremely rare condition and because there are no specific findings on either radiographic or blood examinations pre-treatment diagnosis is difficult. There are around 15 reported cases and in the vast majority of them, the diagnosis was made by nephroureterectomy. Therefore, we consider that the pathological examination is the key to its preoperative diagnosis.

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E-PS-11-001
Metastasis of follicular thyroid carcinoma to the mandible as the first clinical sign: a rare case report
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Background & objectives: Follicular thyroid carcinoma (FTC) metastasizes in 10 to 15% of cases. However, metastasis to the mandible is extremely rare. We describe a
case of FTC in which metastasis to the mandible was detected prior to that of the primary tumour.
Methods: A forty-eight-year-old woman from Fortaleza, Brazil presented to medical service complaining of pain and swelling in left lower jugal mucosa. An x-ray showed an intraosseous lesion in the mandible extending to soft tissues. Incisional biopsy was performed, and the specimen was processed and examined by H&E technique and immunohistochemistry.
Results: Microscopically, the lesion consisted in follicular epithelial neoplasia with colloid production. Immunohistochemistry revealed TTF1 and thyroglobulin expression, indicating metastatic follicular thyroid carcinoma. Subsequent investigation showed primary right lobe follicular thyroid carcinoma, with the mandible metastasis being the single one identified.
Conclusion: Metastatic carcinomas to oral region are rare, accounting for approximately one percent of oral cancer. Metastatic tumours of the oral region are of great importance, since some are responsible for the single signs/symptoms of primary tumours. It is believed that one third of patients with oral methastasis do not have the primary tumour identified. The present case highlights the importance of prompt recognition of FTC metastasis to the mandible, especially when the primary tumour is yet to be identified.

E-PS-11-002
Submandibular myelolipoma with osseous metaplasia: a rare tumour arising in an unfamiliar territory
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Background & objectives: Extra-adrenal myelolipoma is a benign rare lesion with reported sites including the mediastinum, thoracic spine and kidney. Osseous metaplasia has rarely been observed within. We present a never-reported case in the English literature of a submandibular myelolipoma with osseous metaplasia.
Methods: A 76-year-old male presented with a firm left submandibular lesion, measuring 3x2.7cm. On ultrasound (US) and magnetic resonance imaging (MRI) the lesion was well-demarcated and showed fatty areas in the background of heavy calcification. An US-guided biopsy was obtained.
Results: Microscopic examination of the lesion showed lobules of mature adipose tissue, with trilinear hematopoietic elements composed of myeloid cells with few clusters of erythroid cells and megakaryocytes. Extensive areas of osseous metaplasia were seen. No atypical or malignant features were identified. A diagnosis of myelolipoma with osseous metaplasia was made.
Conclusion: This is the first reported case in the English literature of myelolipoma with osseous metaplasia occurring in the submandibular region. Distinguishing this from other possible differential diagnoses including extramedullary haematopoiesis, hamartoma, liposarcoma and teratoma is necessary. We also propose a new name of "Osteomyelolipoma" in exchange of the using of 'osseous metaplasia' as this would reflect the extensive formation of mature bone formation which we believe that it does constitute an integral part of this neoplasm.

E-PS-11-003
Nasopharyngeal Warthin tumour: a forgotten entity that is worth revisiting
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Background & objectives: Extra-parotid Warthin tumour (WT) is rare, with few reported cases in oral cavity, larynx and cervical lymph nodes.

Nasopharyngeal WT is extremely rare, with only a handful reported cases in the literature. We present a case of this rare entity.
Methods: The presented case is of a 77-year smoker man, who presented with a unilateral earache. Nasendoscopy showed a 1x2cm nasopharyngeal mass occupying the post-nasal space and blocking Eustachian tube. These findings were confirmed by radiological imaging.
Results: Microscopic examination showed respiratory-type mucosa with underlying lymphoid rich connective tissue, comprising a cyst lined by a double-layered oncocytic epithelium. A diagnosis of Warthin tumour arising in minor salivary gland tissue in the nasopharynx was made. The differential diagnosis includes extensive Warthin-like/oncocytic metaplasia arising in a cyst wall.
Conclusion: Nasopharyngeal WT is a rare and overlooked entity. Little is known on the biologic mechanism for extraparotideal WT; however, it is thought to be due to entrapment of thymic/lymphoid tissue during the embryonic descent and proliferation of the 2nd, 3rd and 4th pharyngeal pouches.

E-PS-11-004
Biphenotypic sinonasal sarcoma of the frontal sinus
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Background & objectives: We present a case of Biphenotypic Sinonasal Sarcoma of the left frontal sinus.
Methods: A fifty year old woman was presented in our hospital with nasal obstruction and difficulty in breathing. Imaging of the visceral skull revealed a heterogenous destructive mass. Several tissue fragments were taken and sent for histologic examination.
Results: Histologically, the tissue fragments were partly covered by respiratory epithelium. In the adjacent haemorrhagic and myxoid stroma an uncapsulated tumour was observed. It was composed of spindle cells arranged in fascicles and in some areas a herringbone pattern and sparse glandular structures were noticed. Significant mitotic activity or nuclear pleomorphism were not observed. Immunohistochemistry revealed positivity for Vimentin, patchy expression of S100, SMA and negativity for Pankeratin, Ck7, h-caldesmon, Desmin, CD34, SOX-10, STAT-6, EMA, NF, GFAP, FXIIIα, Mart-1 and HMB45. Ki67 was 3-5%. From all the above, the diagnosis of Biphenotypic sinonasal sarcoma with myogenic and neurogenic characteristics was made. Molecular test in combination with Pax-5 positivity confirmed the diagnosis.
Conclusion: Biphenotypic sinonasal sarcoma is a low grade spindle cell tumour. Its molecular signature is a recurrent PAX3- MAML3 gene fusion. It involves various sites in the sinonasal tract and affects females 2 times more often. It grows slowly and can invade local tissues. Half of the patients report local recurrence even years after the first treatment. No death or metastatic disease have been reported so far.

E-PS-11-005
Nasal angiomyolipoma
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Background & objectives: We present a case of angiomyolipoma (AML) of the left nostril.
Methods: An eighty-three-year-old male was presented in our hospital due to epistaxis and difficulty in breathing. Endoscopically, a polypoid lesion of 1,3x 1,3x 0,7cm in dimensions was removed and was sent for histological examination.
Results: Histologically, a well circumscribed, polypoid lesion was seen, lined by respiratory epithelium. The stroma was composed of smooth muscle cells, fat cells and dystrophic thick-walled blood vessels. As a rule, there is coexpression of myoid (Desmin, SMA), lipoid (S100) and melanocytic markers (HMB45). The last marker is usually negative in AMLs of the nasal cavity.
Conclusion: Angiomyolipoma, is a benign mesenchymal neoplasm and is usually associated with Tuberous Sclerosis. Nasal AML is very rare, composed of thick dysmorphic vessels, smooth muscle and adipose tissue. Each component is presented in a variable amount. Surgical excision is usually curative.

E-PS-11-006
Extensive calcification with bone and cartilaginous metaplasia in thyroid papillary carcinoma
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Background & objectives: Bone and cartilaginous metaplasia represent a rare findings in papillary thyroid carcinoma (PTC), reported in association with aggressive behaviour. We report two cases of PTC with extensive calcification, bone and cartilaginous metaplasia and we describe its histopathological features.
Methods: We report the cases of a 79-year-old man and a 40-year-old woman presenting with multinodular thyroid associated to cervical lymphadenopathy. Fine needle aspiration cytology concluded to PTC. Total thyroidectomy with lymph node dissection was performed for the two patients. The Surgical specimens were analysed in the Department of Pathology of the University Hospital of Monastir.
Results: Bilateral thyroid gland involvement by multifocal PTC with extrathyroidal extension and multiple lymph node metastasis was noted in both cases. The tumour had papillary and follicular architecture. Psammoma bodies were absent. In the first case, the stroma contained a large foci of calcification associated to mature bony trabeculae and cartilaginous lobule. Marrow fat tissue was identified between mature bony trabeculae, and occasionally hematopoietic cells were observed. In the second case, the tumour showed foci of mature bone formation associated to lymphocytic thyroiditis.
Conclusion: Among malignant thyroid tumours, papillary thyroid carcinoma most frequently demonstrates calcification and bone metaplasia. Despite its rare occurrence, PTC with osseous metaplasia should be recognized as an histological variant by the WHO classification of endocrine tumours because it is correlated to a poor prognosis.

E-PS-11-007
Ameloblastic fibroma: a rare entity of the mandibule - case report
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Background & objectives: Ameloblastic fibroma is a rare benign tumour. It accounts for 2.5% of all odontogenic tumours and 80% of it occurs in the mandible. It is more common in children. We report the clinicopathological features of this entity as well as the evolutionary aspects.
Methods: A female child aged 7 years consulted for a right mandibular tumefaction first discovered a month ago.
On examination, it was a firm and an encapsulated mass measuring 2.5cm. Imaging showed a radiolucent lesion involving the horizontal branch of the mandible. Surgical enucleation of the mass and gingival biopsy on front of the lesion were done and sent for histopathological examination.
Results: Grossly, we received a white well defined, firm and lobular mass measuring 3cm. In cut, it had a white colour with some calcifications. With the mass we received a gingival fragment measuring 2 cm. Histologic examination showed a cellular connective tissue stroma comprising odontogenic epithelium arranged in the form of islands and cords of varying size and shape. These structures were lined by cuboidal-to-

columnar ameloblast-like cells. The connective tissue component resembled the dental papilla. It was characterized by numerous plump fibroblasts which were angular and oval in shape in a myxoid background. There were no atypia or mitosis. The diagnosis of ameloblastic fibroma was made.
Conclusion: Ameloblastic fibromas are benign neoplasms of odontogenic epithelium and mesenchymal tissues, and as such are categorized as mixed odontogenic tumour. The presence of mitosis should expand the differential diagnosis to include malignant entities such as ameloblastic fibrosarcoma. Immunohistochemistry generally does not aid in differentiating ameloblastic fibroma from other mixed odontogenic tumours. Treatment considered is meticulous enucleation and curettage of surrounding bone. However, concerns regarding its recurrence and its malignant transformation have to be kept in mind and require a long-term follow-up.

E-PS-11-008
Unusual gingival enlargement post radiotherapy: a report of 2 cases
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Background & objectives: Radiotherapy is a cornerstone in the treatment of cancer. However, complications do arise. Radiation-induced sarcomas are rare high-grade malignancies evolving within 3 to 55 years following the radiotherapy. These tumours are associated with poorer prognosis compared to primary sarcomas.
Methods: We report 2 cases of such tumours highlighting the importance of the clinical history of the patient to the pathological diagnosis.
Results: The first case is 49-year-old male treated by radio-chemotherapy 20years ago for an undifferentiated nasopharyngeal carcinoma tumour, presenting with a 4cm ulcerated gingival growth of the posterior region of the maxillary. Our 2nd case is a 71-year-old female who underwent mandibular resection and radiotherapy 2years ago for a gingival moderately-differentiated squamous-cell carcinoma presenting with a 4cm white friable mass lining the radiation site growing alarmingly fast. On biopsy both tumours were poorly differentiated showing elongated fascicles of spindle cells and scattered polygonal cells with a vacuolated cytoplasm, marked nuclear atypia and high abnormal mitotic count. The IHC profile was: vimentin(+), smooth-muscle-actin(+), H-caldesmone(+), Cytokeratin(-), P63(-) concluding to high grade leiomyosarcomas.
Conclusion: A recurrence of the primary tumour should always be ruled out. However, taking into consideration the clinical history of the patient is a valuable clue particularly in cases of former radiation treatment. Radio-induced sarcomas call for heavy medical treatment and extensive surgery to improve survival, thus pathologists should be aware of the rare but very plausible risk.

E-PS-11-009
Case report: a 47-year-old man with a primary intraosseous carcinoma, NOS
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Background & objectives: Primary intraosseous carcinoma (PIOC) is a rare aggressive malignant odontogenic tumour with poor prognosis. We present the case of a 47-year-old man referred by the dentist to the maxillofacial surgery department for investigation of a suspect mandibular ulceration.
Methods: Intraoral examination revealed an ulceration measuring 14/6mm of the right mandibular epithelium between 4.5-4.6 by loss of sensitivity. Radiography showed a unilocular radiolucency extending from the distal side of 4.5 to the ramus. The surgical resection specimen was fixed in 10% formalin and paraffin embedded. HE staining and immunohistochemical tests were performed.
Results: Macroscopically, an ulcerated, grey, infiltrative intraosseous lesion, measuring 14/6/4mm was identified. Microscopic examination revealed an epithelial neoplasm with squamous differentiation, with extensive intraosseous destruction, infiltrating of the surrounding soft tissue. The tumour cells were arranged in nests and islands, showing hyperchromatic nuclei with mild pleomorphism, abundant pale eosinophilic or vacuolar cytoplasm, rare abnormal mitotic figures, but no keratinization. Vascular invasion was present. The tumour had no connection with the gingival epithelium. On immunohistochemistry, the tumour cells were diffusely and intense positive for CK19 and negative for p63. Considering that no oral mucosal dysplasia/carcinoma was identified and the CT-scan revealed no other tumour, the final diagnosis was primary intraosseous carcinoma, NOS.
Conclusion: PIOC is a diagnosis of exclusion. This aggressive central jaw carcinoma, assumed to derive from the odontogenic epithelium needs differential diagnosis with metastases, squamous odontogenic tumour, solid odontogenic keratocyst, keratinizing ameloblastoma and central high-grade mucoepidermoid carcinoma. Histopathological, clinical and radiographic features assure an accurate diagnosis. Due to the high recurrence rate and poor prognosis, PIOC should be aggressively treated. Multimodal treatment has been reported to provide a 3-year survival rate of 40%.

E-PS-11-010
Paraneoplastic Cushing's syndrome associated with aggressive acinic cell carcinoma of the parotid gland
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Background & objectives: Acinic cell carcinoma (ACC) is a rare salivary gland neoplasm, usually low-grade and indolent. We report a rare case of ACC with aggressive behaviour, associated with paraneoplastic Cushing's syndrome (CS) due to ectopic ACTH production.
Methods: The clinical history was collected from the clinical files. Histology and cytology samples were reviewed and immunohistochemistry for ACTH was performed. PubMed search for similar cases was done.
Results: A 60-year-old-man presented with a laterocervical mass. Imaging studies revealed a 4cm parotid gland tumour, homolateral lymphadenopathies and multiple lung, pleural and bone lesions. FNAC/biopsies from the laterocervical mass and one of the lung's nodules revealed tumour compatible with ACC. The patient was admitted for parotidectomy and neck dissection but, on surgery's day, a hypertensive crisis precluded the procedure. The patient remained hospitalized due to further decompensated diabetes mellitus, hypokalemia and dyslipidemia. Serum ACTH/cortisol and 24-hour urine cortisol levels were elevated. ACTH immunohistochemistry was performed in one of the pathology specimen and immunostaining was observed. Diagnosis of paraneoplastic CS due to ectopic ACTH producing metastatic ACC was rendered.
Conclusion: We describe a rare case of an usually indolent tumour that presented ab initio with disseminated metastatic disease. Furthermore, three months after the diagnosis the paraneoplastic CS developed, potentially creating diagnostic questions as this syndrome is more frequently associated with tumours like lung small cell carcinoma or carcinoids. To our knowledge this is the tenth case described with this association. Due to its rarity, increased awareness of this phenomenon can avoid potentially misdiagnosis and delays in the treatment.

E-PS-11-011
Melanotic schwannoma: a case report
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Background & objectives: Melanotic schwannoma is a nerve sheath tumour with a uniform composition of variably melanin-producing Schwann cells and metastatic potential. It is an uncommon neoplasm, accounting for less than 1% of all nerve sheath tumours.
Methods: We report a case of a 64 years-old woman having an 8cm mass on the left lateral region of the neck for many years, that lately has enlarged. FNA showed a melanotic schwannoma and radical resection was performed. The tumour was located under the vessels of the spine, below the n.vagus(VI) and seemed to becoming out of the ganglion.
Results: Macroscopically the tumour an ovoid well circumscribed mass covered by a thin fibrous membrane, measured 8cm. The cut surface had the consistency of tar. Microscopical examination showed plump spindle and epithelioid cells arranged in interlacing fascicles and nests, with round or ovoid nuclei, containing delicate chromatin and small distinct nucleoli. Accumulation of melanin was noticed in neoplastic cells and associated melanophages. Necrosis was present and Ki67 was approximately 25% (4mitoses/10 HPF). Immunohistochemical staining for S100, SOX10, HMB45, MelanA, p16, collagen IV and Vimentin produced positive results. BRAF V600E was not expressed in tumour cells.
Conclusion: A diagnosis of MMNST (malignant melanocytic nerve sheath tumour / melanotic schwannoma) was performed, in the differential diagnostic context of which is malignant melanoma. Four months after surgery an extradural metastasis in the L3-L4-S1 spinal region occurred, that was successfully removed. Two months after the patient is free of recurrence.

E-PS-11-012
Unexpected location of adult type rhabdomyoma
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Background & objectives: Rhabdomyoma is a benign tumour with skeletal or cardiac muscle cell differentiation, and it is divided into foetal, juvenile, adult subtypes on the basis of histology. Common localizations are the parapharyngeal space, larynx, submandibular, paratracheal region, tongue.
Methods: We present a case localized to the nasopharyngeal area in a 56-year-old man. Examination of the nasopharynx showed an irregular area of 1x0.5 cm in the left half of the nasopharynx. Microscopic examination was performed after surgical excision. Desmin and S100 markers were used for immunohistochemical evaluation.
Results: The histology shows polyglonal tumour cells, which are described as "spider cells"; no significant and mitotic activities or atypia can be detected. Tumour cells were desmin positive and negative for S100. Diagnostically, the histological findings are compatible with adult type rhabdomyoma.
Conclusion: Only 4 cases of nasopharyngeal rhabdomyoma have been reported to date. We report on a patient with a tumour manifestation that fifth in the literature: a rhabdomyoma of the adult type located in the nasopharynx.

E-PS-11-013
Expression of SDH subunits in middle ear paragangliomas
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Background & objectives: Middle ear (ME) paragangliomas (PGLs) belong to the most hereditarily driven of all human tumours and are associated with several genes, including *SDHx*. Immunohistochemistry (IHC) of SDH subunits can identify the germline mutations in the corresponding genes.
Methods: We performed the analysis of expression SDH subunits in 14 MEPGLs using IHC. Immunoreactions were performed with the following primary antibodies: SDHA, monoclonal, clone 2E3GC12FB2AE2; SDHB, monoclonal, clone 21A11AE7; SDHC, monoclonal, clone EPR11035(B); SDHD, polyclonal from Abcam (UK). SDHB staining was assessed as positive, negative, or weak diffuse. IHC of SDHA, SDHC, and SDHD was scored as positive or negative.
Results: In all tumours, we detected positive staining of SDHA and SDHB. In one sample, negative SDHD expression was detected. In the same tumour, we found negative immunostaining of SDHC. Notably, in six tumours we observed an SDHC expression pattern that looks like weak diffuse staining; it was defined as the positive expression of the subunit.
Conclusion: IHC of the SDHB subunit has been proposed as a useful method to predict underlying *SDHx* mutations of hereditary PGLs. Negative or weak diffuse staining of SDHB is associated with the disruption of the SDH complex caused by germline mutations in any *SDHx* genes. In the study cohort, we did not find changed SDHB staining, which can indicate the absence of *SDHx* pathogenic variants.
This work was performed using the equipment of EIMB RAS "Genome" centre (http://www.eimb.ru/ru1/ckp/ccu_genome_c.php).

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E-PS-11-014
Epitheloid haemangioendothelioma of the nasal cavity: a challenging diagnosis
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Background & objectives: Epithelioid haemangioendothelioma (EHE) is an unusual vascular neoplasm of intermediate malignancy. It has an indolent course, with the potential for local recurrence. We aim to describe the pathological aspects of the EHE and discuss the main differential diagnoses.
Methods: We presented a case of a 39-year-old Tunisian woman, with personal and family history of allergic rhinitis. She presented an intermittent epistaxis resistant to the medical treatment for 2 months. A nasal endoscopy was done and showed a polyp of the right nasal septum, bleeding on contact. An endoscopic resection was performed.
Results: The pathological examination showed a firm polyp with brownish cut section and myxoid appearance. Histologically, the surface squamous epithelium was widely ulcerated with a fibrino-leukocyte coating. The axis of the polyp showed a vascular tumour proliferation made by epithelioid endothelial cells organized in nests and primitive vascular formations. The tumour cells had a moderately abundant acidophilic and vacuolated cytoplasm. Occasionally, erythrocytes were seen within the cytoplasmic vacuoles. The mitotic activity was quite high. The stroma-reaction varied from fibro-hyaline to myxoid. Necrosis was absent. The immunochemical analysis showed CD31, ERG and FLI1 cells tumour positivity. The diagnosis of EHE of the right nasal septum was retained.
Conclusion: EHE, first reported by Weiss and Enzinger, is an uncommon vascular tumour of soft tissue. EHE has clinical and histological features intermediate between those of benign haemangioma and conventional angiosarcoma. It is occasionally seen in the soft tissue of the head and neck area. Due to its rarity and histological similarity to other tumours, the diagnosis of EHE can be challenging. Surgical excision is the treatment of choice when it is limited to the nasal cavity.

E-PS-11-015
Carcinoma ex pleomorphic adenoma presenting two uncommon components: apocrine epithelial–myoepithelial carcinoma and squamous cell carcinoma
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Background & objectives: Carcinoma ex pleomorphic adenoma (Ca-ex-PA) is defined as a carcinoma arising in the epithelial and/or myoepithelial component of a PA. The carcinomatous component encompasses various histological tumour types including epithelial–myoepithelial carcinoma (EMCa) and rarely squamous cell carcinoma (SCC).
Methods: We describe a case of hybrid Ca-ex-PA with apocrine EMCa and SCC components. A 52-years old male presented with a rapidly growing extensive mass expanding from submandibular region to parapharyngeal space. Both, submandibular and parapharyngeal locations were biopted and the initial diagnosis was simultaneous neoplasms: Ca-ex-PA and SCC, respectively. The case was referred to our department for histopathological review.
Results: Histologically, the sample from the submandibular region presented a neoplasm arranged in a multinodular pattern, consisting of PA morphology areas and carcinomatous bilayered tubular structures. The inner/ductal cells were eosinophilic with apical snouts in the lumina and presented high-grade nuclear atypia, high mitotic activity with atypical figures. The outer/myoepithelial cells were polygonal with clear cytoplasm forming more than one layer. Immunohistochemically the cells were: luminal-AR[+], mammaglobin[+], GCDFP15[+], GATA3[+], CK7[+], HER3+, abluminal-p63 [+], p40[+], S100[+]. The parapharyngeal space sample evaluation revealed an area of infiltrative squamous differentiation without relation to the epidermis and small foci of PA. The Ki-67 index for SCC fields was 50%. PLAG1 rearrangement by FISH was confirmed for both glandular and squamous components.
Conclusion: The final diagnosis was Ca-ex-PA with apocrine EMCa and SCC components. The FISH study was crucial for diagnosis as it had revealed a PLAG1 rearrangement in samples form submandibular region and parapharyngeal space, which confirms that both carcinomatous components developed within PA. Both neoplasms are exceedingly rare, moreover their coexistence have not been previously documented. Pathologists should be familiar with the Ca-ex-PA phenomenon with multiple components and use molecular testing for ambiguous cases of simultaneous neoplasms.

E-PS-11-016
Recurrent and metastasizing parapharyngeal pleomorphic adenoma: a paradoxical behaviour
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Background & objectives: De novo occurrence of pleomorphic adenoma in the parapharyngeal space is rare [1][7][8]. Moreover, histologically benign parapharyngeal pleomorphic adenoma that manifests local or distant metastasis are even rarer with no reported cases found in literature [8].
Methods: A 72 year old lady came with dysphagia, odynophagia and sore throat for 1 month at initial presentation in 2014. She was diagnosed with left parapharyngeal pleomorphic adenoma with the size of 65x40x25mm. A transcervical excision of the mass was performed and the excision margins were free.
Results: She returned with multiple recurrences in 2017, 2018 and 2020 with regional metastasis to level Ib node in 2017, followed by metastasis to level Ia, III and IV nodes in 2020. She is still under regular otolaryngology clinic follow up.
Microscopy: Review of all H&E slides from 2014 till 2020 show similar well-circumscribed and partially encapsulated triphasic tumour composed of epithelial cells, myoepithelial cells and chondromyxoid stroma with bland cytology and low mitotic activity (average of 2 per 2mm2). There are no necrosis and perineural or vascular invasion. Immunohistochemical profile: CK AE1/AE3 and CK7 highlight the epithelial component whereas SMA and p63 highlight the myoepithelial component.
Conclusion: Pleomorphic adenoma can metastasize while preserving its benign cytological features and thus, must be kept as a diagnostic consideration in known cases of pleomorphic adenoma [1]. At present, there are no reliable histological, immunohistochemical or molecular parameters to predict the metastatic potential of pleomorphic adenoma [2][6]. However, local recurrence after surgical excision is shown to be a risk [2][5]. Therefore, further research is required to identify the biological reasons behind the aggressive behaviour of the tumour.

E-PS-11-017
Lymphoepithelial cyst of the tonsil: a case report
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Background & objectives: Oral lymphoepithelial cysts are uncommon benign lesions that develop within the oral and pharyngeal lymphoid tissue. Tonsillar involvement usually presents itself as a painless yellowish/ white nodule. Herein, we report a case of lymphoepithelial cyst (LEC) arising in the tonsil.
Methods: We will describe a case of lymphoepithelial cyst of the right tonsil in a 20-year-old woman. The patient complained of a lump in the throat and underwent excisional biopsy. There were no postsurgical complications.
Results: Grossly, the lesion appeared pedunculated, cystic, with soft whitish material in the lumen. The greatest diameter of the lesion was 1.4 cm. Histopathological features showed a cystic cavity containing keratin, inflammatory cells and desquamated squamous cells. The cystic wall was lined with parakeratinized stratified squamous epithelium, surrounded by lymphoid tissue with germinal centres.
Conclusion: LEC as a benign lesion can be found in different parts of the body, including the pancreas, mediastinum, thyroid and head and neck region. Despite its rare occurrence, LEC should be considered in the differential diagnosis of tonsillar nodules.

E-PS-11-018
Combining nanostructured microfluidic chip with pMHCI-pentamer enables enumeration and functional assessment of circulating antigen-specificCD8+T cells in HPV-associated head and neck squamous cell carcinoma
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Background & objectives: Antigen-specific CD8+ T cells enable important form of immunotherapy, technology that requires a small amount of blood sample and high sensitivity is in urgent need to detect and characterize circulating rare antigen-specific CD8+ T cells.
Methods: Here, by uniquely integrating several coherent strategies including covalent chemistry mediated antigen-specific CD8+ T cells capture/release, peptide MHCI-pentamer, nanostructured substrates, and a PDMS chaotic mixer, a Nanovilli-pMHCI-Pentamer capturing system is developed to capture circulating rare HPV16-E711-20-specific CD8+T cells, followed by disulfide cleavage-driven release, and then to further analyse the response of HPV16-E711-20-specific CD8+T cells to HPV16-E711-20 antigen.
Results: We have successfully developed and validated a novel antigen-specific CD8+ T cells purification system, i.e., CTL-NanoChip, which could achieve a purity above 86.55% even when the target cells made up less than 0.01% (10/106) of the total cells. These data promise the CTL-NanoChip's ability to rapidly and effectively isolate rare antigen-specific CD8+ T cells. By coupling CTL-NanoChip with a downstream

functional assay to quantify CD8 activated-related mRNA transcripts and to detect the killing ability and IFN-γsecretion ability of antigen-specific CD8+ T cells, these data demonstrate the CTL-NanoChip's ability to maintain the well-preserved integrity and biological activity of recovered antigen-specific CD8+ T cells.
Conclusion: This nano-system, denoted CTL-NanoChip, could utilize streptavidin-modified nanovilli chip and biotin-modified peptide-MHC-pentamer complex to dynamically monitor the count and function of circulating rare antigen-specific T cells using a small amount of peripheral blood samples, which provided a feasible method to facilitate T cell-based immunotherapy through predicting the response to checkpoint inhibitors and monitoring the efficacy of CART-cell therapy or adoptive cellular therapy.

E-PS-11-020
Mixt plexiform and desmoplastic ameloblastoma
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Background & objectives: Ameloblastoma is a benign but aggressive/destructive epithelial odontogenic tumour, with the capacity to attain great size, invade bone and adjacent structures. Plexiform and desmoplastic types (especially mixed forms) are rare odontogenic lesions, with radiographic and pathologic features of jaw cysts.
Methods: A 29-year-old male patient admitted to the dentist with painless swelling on manbular region. Clinical examination revealed a mass in left side of mandibula near the 2. Molar tooth. Panoramic radiograph disclosed a well corticated radiolucent lesion 2x1,5 cm in diameter and excisional biopsy was performed.
Results: We received haemorrhagic white soft tissue fragments. Microscopically mixture of dense collagenous stroma with compressed, angular islands of odontogenic epithelium (desmoplastic area) and anastomosing odontogenic epithelial cells in fibrous tissue (plexiform areas) were seen. Odontogenic epithelial islands composed of peripheral palisading columnar cells were at basal layer, hyperchromatic cells were shown reverse polarization away from basement membrane. Infiltrating islands of atypical basaloid cells with peripheral palisading and separation artifact of peritumoral stroma were evident. Necrosis, mitotically activity and haemorrhage are not seen. Ki67 proliferation index was 1%. On immunohistochemistry, tumour was positive for CK5, CK19, P63 and CD56 (preferentially expressed in the stellate reticulum-like cells).
Conclusion: Every radiolucency of the jaw should be closely distinguished from mimickers with pathological examination since ameloblastoma shares significant clinical and radiographic similarities with odontogenic cysts and malignant tumours. Incisional biopsy and aspirational cytology may not be able to reflect the true nature of the lesion.

E-PS-11-021
A not-so incidental case of papillary thyroid microcarcinoma
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Background & objectives: Papillary thyroid microcarcinomas are typically indolent neoplasms. Approximately one third of adults have papillary thyroid microcarcinomas, most of which never progress to metastatic cancer. We report an extremely rare case of papillary thyroid microcarcinoma metastasis presenting as a neck mass.
Methods: An 83-year-old male presented with a left level II neck mass. CT neck and thorax identified an avidly enhancing soft tissue mass at the common carotid bifurcation. Cerebrovascular duplex scan confirmed a non-vascular entity, separate from the common carotid artery, which was positive for thyroid cells on fine-needle-aspiration. The patient underwent a total thyroidectomy and selective lymph node dissection.
Results: Dissection of the left neck mass revealed a 42mm, well-circumscribed cystic entity with calcification. Histologically, this mass was identified as metastatic papillary thyroid carcinoma, entirely replacing a lymph node.
Curiously, the only abnormalities within the thyroid were two foci of papillary thyroid microcarcinoma, located within the right and left thyroid lobes, measuring 2mm and 1.5mm respectively.
Ectopic thyroid tissue was outruled as the primary source of malignancy and there were no larger foci of papillary thyroid carcinoma elsewhere in the thyroid.
Following multidisciplinary discussion, the presence of multifocal papillary thyroid microcarcinoma was identified as the most likely origin for this metastatic deposit, with a final stage of pT1a (m) N1b.
Conclusion: The vast majority of papillary thyroid microcarcinomas are not aggressive, demonstrate an indolent behaviour and have an excellent prognosis. However, very rare cases of distant metastasis (0.7%) can occur. Male patients with bilateral, multifocal lesions are reportedly more likely to develop lymph node metastasis from papillary thyroid microcarcinomas.
This unusual case represents a very rare and challenging example of metastatic papillary thyroid microcarcinoma, which presented as a large left neck mass, and highlights the importance of a multidisciplinary team approach.

E-PS-11-022
Expression of Claudin-1 in laryngeal squamous cell carcinomas (LSCCs) and its significance
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Background & objectives: A large body of scientific evidence points to the important roles of tight junction proteins in tumour development in many body sites. The author sheds some light on the expression and possible role of claudin-1 in laryngeal squamous cell carcinomas.
Methods: This study analysed the expression of claudin-1, using immunohistochemistry, in a tissue microarray of 80 cases of laryngeal cancers. Clinicopathological parameters were analysed according to claudin-1 expression in the microarray. Furthermore, the expression of slug/snail1, an Epithelial-Mesenchymal Transition (EMT) linked protein, was analysed by immunohistochemistry in the same microarray, and the expressions of the two proteins were assessed for correlation.
Results: A significant majority of laryngeal squamous cell cancers exhibited positive expression of claudin-1 proteins. The majority of those tumours expressed claudin-1 in their cytoplasm. The overall majority of those same tumours also exhibited a cytoplasmic shift of the slug-snail-1 protein from the nuclei to the cytoplasm. There was also evidence of correlation of the two proteins' expressions in the cytoplasm of laryngeal tumours.
Conclusion: The above may suggest a role for claudin-1 in the development and progression of laryngeal squamous cell carcinoma. Overall, claudin-1's aberrant expression in laryngeal cancer is in line with evidence seen in other head and neck cancers. Its co-expression with slug/snail-1 in LSCC patients should be investigated further to understand the nature of the relationship of the two proteins in LSCC and their possible contribution to its development and progression.

E-PS-11-023
Tenosynovial giant cell tumour of the temporomandibular joint: case report and literature review
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Background & objectives: Tenosynovial giant cell tumours(TGCTs) are benign lesions affecting tendon spaces, sheats, bursae of synovia in patients between ages 30-40. Mostly occurs in large weight-bearing joints.

TGCT of temporomandibular joint(TMJ) is very rare, present with preauricular swelling, trismus, clicking of TMJ.
Methods: 68-year-old male presented with the left painless facial swelling, tinnitus and pain with neck movements for two years. He had no history of chemotherapy or radiotherapy. Imaging showed a 40 x 28 x 27 mm, solid mass in the deep parotid gland which has a cystic component in the middle and extension into temporomandibular joint, mandibula, adjacent muscle.
Results: On gross examination of the resection specimen was 4.6 × 2.6 × 1.9 cm, nodular mass. The cut surface showed tan-reddish tissue with dense haemorrhage. Microscopically, the lesion showing groups of pigmented histiocytes, dispersed osteoclasts and rare typical mitosis, consists of vesicular nucleus and oval-spindle cells with eosinophilic cytoplasm. Focal ossification was present. Immunohistochemical analysis showed partially positive staining of the lesional cells for CD68, with negative staining for HMB45, Melan A, Desmin, ALK, EMA, HMW+ LMWCK, S-100 protein, SMA. There is no loss of expression with INI-1. Ki67 proliferation index was lower than 10%.
Conclusion: TGCT of the temporomandibular joint may present clinically and radiologically as a primary parotid gland lesion. Giant cell-rich lesions are uncommon in salivary glands. It is important to keep this entity in the differential diagnosis of giant cell-rich lesions in the parotid gland.

E-PS-11-024
Inflammatory myofibroblastic tumour, an uncommon diagnosis of head and neck lesions: two cases reports and review of the literature
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Background & objectives: Inflammatory myofibrosblastic tumours (IMT) rarely evolve head and neck, accounting for 14% of all lesions. Their pathological diagnosis can be challenging with frequent inconclusive biopsies. Objective: to put forward the clinicopathologic features of two IMT of the head and neck.
Methods: The first case is about a 46-year-old women, presenting with an expansive submucosal mass of the posterior and lateral nasopharyngeal right wall on CT scan. The 2nd case is about a 26-year-old man presenting with 1 cm polypoid mass involving right true vocal cord.
Results: Histological assessment of nasolaryngeal biopsies and of the vocal cord mass excision showed similar features. They revealed a deep submucosal tumour mainly composed of spindle or stellate cells with mild fasciculated arrangement pattern. There were no cellular atypia nor mitosis. Stroma was oedematous, with focal hyalinization and prominent inflammatory component, predominantly composed of lymphocytes, plasma cells, and eosinophils. The surface was not ulcerated. Immunohistochemical study made on the vocal cord mass revealed diffuse expression of smooth muscle actin and ALK by spindle cells.
Conclusion: IMT of head and neck are rare. Pathologist must pay attention to misinterpret inflammation and myofibroblastic cells as inflammatory and reactive change, particularly in submucosal tumour biopsies.

E-PS-11-025
Angiosarcoma of parotid gland - a 10 years retrospective study
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Background & objectives: Parotid glands are an unusual site for primary and metastatic angiosarcomas, representing together with oral cavity and other salivary glands 2% of all angiosarcomas. Prognosis is not well-known due to rarity of the cases in literature.
Methods: In the last ten years (2011-2021), at our institution, a total of three angiosarcomas of parotid gland were studied. Patients were males, aged between 51 and 80 years old, of which two were metastatic angiosarcomas from the scalp submitted to radiotherapy. The youngest patient was diagnosed with primary neoplasia and presented a vocal cord epidermoid carcinoma previously.
Results: Cell-blocks paraffin-embedded revealed epithelioid neoplastic cells with marked atypia, eosinophilic cytoplasm with poorly-defined borders as well as round nucleus with irregular borders. Both, primary and secondary, demonstrate high mitotic activity. Primary tumour cells were positive to CD31 and ERG and negativity for CK5.6, CK7, p40, TTF1, SOX10 and CD10. One of the secondary tumours expressed CD31 and CD34 positivity and MNF116 negativity and the other positivity for CD31, ERG and WT1.
Conclusion: Primary and secondary angiosarcoma of parotid gland are rare, usually presenting unresectable and metastatic stage. Therefore, the diagnosis can be achieved with confidence by cytology which will determine the outcome.

E-PS-11-026
Molecular pathology of undifferentiated thyroid carcinoma with NRAS mutation
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Background & objectives: Undifferentiated thyroid carcinoma is a rare pathological entity with an aggressive course and invariably fatal with a median survival of only 6 months, representing less than 5% of all thyroid cancers.
Methods: A sixty-year-old man presented in our hospital with a sore unilateral cervical mass, rapidly growing in the previous ten days. Ultrasound revealed a hypoechogenic and heterogeneous massive nodule. TAC showed carotid and jugular involvement. Tracheostomy was performed as well as a cellblock of thyroid and cervical adenopathy. Molecular analysis were run to test BRAF and NRAS mutation.
Results: Fine needle aspiration from thyroid identified dyscohesive and pleomorphic cells with enlarged nuclei as well as broad cytoplasm and frequent mitotic figures. The tumour cells were positive for TTF1 and negative for thyroglobulin, neuroendocrine and calcitonin markers. The molecular study was positive for NRAS mutation. The cytopathology interpreted the lesion as an undifferentiated carcinoma of the thyroid gland, possibly with follicular vs follicular variant of papillary carcinoma.
Conclusion: Molecular pathology is recommended in order to predict the outcome and consider the appropriate treatment, mainly in metastatic undifferentiated carcinomas or inoperable cases. In this particular case, this patient had NRAS mutation, therefore not benefiting from EGFR treatment.

E-PS-11-027
Primary epithelioid angiosarcoma of tonsil
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Background & objectives: Squamous cell carcinomas constitute the most frequent malignant neoplasms of head and neck region (including tonsils). A primary tonsillar angiosarcoma is extremely rare.
Methods: We hereby present a 82-year-old male admitted to our hospital due to massive haemoptysis, necessitating 10 units of packed red blood cells. During endoscopy, a tumour on the left tonsil was found; emergency tonsillectomy was performed. A 5.5 x 2.5 x 2.4 cm, 14.2 gram tonsil contained a 1.3 cm ulcerated, purplish tumour.
Results: Histologically, the tumour consisted of multiple anastomosing vascular channels lined by atypical endothelial cells with severe nuclear pleomorphism. Necrotic areas were seen. Neoplastic cells were

immunostained for CKAE1/AE3, CK8/18, ERG and CD31. A diagnosis of epithelioid angiosarcoma was rendered. Further examination with CT scan and PET CT revealed no other foci.
Conclusion: Due to their morphology and immunopositivity for cytokeratins, primary epithelioid angiosarcomas of head and neck may mimic poorly differentiated squamous cell carcinomas, especially of the acantholytic subtype; they must, therefore, always be included to our differential diagnosis.

E-PS-11-028
Tracheal deep benign fibrous histiocytoma: case report and literature review
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Background & objectives: Deep benign fibrous histiocytoma(BFH) is a benign neoplasm of mesenchymal origin composed of histiocytes and fibroblasts that arises in subcutaneous or deep soft tissue. Deep BFH's uncommon and poorly recognized tumour and form located in trachea is even more rare.
Methods: A 71-year-old male patient was admitted to the hospital with dyspnoea. The mass was observed in the trachea on CT imaging. In the bronchoscopy performed, a 1.5 cm diameter thick stalked polypoid lesion was seen on the anterior wall of the trachea and was excised.
Results: Microscopically, a subepithelial localized tumoral lesion that ulcerating the surface was observed. The tumour was composed of spindle-shaped cells arranged in a storiform pattern, with vesicular nucleus with inconspicuous nucleoli, eosinophilic cytoplasm and no atypia. There were 3 typical mitoses/10 HPFs. Pigmented macrophages and multinucleated histiocytes accompanied the tumour. Immunohistochemically, SMA was focally positive in tumour cells whereas pan-CK, S100, desmin, CD34, STAT6, HHV8, EMA, CD68, and P40 were negative. Ki67 proliferation index was 20%. In view of the morphological and immunohistochemical findings, a deep benign fibrous histiocytoma was diagnosed.
Conclusion: BFH is a benign mesenchymal tumour, its presence in deep organs, especially in the head and neck, is rare. There have been only a few case reports of BFH of the larynx. Deep BFH usually present as painless well-circumscribed lesions causing symptoms due to pressure effects depending on size and site of involvement. It's difficult to diagnose deep BFH due to its histological features resembling other mesenchymal tumours. Its diagnosis is challenging and rests on characteristic histopathological and immunohistochemical features.

E-PS-11-029
A rare metastasis of renal cell carcinoma: gingiva
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Background & objectives: Metastasis of malignant neoplasms to the oral cavity is rare and almost exclusively by hematogenous route. Metastasis to bone, especially jaws, is more frequent than the metastasis to soft tissue and affects 40-70 years old.
Methods: A 73-years-old male presented with an intraoral soft tissue tumour. The lesion was excised with pre-diagnosis as peripheral giant cell granuloma. On histopathological examination, there were epithelial tumour nests consisting of cells with clear cytoplasm. Immunoexpression with vimentin, pancytokeratin, CAIX, CD10, EMA and PAX8 were detected. It was reported as renal cell carcinoma metastasis to gingiva.
Results: The gingiva is the most common site for metastasis in the soft tissue of the oral cavity (more than half of cases) because of it is fine capillary vessels. The most common primary malignancy in males is lung, followed by kidney and skin. In women, the most common primary malignancy is breast. In our case, soft tissue tumour in the gingiva was in the maxillary anterior and premolar region, and radiological resorption of the underlying alveolar bone was not observed. The patient had left nephrectomy with a diagnosis of clear cell renal cell carcinoma 2 years ago. The patient died 4 months after the diagnosis of gingiva metastasis.
Conclusion: Metastatic intraoral soft tissue masses have clinical manifestations similar to traumatic or reactive hyperplastic lesions. Anamnesis and radiological imaging methods are important to find the primary malignancy. In microscopic examination, tumour pattern, cell features and immunohistochemical methods may guide for primary malignancy. For the diagnosis of clear cell renal cell carcinoma metastasis, compact nests and sheets of cell with distinct membranes and clear cytoplasm are remarkable, and there may be clues of vascularization, blood lakes and intratumoral haemorrhage.

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E-PS-12-001
Tumour-like alveolar echinococcus
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Background & objectives: Alveolar echinococcus is a rare parasitic disease caused by fox tapeworm Echinococcus multilocularis and it is characterized by an asymptomatic incubation period of many years and the slow development of a primary tumour-like lesion.
Methods: Here we present a case diagnosed in our pathology department. 70-year-old female patient had epigastric pain and fatigue. Radiologically, there was mass lesions with heterogenous lobule contours and cavitation scattered in both lung parenchyma, some in conglomerated form and the liver and the right surrenal gland had mass lesion and calcifications. Wedge resection of the lung was performed.
Results: On macroscopic examination of the lung parenchyma, there were millimetric multilocular cysts. Histopathologically examination revealed thin walled multiloculated cystic structures in the lung parenchyma. There were areas with necrosis in the inner parts of these cystic structures and sharp-edged, birefringent structures, which are likely to be microbiological factors, were seen. Lung parenchyma contained inflammatory cells, fibrotic and anthracotic areas. There was histochemically staining with gomori-methenamine-silver and periodic-acid-schiff in the cystic laminated layers.
Conclusion: Alveolar echinococcus is a rare tumour-like parasitic disease. Humans are accidental intermediate hosts that are infected with contaminated food. It is relatively common in pandemic areas in the liver and lung. Serologic tests and histopathological examinations can produce a diagnosis.

E-PS-12-002
When schistosoma meets an ovarian fibroma - a case report
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Background & objectives: Urogenital schistosomiasis may have different presentations, particularly in women. It is considered to be a risk factor for human immunodeficiency virus (HIV) infection. Lower genital lesions may be easily accessed, although, in the Upper genital tract (UGT), may not.
Methods: We present a case of an Angolan 29-year-old woman, without relevant medical background, who was referred to our hospital due to a pelvic tumefaction. A petreal pelvic mass was palpated at physical exam. The ultrasonography and CT-scan described a right ovarian tumour and right oophorectomy was proposed, and performed.

Results: On gross dissection, the ovary weighted 1605g and measured 20x16.5x7cm, with smooth external surface. Section surface was solid, white and fasciculate. Histology showed a monotonous fusocellular proliferation, without necrosis or cellular atypia, strongly immunoreactive for WT1 and weakly positive for ER, calretinin and actin and negative for inhibin and desmin. The final diagnosis was of ovarian fibroma – a benign tumour. Incidentally, in one section, chronic inflammatory granulomatous reactions with eosinophils and foreign body multinucleated giant cells were found, surrounding structures that were compatible with Schistosoma eggs.
Conclusion: Schistosomiasis remains the second most frequent parasitic infection worldwide, affecting especially many African regions. It is a chronic infection that can have a large impact on female health status, since it can manifest as menstruation disorders, dyspareunia, infertility, pregnancy complications and be considered a risk factor for HIV infection. Schistosomiasis in the UGT is a rare disorder which may have an important influence in women's health and is poorly understood, hence the importance raising awareness to it.

E-PS-12-003
A rare case of huge hydatid cyst in spleen
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Background & objectives: We describe a rare case of echinococcus in a 64-year-old woman localized in the spleen. Echinococcus granulosus is quite common in Greece but rarely localized in the spleen.
Methods: Clinical examination and laboratory tests including ultrasound and computed tomography were performed. The patient underwent splenectomy, and the recessed organ underwent pathological examination.
Results: The patient presented with fever and with a feeling of fullness in the right abdomen. Clinical examination as well as ultrasound and CT scans revealed a cyst in the spleen of the patient which then underwent splenectomy. The pathology lab received a 470 gram spleen of 15X10X7.5 cm. After dissection an 8 cm cyst was found containing membranes and small cystic formations containing clear liquid. Moreover, classifications were observed in the walls of the cyst. The diagnosis was echinococcus cyst with multiple daughter cysts and scolices.
Conclusion: Greece ranks 1st in Europe and 2nd worldwide in echinococcus cases. The non-specific sub-clinical presentation makes the timely diagnosis and treatment of the disease almost impossible. Complications following rapture of the echinococcus cyst are severe and require immediate medical assistance. Localization in the spleen although rare can cause severe problems if not diagnosed and treated in early stages.

E-PS-12-004
Unusual presentation of pseudotumoral epidural schistosomiasis: a case report
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Background & objectives: Schistosomiasis is a highly frequent disease in less developed countries. The nervous system is the second most affected site, responsible for 20-30% of the cases. Commonly seen in myeloradicular location, the diagnosis is often presumptive, with rare epidural presentation.
Methods: A 26-year-old male, paraplegic patient, native of Cape Verde, looked for medical assistance in Fortaleza, Brazil. The magnetic resonance imaging (MRI) showed a 4.4 cm cystic lesion in the spinal posterior epidural space, at T8-T10 level, suspicious for neoplasm. Laminotomy and excision were performed. The histopathology report showed a granulomatous lesion with structures compatible with Schistosoma mansoni (SM) eggs.
Results: When outside the portal venous system, the SM manifestations are considered "ectopic" and can occur at any stage of the disease. The gap between the infection and the onset of symptoms can take days or years, what makes it important to ask about previous contact with water reservoirs, reported in most of the diagnosed cases, and confirmed by our patient during his childhood in Africa. Even when the clinical suspicion is neoplasia, the pathologist must be aware of parasitic lesions that can mimic other conditions.
Conclusion: The anatomopathological report revealed a granulomatous chronic inflammatory process with ovoid structures compatible with S. mansoni eggs. Although the diagnosis is often presumptive, the difficulty of recognizing the disease and operational issues have been described by health professionals as causal factors of the low frequency of diagnosis. The authors emphasize the importance of being aware of the parasitic nature of resected lesions, even in the absence of clinical suspicion.

E-PS-12-005
Coronavirus: features of morphology
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Background & objectives: Humanity has been familiar with the coronavirus, 3 out of 7 coronaviruses can cause severe damage to the lung tissue. In humans, the disease ranges from asymptomatic carriage to the development of severe forms of ARDS and pneumonia.
Methods: Analysed the results of 30 autopsies: 8 women and 22 men. The average age of women is 71.1 ± 7.8. The average age of men is 68.0 ± 11.4. The incubation period was estimated at 2-14, with an average of 3-5.2 days. The hospital stay was 12.5 ± 8.5 days, while 45.8% died in the first 7 days of hospitalization.
Results: At autopsy, lung damage was varied - from a bilateral pathological process to a lobar, segmental or focal lesion. Microscopic examination revealed changes in the interstitial tissue, diffuse damage to the alveoli, the picture of "hyaline" membranes. Exudative changes: intraalveolar oedema, erythrocytes, lymphocytes and plasma cells. With the addition of bacterial or fungal flora, a combined viral-bacterial or viral-fungal lesion of the lung tissue developed. Bacteriological examination revealed pathogenic flora in 87.5%. Staphylococcus aureus was found in 29.1% (57.1% - Staphylococcus aureus, 28.5% Staphylococcus Epidermidis, 14.2% Staphylococcus Haemolyticus). In 45.8% of cases kl.pneumoniae was found, in 8.3% of cases E. coli, in 4.1% - candidiasis in combination with kl. pneumonia.
Conclusion: Thus, the analysis of autopsy studies showed that the main percentage of victims of coronavirus infection falls on the older age group with a premorbid background, aggravated by a number of chronic diseases. When staying in the hospital for more than 7-10 days, the addition of a bacterial infection was noted.

E-PS-12-006
Visceral leishmaniasis: case report of a rare disease in south-eastern Brazil
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Background & objectives: To report a case of visceral leishmaniasis, a rare disease in south-eastern Brazil.
Methods: Review of medical record and anatomopathological report. The bone marrow specimen was fixed in formalin, decalcified with ethylenediaminetetraacetic acid and subjected to histological processing.
Results: Female, 38 years old, is referred from her city to the haematology team due to a clinical suspicion of lymphoma. At the initial

evaluation, the patient had lymphadenomegaly, hepatosplenomegaly, fever and jaundice. Laboratory tests showed pancytopenia. The investigation continued with bone marrow biopsy, which exhibited hypocellularity for age and the presence of multiple amastigotes phagocytosed by macrophages, confirming the diagnosis of visceral leishmaniasis infection. The patient was treated with liposomal amphotericin B (6 ampoules/day). There was clinical and laboratory improvement after treatment, the patient was discharged and started the follow-up with the infectiology team.
Conclusion: Visceral leishmaniasis is a rare disease in south-eastern Brazil. Brazilian epidemiological data show that 100 cases of the disease were reported in the state of São Paulo in 2019, leading to an incidence of 1 case per 440.000 inhabitants. Bone marrow biopsy, although an invasive procedure, gives precise diagnosis of visceral leishmaniasis and may be considered when indicated.

E-PS-12-007
An uncommon testicular tumour mimic: a case report
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Background & objectives: Infectious processes can clinically mimic testicular tumours, by taking the form of space-occupying lesions/pseudotumours which render challenging radiological differential diagnosis, namely in the setting of lesions ineligible for biopsy. Herein, we present an instance of unsuspected active tuberculous orchiepididymitis.
Methods: A 75-year-old male, with previously diagnosed non-muscle invasive bladder cancer (NMIBC) managed through intravesical Bacillus Calmette-Guérin (BCG) instillation, presented with recurrent testicular pain. The ultrasound showed bilateral hydrocele and a heterogeneous hypervascular 2.4x1.9cm testicular nodule. The patient underwent antibiotherapy, without symptomatic improvement, and hence bilateral hydrocelectomy was performed. Due to sustained clinical suspicion of neoplasm, the testicle was later excised.
Results: A 4x2.2x1.9cm orchidectomy specimen was received. Gross sectioning revealed a 1.9x1.9x1.6cm nodule in the lower pole, with caseous-like central necrosis and with a yellow-brownish rim. Histologically, an inflammatory process involved both the epididymis and the testicular parenchyma, displaying confluent epithelioid granulomas with extensive necrosis, rare multinucleated giant cells and Schaumann bodies. Acid fast bacilli were highlighted by Ziehl-Neelsen stain in the necrotic debris. No neoplastic tissue or additional microorganisms were identified. Taking the clinical background of BCG therapy into account, the findings of active tuberculosis were regarded as BCGitis.
Conclusion: NMIBC patients treated with BCG may suffer iatrogenic genitourinary or even systemic infection, which may force therapy termination. Tuberculous orchiepididymitis has been scarcely described, occurring as late as 56 weeks after the last instillation. Mycobacterial traces may be detected in about half of the cases, highlighting the feasibility of a diagnosis through less invasive procedures; however, a negative microbiological study does not exclude the possibility of a BCG infection. The patient has since undergone anti-tuberculous therapy and remains clinically stable.

E-PS-12-008
Solitary coin lesions of the lung: a case report of pulmonary dirofilariasis
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Background & objectives: Solitary coin lesions of the lung have a broad differential diagnosis including benign disease processes and malignancies. The purpose of this case is to present a rare pathology in our country and a literature review.
Methods: We report the case of a 38-year-old immunocompetent man who presented to his family doctor with wrist joint pain; bilateral palmar, left foot, lower lip and gluteal oedema; epigastric pain and diarrhoea. He was a former smoker who had quit 4 years ago. On physical examination, the patient had sting injuries of insect or flea and an antihistamine was prescribed.
Results: Two days later he presented to the emergency department with angioedema of the right hemiface. He had no respiratory or gastrointestinal complaints neither fever or other constitutional symptoms. Laboratory studies showed eosinophilia (12.5%). Computed tomography of the chest revealed a well-defined 4 cm nodule located on the middle lobe. A VATS wedge resection of the lesion was performed. On microscopic examination a well-circumscribed necrotic nodule was identified, containing Charcot-Leyden crystals and remnants of Dirofilaria sp., surrounded by a granulomatous inflammatory process in the periphery, with no evidence of neoplastic cells.
Conclusion: Pulmonary dirofilariasis is a rare condition most often caused by Dirofilaria immitis, a zoonotic nematode transmitted to humans by mosquitos. Filarial larvae enter the subcutaneous tissue, travel to the pulmonary vasculature and lodge in small arteries, producing infarcts. These are visible on chest radiographs as 'coin lesions'. Although these lesions are usually identified by chance in asymptomatic patients, they are often assumed to be malignant. It is therefore crucial to include dirofilariasis in the differential diagnosis of pulmonary coin lesions.

E-PS-12-009
Strongyloidiasis: an unexpected diagnosis on gastro-intestinal biopsies
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Background & objectives: Strongyloidiasis is one of the most common digestive parositosis in the world with more than 70 million people infested, that is barely known in non-endemic regions. Objective: to show the clinical and pathological aspects of gastrointestinal anguillulosis.
Methods: We report a case of gastrointestinal strangylodosis diagnosed on gastric and duodenal biopsies.
Results: The patient is a 68-year-old man presenting with chronic diarrhoea, vomiting and fatigue. The performed explorations revealed hypereosinophiilia, with negative parasitological stool examination. The gastroduodenal endoscopy was held revealing erosive gastritis and duodenitis lesions with whitish stipplings in the duodenum. Multiple biopsies were conducted. The duodenal biopsy revealed an eroded mucosa with subtotal villous atrophy, hyperplastic crypts, a regenerative epithelium and cryptitis. The chorion contained an active lymphocytic inflammatory infiltrate, rich in eosinophilic polynuclear cells. The bottom of the crypts were occupied by PAS positive eggs and eelworm larvae, extending to the antral and antrofundic regions. Antral and antro-fundic biopsies showed active chronic pangastritis lesions without HP nor glandular atrophy.
Conclusion: Histological examination of gastroduodenal biopsies may be the key exam for the diagnosis of gastrointestinal strongyiloidiasis, particularly in when parasitologic analysis is negative.

E-PS-13 | Molecular Pathology E-Posters

E-PS-13-001
NTRK rearrangement in MSI-H and KRAS, NRAS and BRAF wild-type colorectal carcinomas
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Background & objectives: Colorectal carcinomas (CRC) with microsatellite instability (MSI-H) and KRAS, NRAS and BRAF wild-type (wt) present a high frequency of rearrangements in NTRK gene. Our objective is to study the status of NTRK and to confirm results with different molecular methodologies.
Methods: From 2015 to 2017, 18 cases with MSI-H by immunohistochemistry (IHC) and BRAF wt by pyrosequencing are retrieved.
From 2017 to present, 288 MSI and KRAS/NRAS/BRAF studied cases are recovered.
In our series, 7 MSI-H and KRAS/NRAS/BRAF wt cases are selected, in 5 of them NTRK was performed (IHC, Genefusion Idylla assay and NGS).
Results: Of the 5 cases, 1 case (20%) was positive and 4 cases (80%) were negative. Positive NTRK case was confirmed with all methodologies.
One case wasn't analysed by NGS due to technical difficulties (poor DNA libraries).
One of the NTRK negative cases showed an FGFR2 rearrangement by NGS.
NTRK positive case showed cytoplasmatic and membranous staining by IHC, GeneFusion assay indicated NTRK1 gene positive and NGS confirmed NTRK1/TPM3 rearrangement.
Conclusion: In our series, 20% (1/5) of MSI-H KRAS/NRAS/BRAF wt CRC were NTRK rearranged.
All methodologies were optimal to detect NTRK rearrangements.
Different methodologies provide complementary information about rearrangements, being NGS the most specific.
NGS presents technical limitations in a percentage of cases but offers the most comprehensive multi-gene analysis.

E-PS-13-002
Complete pathological response to crizotinib in a gastric inflammatory myofibroblastic tumour carrying TFG-ROS1 fusion
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Background & objectives: Almost 60% of inflammatory myofibroblastic tumours (IMT) carry ALK gene rearrangement. Recently, other gene fusions have been reported. Our aim is to describe the histologic changes seen in a gastric IMT carrying a TFG-ROS1 fusion with complete response to crizotinib.
Methods: We present a rare case of a gastric unresectable IMT with TFG-ROS1 fusion on a 32-year-old man with no medical history. Next-generation sequencing (NGS) OncomineTM Focus Assay (ThermoFisher Scientific) was initially performed to confirm the diagnosis. Morphological and immunohistochemical features of the resection specimen after neoadyuvant therapy with ROS1/ALK/MET tirosin kinase inhibitor crizotinib are described.
Results: The diagnosis of IMT was established after endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA). NGS OncomineTM Focus Assay revealed a TFG-ROS1 fusion involving exons 1–4 of TFG and exons 35–43 of ROS1. The patient received crizotinib during one year before surgery. Examination of the resection specimen demonstrated a 7 cm mass involving the gastroesophageal union and the stomach. Pathologic examination showed a stromal sclerohyaline change composed predominantly of thick haphazardly arranged collagen fibres with cracks intermixed with slightly atypical spindle cells with fibroblastic appearance. Immunohistochemically, atypical spindle cells showed negative staining for SMA, desmin and ROS1. Focal areas of neo-ossyfication, lymphoplasmacytic inflammation, reactive lymphoid aggregates and dystrophic calcifications were also identified.
Conclusion: Currently, reports describing complete pathological response to crizotinib in patients with IMT are quite limited. To the best of our knowledge this is the first case that details the histologic changes after tirosin kinase inhibitor crizotinib and also supports cytological samples as a valid source of high-quality DNA for next generation sequencing (NGS) analysis.

E-PS-13-003
A possible off-target resistance mutation in a metastatic thyroid carcinosarcoma harbouring a NTRK3 gene fusion
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Background & objectives: Neurotrophic-tropomyosin receptor kinase (NTRK) genes are implicated in the neuronal cell physiology. NTRK genetic alterations promote oncogenesis in various types of tumours. Although rare, NTRK gene fusions demonstrate specific druggability. Resistance mutations have been described but are still largely unknown.
Methods: A 80 y.o. female with a forty-year past medical history of right hemithyroidectomy presented with shortness of breath. Multiple hypermetabolic pleural nodules associating pleuresia were found. A biopsy revealed a pleural metastasis of a thyroid carcinosarcoma, associating a double component: epithelioid (papillary architecture, positive for AE1/AE3, TTF-1, PAX8 and Thyroglobulin antibodies) and sarcomatoid (spindle-cell architecture, positive for Vimentin only).
Results: A ETV6-NTRK3 fusion transcript was detected by Next Generation Sequencing (NGS) using a RNA Oncomine Focus Assay panel. Treatment with Larotrectinib was started, with a spectacular, but partial response. However, after 6 months, the patient developed paraparesis. The spinal MRI showed multiple lytic bone infiltrates, invading the spinal canal and compressing the spinal cord. Surgical decompression was performed, as well as biopsies, which revealed a bone metastasis of the previous tumour, comprising only the sarcomatoid component. Molecular analysis confirmed the previous fusion, as well as a p.R88Q mutation of the PIK3CA gene, which was not detected previously. The patient succumbed before any other new treatment was given.
Conclusion: Although rare, NTRK gene alterations characterize oncogenic pathways in different types of tumours. Tumours harbouring NTRK gene fusions can be successfully treated with TRK inhibitors. On the other hand, resistance mutations may appear, leading to changes in treatment strategy. In the current case report, a NTRK downstream pathway mutation was demonstrated using NGS techniques. This PIK3CA gene mutation could be hypothesized as an off-target resistance mutation. However, tumour heterogeneity cannot be excluded. Further studies are needed to support our hypothesis.

E-PS-13-004
A comparative study between neoplastic nuclei percentage and allelic fraction in lung carcinomas analysed by NGS
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Background & objectives: Accurate definition of malignant cell fraction is pivotal to determine the quantity of tumour DNA/RNA acceptable for molecular testing. Our aim was to verify the correlation between neoplastic nuclei percentage(NNP) and allelic fraction(AF) detected by NGS in a series of lung cancer.
Methods: We revised the data resulting from NGS analysis of 349 lung carcinomas, studied in our Institute from January-May2020. We selected and analysed 320 cases, that presented at least one mutation, aiming to verify a correlation between morphological assessment of NNP, made by a pathologist/technician, and the allelic fraction detected. All cases with lower NNP(5-10%) were reviewed by another pathologist.
Results: The genes more frequently mutated were: KRAS (40%), EGFR (33%), BRAF (6%), HER2 (5%) and MET (2,5%). In 248 cases (77,5%) we observed an expected relation between NNP and AF of the mutated gene by NGS, in other words a relation approximately from 2:1. In 72

cases (22,5%) there was no correlation, with a low NNP compared to the AF. These cases were re-evaluated by another pathologist in order to exclude an inter-observer disagreement in the estimation of NNP. Nevertheless, the absence of correlation was confirmed.
Conclusion: In most of the cases(77,5%) there was a good agreement between the estimation of NNP and the AF. However, in 22,5%cases there was possible underestimation of the NNP, which has been demonstrated in other studies. Tumour heterogeneity, differences between the real number of neoplastic nuclei observed and those dissected for NGS, due to different section levels of cutting and a rare possibility for a double/triple hit in some of the genes, can explain the discrepancies found in about(1/4)of the cases.

E-PS-14 | Nephropathology E-Posters

E-PS-14-001
Renal malakoplakia: an unexpected diagnosis
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Background & objectives: Malakoplakia is an uncommon granulomatous infectious process resulting from partially digested phagocytosed bacteria, most frequently observed in the urinary tract as a recurrent infection complication. We report a case of renal malakoplakia in a patient with history of renal transplantation.
Methods: A 61-year-old female, submitted to renal transplantation in February 2019 due to advanced renal chronic disease, developed severe urosepsis Escherichia coli-related and concomitant graft dysfunction in November 2019. Renal biopsy was hence performed to assess signs of rejection, using ancillary studies of the department's protocol and also Gram, von Kossa and Prussian blue stains.
Results: Two core biopsies of 7 and 12 mm were received, comprising a total of 16 glomeruli. There were no signs of rejection. Noteworthy, in 60% of the sample, there was architectural effacement and it was possible to identify numerous interstitial histiocytic foamy cells (confirmed with immunohistochemical staining for CD68) with several basophilic cytoplasmatic inclusions, evidentiated by von Kossa and Prussian blue stains, consistent with Michaelis-Gutmann bodies. Given these morphologic findings and histochemical results, a diagnosis of malakoplakia was made.
Conclusion: Malakoplakia may occur in many organs, namely in the urinary tract and especially in the bladder where E. coli is the most frequent infectious agent. Our case highlights how the detection of malakoplakia emphasized that the infectious process had extended proximally throughout the whole urinary tract and was the culprit of the clinical renal dysfunction, offering an immediately manageable condition. However, despite immunosuppression readjustment and antibiotherapy, the patient briefly progressed to dialysis.

E-PS-14-002
Lysozyme amyloidosis - challenges of a rare diagnosis
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Background & objectives: Lysozyme amyloidosis is an extremely rare and probably under-diagnosed form of hereditary amyloidosis, with around fifty reported cases. Lysozyme amyloid deposits typically accumulate in the kidney, liver, gastrointestinal tract and spleen. We herein report a case of this rare entity.
Methods: A 43-year-old female, with a previous history of hypertension and atrophic gastritis, and no relevant family history, was admitted in our institution with acute kidney injury, a proteinuria of 0,5g/L and marked cholestasis. Abdominal ultrasonography showed hepatomegaly. Considering clinical features and an appropriate autoimmune panel, the diagnosis of primary biliary cholangitis was proposed. Kidney and liver biopsies were performed.
Results: Kidney biopsy showed amyloid deposits within the glomeruli, interstitium and vessel walls. There was also severe interstitial fibrosis and tubular atrophy. Amyloid typing by immunohistochemistry showed expression of lysozyme and serum amyloid A (SAA). Immunofluorescence for light chains (kappa and lambda) was negative. SAA concentration was in the normal range. On liver biopsy there were no bile duct lesions, and amyloid deposits (positive for lysozyme and SAA) were found within vessel walls. On follow-up kidney function progressively deteriorated to pre-dialysis stage. Cardiac involvement was suspected due to concentric left ventricular hypertrophy. Mass spectrometry of amyloid deposits and genetic study of lysozyme gene is ongoing.
Conclusion: The variable penetrance of hereditary forms of amyloidosis often results in absence of a positive family history which, allied to significant overlap of symptoms between these and other forms of primary amyloidosis, makes correct diagnosis a challenge. Heterogeneity of amyloid proteins, lack of specific antibodies for different amyloid proteins and high background staining are some of the difficulties of amyloid typing by immunohistochemistry. In equivocal cases or when less common/unusual amyloid types are suspected mass spectrometry could be helpful.

E-PS-14-003
Coexistence of lupus nephritis and thin basement membrane. Case report
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Background & objectives: Kidney biopsy plays an important role for an accurate lupus nephritis (LN) diagnosis, treatment choice and prognosis evaluation. Eventually, the biopsy can diagnose coexisting kidney entities, which may have an impact on prognosis.
Methods: We present the case of a middle-aged woman diagnosed with systemic lupus erythematosus (SLE) 15 years before. She presented a LN flare with haematuria, proteinuria, positive anti-DNA, and a decrease in complement levels, after withdrawal of immunosuppression. Prednisone and mycophenolate mofetil (MMF) were restarted, and a kidney biopsy was performed.
Results: The light microscopy study showed glomeruli with mildly increased mesangial matrix and cellularity. There were also focal endocapillary hypercellularity, without extracapillary proliferation. Immunofluorescence showed intense positivity in mesangial area and capillary loops of IgM, C3 and C1q. These findings were compatible with class III LN according to the International Society of Nephrology/Renal Pathology Society Classification for Lupus Nephritis (2018), with an activity score of 5/24 and a chronicity score of 1/12. The electron microscopy shows subendothelial structured electron dense deposits with fingerprint-like morphology and a diminished thickness of glomerular basement membrane (214 nm). The findings were consistent with class III LN with thin glomerular basement membrane (TGBM).
Conclusion: Thin glomerular basement membrane is a common ultrastructural finding in patients with other glomerulopathies, including lupus nephritis. Electron microscopy is a key technique for a complete evaluation of renal histology. There is missing information about the relevance of this finding on the clinical evolution of other glomerular diseases and the nature of the association.

E-PS-14-004
Histological features of unusual cases of ANCA associated glomerulonephritis in children
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Background & objectives: Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis is a rare but severe condition in childhood. Clinical presentation and pathology is often heterogeneous and treatment is not well defined for this population.
Methods: We describe two cases of ANCA vasculitis in children with renal involvement, who had a kidney biopsy for diagnosis.
Cases description: First case is a 2-year-old boy with end-stage renal disease (ESRD) because of rapidly progressive glomerulonephritis. He was diagnosed when he was 3 months old during a hospital admission because of a suspected Urinary tract infection.
Results: He started with oliguria, haematuria, proteinuria, elevated serum creatinine and refractory hypertension with positive A-ANCA, requiring continuous hemodiafiltration. The kidney biopsy showed an extensive global glomeruloesclerosis and few viable glomeruli with pauci-immune extracapillary proliferative glomerulonephritis, with fibrocellular and fibrous crescents (sclerotic class). Despite treatment with steroids and rituximab he is on peritoneal dialysis and is awaiting a kidney transplant. Last case is a previously healthy 5-year-old patient who presented with nephritic syndrome of torpid evolution and low C3 levels. Renal function worsened progressively, and he needed extrarenal depuration techniques. P-ANCA was positive and kidney biopsy showed diffuse crescentic glomerulonephritis, with crescents` formation in above 70% of glomeruli.
Conclusion: The direct immunofluorescence showed C3 positive staining(2+) in mesangium and glomerular capillary wall. Genetic test for complement disorders was negative. He received two doses of rituximab, ten plasmapheresis sessions and intravenous and oral corticoids with clinical improvement. Five months after treatment, he has normal GFR.
Conclusion: kidney biopsy is important for renal vasculitis diagnosis in children, were there is a broad differential diagnosis. The Treatment of paediatric ANCA-vasculitis is based on adult guidelines. More studies are needed to establish therapy.

E-PS-14-005
IgA nephropathy in patient with X-linked Alport syndrome – a case report
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Background & objectives: X-linked Alport syndrome (AS) is caused by COL4A5 mutation and presents as a progressive nephritis with haematuria, sensorineural hearing loss, ocular abnormalities, and early progression to end-stage renal disease. We present a 23-year-old male with X-linked AS and IgA nephropathy.
Methods: At the age of 3 the patient presented with haematuria and proteinuria, underwent kidney biopsy and was diagnosed with AS. At the age of 21, diagnosis was confirmed by genetic testing. A pathogenic splice-site variant COL4A5 c.991-1G>C was found. During a 20-year follow-up, patient presented with haematuria, average 24-hour proteinuria of 1.5 g, keratoconus, hearing loss and preserved renal function.
Results: At the recent follow-up (patient's age 23) 24-hour proteinuria was 8.9 g. The second kidney biopsy was performed. Light microscopy showed perihilar focal segmental glomerulosclerosis, diffuse mesangial and focal endocapillary hypercellularity, and necrosis in one glomerulus. Minimal interstitial fibrosis and tubular atrophy was noted. Immunofluorescent microscopy showed global granular positivity (+) for IgA, IgM and C3, and weak positivity for kappa and lambda light chains. Electron microscopy showed classic AS morphology combined with numerous mesangial and some subendothelial, intramembranous and subepithelial deposits. A diagnosis of Alport syndrome with IgA nephropathy was made. Oxford score was M1, E1, S1, T0, C1.
Conclusion: Genetic testing has increasingly been applied to confirm diagnose of AS. However, kidney biopsy is still the only method that gives a precise insight into the condition of the kidney tissue and can detect other diseases which can be overlooked with genetic testing only.

E-PS-14-006
Multiorgan transplantation from a deceased donor with intravascular large B-cell lymphoma: a case report
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Background & objectives: Intravascular large B-cell lymphoma (IVLBCL) is a rare subtype of non-Hodgkin lymphoma (<1%), characterized by atypical lymphocytes accumulated within small blood vessels. IVLBCL has an uncommon clinical presentation and poor prognosis frequently diagnosed post-mortem. Renal involvement is rarely described.
Methods: This report presents the transplantation of two kidneys and the liver from a deceased donor with a Cerebral Vascular Accident (CVA). Routine preimplantation biopsies are performed in all kidney transplant recipients at our centre for assessing basal donor derived histological lesions. An IVLBCL lymphoma was diagnosed in the preimplantation biopsy at day +0 in one of the kidney graft.
Results: After a multidisciplinary discussion, we opted to remove the renal allografts from the two recipients, which confirmed the presence of the IVLBCL in both kidneys. A histological examination showed infiltration of the renal parenchyma by abnormally large lymphoid cells with prominent nucleoli, consistent with lymphoma. These cells proliferated in the lumina of glomerular, peritubular, and interstitial capillaries. Immunophenotyping showed the expression of LCA, CD20, CD79, and MUM1, whole CD10 and CD30 were negative. The Ki67 index was 95-100%, reflecting a high proliferative activity.
Conclusion: Kidney biopsy remains a valuable tool in assessing the quality of the organ donor. For instance, it is the only procedure capable to detect the presence of malignant lymphoproliferative diseases of non-forming solid masses non-detected by imaging study. Our case highlights the value of performing harvest biopsies as a tool to exclude rare donor-derived tumours.

E-PS-14-007
Anti-glomerular basement membrane disease, a case report of an uncommon entity
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Background & objectives: Anti-glomerular basement membrane (anti-GBM) disease is a rare small vessel vasculitis that can affect both the glomerular and pulmonary capillaries. We aim to describe the case of a 40-year-old woman who presented acute renal failure due to anti-GBM antibody-positive vasculitis.
Methods: Study of glomerular disease revealed elevated titers of anti-GBM antibodies. The patient was started on haemodialysis and treated with methylprednisolone pulse therapy, followed by oral prednisone and cyclophosphamide pulse. A renal biopsy was requested. Light microscopy with histochemical stains and direct immunofluorescence were realized.
Results: Renal biopsy showed 21 glomeruli, one of which was sclerosed. The remaining were severely affected. They exhibited extensive disruption of Bowman's capsule, lysis of the glomerular tuft, and cellular crescents formation, most of them associated with segmental fibrinoid necrosis and neutrophilic infiltrate with karyorrhexis. Tubulointerstitial component revealed varying degrees of interstitial oedema, interstitial

leukocyte infiltration, tubulitis, and tubular epithelial simplification most pronounced adjacent to inflamed glomeruli. Direct immunofluorescence study showed exclusively linear deposits of IgG along the glomerular capillary basement membrane.
Conclusion: Anti-GBM usually presents as rapidly progressive glomerulonephritis (RPGN), with or without pulmonary haemorrhage. Crescent formation is the histopathologic hallmark of the anti-GBM disease. The proportion of crescents observed in the biopsy sample correlates strongly with the degree of renal impairment at presentation. Since it can lead to rapid deterioration in kidney function, prompt diagnosis and treatment are very important to improve outcomes.

E-PS-14-008
Membranous nephropathy after hematopoietic stem cell transplantation: renal manifestation of graft versus host disease (GVHD)?
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Background & objectives: Nephrotic syndrome (NS) after allogeneic hematopoietic stem cell transplantation (HSCT) is a rare phenomenon, generally associated with acute or chronic GVHD. Most cases correspond to membranous nephropathy or minimal change disease that appear after changes in immunosuppression treatment.
Methods: We describe a clinical case of membranous nephropathy after HSCT diagnosed by renal biopsy from which we will review the clinical-pathological characteristics and the main series published in the literature covering this topic.
Results: A 66-year-old woman with chronic myeloid leukaemia treated with HSCT who 24 months later, initiated NS with normal immunological analysis and proteinogram. A renal biopsy revealed thickening of the glomerular basement membrane and spike type projections with rigid capillary lumens. The tubulo-interstitial component showed mild toxicity due to calcineurin inhibitors with minimal inflammatory infiltrate. By immunofluorescence, a global and diffuse granular deposit and intense subepithelial distribution for IgG+C3 was observed, being diagnosed with membranous nephropathy.
After diagnosis, blood Anti-PLA2R and Anti-thrombospondin were negative and treatment with steroids at a dose of 1mg/kg/d and tacrolimus was started, combining diuretics and ACEIs as concomitant antiproteinuric management.
Conclusion: Glomerular lesions after HSCT with nephrotic syndrome are usually due to membranous nephropathy or minimal change disease. Most are associated with concomitant GVHD and have a median onset of 20.5 months after HSCT, frequently related to changes in immunosuppression treatment. Clinical suspicion and renal biopsy allow a specific diagnosis. Regarding treatment, the main case reports document a combination with steroids and immunosuppressive medications, although in some cases steroid monotherapy may be sufficient.

E-PS-14-009
Large B-cell lymphoma presenting as acute kidney injury: a case report
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Background & objectives: Although rare, the pattern of kidney injury in non-Hodgkin lymphoma is diverse, ranging from glomerular nephropathies, interstitial diseases and intravascular lymphomatous infiltration. We report a case of large B-cell lymphoma with acute kidney injury (AKI) as the sole clinical manifestation.
Methods: A 69-year-old male with a history of hypertension and diabetes mellitus was admitted for AKI (serum creatinine was 5.6mg/dL). He had no proteinuria or haematuria. Lab tests also showed are generative normocytic anaemia and mild lymphopenia. A whole-body native CT scan was unremarkable. Bone marrow biopsy showed no signs of a lymphoproliferative or neoplastic process.
Percutaneous kidney biopsy (KB) was performed.
Results: Histological examination of KB showed almost complete replacement of the interstitium with a population of large lymphoid-like cells which were arranged in a vague nodular pattern. The infiltrating cells had a large size with a big nucleus and visible nucleoli. The glomeruli demonstrated ischemic changes. Immunofluorescence and electron microscopy were unremarkable. IHC demonstrated infiltrating cells positive for CD20, BCL6, and MUM1 and negative for CD5 and CD10. Ki67 positivity was estimated at 75%. A diagnosis of non-Hodgkin diffuse large B-cell lymphoma was made.
FDG PET-CT showed a diffusely intense FDG uptake in both kidneys, liver and testes with a standard uptake value of 5.5.
Conclusion: The patient was started on anthracycline-containing chemotherapy associated with rituximab (R-CHOP).
Diffuse large B-cell lymphoma infiltrating the kidney is a rare finding. The present case highlights the importance of renal biopsy in early diagnosis and prompt treatment of patients presenting with AKI.

E-PS-14-010
Infection-related glomerulonephritis due to Haemophilus influenzae: a case report
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Background & objectives: Infection-related glomerulonephritis (IRGN) is an immune complex mediated disease associated with nonrenal infection by certain bacteria strains, most frequently Steptococcus spp. and Staphylococcus spp. We report a rare case of non-IgA IRGN associated to Haemophilus spp.
Methods: A 60-year-old male patient presented with acute nephritic syndrome (haematuria with dysmorphic red blood cells, 24h proteinuria 0.6g, serum creatinine 7mg/dL). Two weeks before admission he suffered an episode of pharyngitis.
Percutaneous kidney biopsy (KB) was performed and the specimen was assessed by light, immunofluorescence and electron microscopy. Identification of Haemophilus spp. was performed according to standard microbiology laboratory procedures.
Results: The patient had hypocomplementemia with a low C3 and a normal C4. Moreover, ASO level, ANA, dsDNA, ANCAp and ANCAc were negative. Haemophilus influenzae was isolated from a pharyngeal exudate.
The KB showed 10 glomeruli out of which 4 were globally scarred. Most of the glomeruli demonstrated endocapillary hypercellularity with frequent neutrophils in the capillary lumens. Some glomeruli demonstrated a mesangial hypercellularity. Few tubules had intraluminal red blood cells casts. Immunofluorescence microscopy showed bright (3+) granular deposits for C3 and IgG. Electron microscopy showed small electron dense immune complex type deposits located in the subendothelial areas and a few subepithelial humps. The diagnosis was diffuse proliferative infection-related glomerulonephritis.
Conclusion: The patient was started on antibiotherapy according to the antibiogram, and on prednsione 0,5mg/Kgc. At one month from diagnosis his serum creatinine decreased to 1.9mg/dL and the C3 was in normal limits.
There are only few case reports of Haemophilus spp. associated with IRGN. Usually, the pathological pattern of injury resembles IgA nephropathy. We report a rare case of non-IgA infection-related glomerulonephritis associated to Haemophilus spp.

E-PS-15 | Neuropathology E-Posters

E-PS-15-001

Secondary gliosarcoma with osteoblastic and chondroblastic differentiation and associated gossypiboma

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Background & objectives: Gliosarcoma (GS) is a rare biphasic variant of IDH-wildtype glioblastoma (GBM). When diagnosed after a high-grade glioma, GS is classified as secondary (SGS).
We report an SGS with a predominance of malignant osteoid-chondroid mesenchymal component, together with a gossypiboma.
Methods: A 59-year-old man had an IDH-wildtype GBM WHO grade IV partially removed and underwent radiotherapy with concomitant temozolomide (TMZ) and a further six cycles of maintenance TMZ. Fourteen months after surgery the patient worsened headaches and RMI confirmed tumoral progression by showing a partly calcified tumour on the irradiated area. The lesion was incompletely excised.
Results: Histologically it was a malignant tumour with an astrocytic component globally identic to the GBM diagnosed before but intermingle with a significant mesenquimatous component constituted of malignant-appearing cartilage and bone tissue, resembling chondroblastic osteosarcoma. GFAP was diffusely positive on the glial component and showed perivascular positivity on the sarcomatous areas. P53 was positive in both components. At the lesion's periphery we identified necrosis and basophil amorphous material, compatible with surgical haemostatic material, surrounded by macrophages and giant multinucleated cells.
Our diagnosis was of SG with osteoblastic and chondroblastic differentiation and an associated gossypiboma.
The patient needed subsequent admissions for surgical site infection treatment but unfortunately died 52 days after surgery.
Conclusion: Current molecular evidence supports a monoclonal origin of both glial and sarcomatous components, the latter usually presenting as a fibrosarcoma-like proliferation. Osteoid and chondroblastic differentiation are exceptionally rare morphologies of this uncommon GBM variant, with only a few described cases in SGS.
SGS's patients harbour an unfavourable prognosis, and further research is required to better understand this tumour.
Foreign body reaction to the haemostatic material was an additional finding.

E-PS-15-002

Pure sellar gangliocytoma: a case report

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Background & objectives: Gangliocytomas (GCs) are benign neuroepithelial tumours accounting for less than 1% of intrasellar lesions. Most coexist with a pituitary adenoma and patients commonly have endocrine manifestations.
We report a case of a GC without an associated adenoma or hormonal elevation.
Methods: A 40-year-old woman with depressive disorder presented sudden psychotic behaviour. CT revealed no signs of acute vascular lesions but showed an expansive lesion on sella turcica, suggestive of a pituitary macroadenoma. MR confirmed a 2.4 cm lesion with supra and slightly infrasellar extension. The patient had no endocrine manifestations, and hormonal levels were normal.
Postoperative MR showed complete tumour resection.
Results: All fragments were included for histopathological examination, revealing a population of mature ganglion neurons on a neuropil fibrillary background with scattered and perivascular lymphocytes. On immunohistochemistry ganglion neurons expressed synaptophysin, chromogranin, neurofilament, and also ACTH. The other pituitary hormones were negative.
Fragments of normal pituitary were observed, but there was no evidence of hyperplasia or adenomatous component.
Complete tumour resection combined with adenoma absence on histopathological analysis prompted a diagnosis of isolated/pure gangliocytoma.
Four months after tumour resection, the patient is asymptomatic.
It is unlikely that the psychotic symptoms were related to the lesion.
Conclusion: Pure CGs are exceedingly rare sellar tumours, with only 21 cases reported. Its diagnosis relies on histopathological analysis, as image studies cannot differentiate pure CGs from mixed gangliocytoma-adenoma or conventional pituitary adenoma.
In the case we present, although ACTH was detected by immunohistochemistry, there was no peripheral hormonal secretion. ACTH expression on pure sellar CGs supports the theory that tumour cells represent a spectrum of mixed adenomatous and gangliocytic features.

E-PS-15-003

The distribution of cases of atypical meningioma based on age and gender in West Romania

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Background & objectives: Atypical meningioma is a tumour with an unpredictable evolution, a complete resection usually not being possible. The purpose of this paper is to determine the incidence rate of atypical meningioma based on the gender and age of patients.
Methods: Based on the pathological reports from the archives of our Pathology Department, a retrospective study involving 692 patients diagnosed with brain tumours during 2018-2020 was conducted. The parameters chosen for this study were the type of tumour (atypical meningioma), age of patients, and gender.
Results: Out of the total number of 692 patients, 138 (19.94%) were diagnosed with meningioma, and out of the total cases of meningioma, 47 (34%) were atypical meningioma (Grade II). The youngest patient was a 30-year-old male and the oldest was an 84 years old woman. The average age at the time of diagnosis was 62.33 years; 61% of the patients are females, with an average age of 63.1 years, whilst the average age in men is 62.4 years. Men tend to be more affected by this pathology at the ages of 65-75, not exclusively, whilst females are more prone to suffer from atypical meningioma at 45-65 years.
Conclusion: To conclude, atypical meningioma is a tumour of the nervous system that appears with predilection in women, at a younger age than in men. It must be stated that at the age of 60-70, the ratio between females and males tends to become relatively even. The results of our paper are in concordance with the international dedicated literature.

E-PS-15-004

An extremely rare case of giant cell tumour of the clivus

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Background & objectives: We present a case of a giant cell tumour of bone (GCTB) arising from the clivus.
Methods: A 36-year-old male arrived at our hospital with diplopia and a history of headaches during the last year. Computer tomography showed a mass of clivus extending to the sella turcica. We received several brown coloured, elastic specimens with total dimensions 3.2X3X0.5cm.
Results: Histologically, the neoplasma consisted of mononuclear cells, mainly round and focally spindle, in a vascular background with haemorrhage and haemosiderin pigment, separated by fibrous septa, without atypia

and 2-7 mitoses/high power field, and of numerous evenly distributed multinucleated osteoclast-like giant cells, without atypia or mitoses. Immunohistochemical study showed positivity against CD68, PGM1 whereas it was negative against CKAE1/AE3, GFAP and S100. Ki67 (MIB1) was positive in 7% of the neoplastic nuclei. Hyperparathyroidism was excluded. Thus, the diagnosis of giant cell tumour of bone was concluded.
Conclusion: GCTB is an uncommon, usually benign neoplasm of early adulthood, showing predilection for epiphyses of long bones. Skull GCTBs are extremely rare (0.51% of all GCTBs), especially those originating from the clivus. Surgery with complete resection is the current treatment of choice, though it is difficult to achieve.

E-PS-15-005
Giant thoracic paraspinal ganglioneuroma
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Background & objectives: Ganglioneuromas are rare benign tumours arose from neural crest cells of the autonomic nervous system. Well differentiated and usually asymptomatic, a favourable prognosis is expected after treatment. We report a case of a massive ganglioneuroma in a 14-year-old male.
Methods: A large paraspinal mass extended from T6 to T11 vertebrae was resected after a thoracotomy and fragments were sent to a histopathological examination. Gross description consisted of a well circumscribed, firm, encapsulated white-yellow tumour measuring 17×14×15 cm.
Results: Histologically, the tumour composed of scattered mature ganglion cells, Schwannian dense stroma and multiple mature nervous structures with fibrous areas. Within the stroma, fascicles of elongated Schwann cells with a single spindle-shaped wavy tachychromatic nucleus were present. Ganglion cells showed abundant eosinophilic cytoplasm with a single eccentric nucleus and prominent eosinophilic nucleolus. There were no significant atypia or mitoses found. Immunohistochemistry showed positive strains for S100 in both types of cells, Glial fibrillary acidic protein (GFAP) in Schwann cells, synaptophysin and chromogranin in ganglion cells, aiding in the diagnosis of ganglioneuroma. Ki67 marker was positive in under 1% tumour cells within the evaluated mass.
Conclusion: Ganglioneuromas represent a diagnostic challenge and constitute a problem of differential diagnosis with other intra-thoracic tumours, neurogenic tumours (ganglioneuroblastoma, neuroblastoma) or nerve sheath tumours (neurofibroma). Being asymptomatic as it grows slowly, it is usually an incidentaloma. Having such large dimensions when found, compressive symptoms may appear, but they fade away after surgical resection. Long term follow-up is recommended as rare cases of malignant transformations of Schwann cells were reported.

E-PS-15-006
Diffuse melanin pigmented neoplasm in the middle line of the CNS: primary CNS melanomatosis
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Background & objectives: We present a case of melanomatosis, a malignant diffuse primary melanocytic tumour of the CNS. It can clinically mimic a wide variety of conditions, including lymphoma, leukaemia, metastatic carcinoma, subacute meningitis, viral encephalitis hypotrophic cranial pachymeningitis and others.
Methods: A 58-year-old man was admitted to the Neurosurgery Department with obstructive hydrocephalus. Brain MRI with godalinium contrast showed a lesion of abnormal signal located in the middle line. Ventriculoscopy revealed dissemination, probably by melanocytes of the choroid fissure, septum pellucidum, infundibulum, tuber cinereum, mammillary bodies, floor of 3rd ventricle and wall of basal artery. Biopsy was performed.
Results: We received five black pigmented specimens of maximum diameter 0,1-0,15cm. microscopic examination showed brain tissue infiltration by epithelioid cells containing melanin pigments in the cytoplasm, with focal pleomorphic features. There was no sign of necrosis, anaplasia or increased mitotic activity. Melanin bleaching was performed before immunohistochemistry. The cells stained diffusely positive for Mart1, HMB45, SOX10, foca;;y positive for S100 protein and negative against GFAP, synaptophysin, CD34. Ki67 proliferation index (M1B1) was estimated 5%.
A full body scan was unremarkable in other sites and clinical examination didn't reveal any dermal melanocytic lesion. Diagnosis of melanomatosis was established. The patient died about 3 weeks after administration.
Conclusion: Correlation of clinical, histological and imagine results as well as intraoperative state is mandatory. When dealing with melanin pigmented lesions of the CNS. Metastatic melanoma and other primary tumours of the CNS undergoing melanisation (melanocytic schwannoma, medulloblastoma, paraganglioma, various gliomas, meningiomas with melanocytic colonization) must be safely ruled out.

E-PS-15-007
Thymic carcinoma metastasizing to the brain: a case report
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Background & objectives: Thymic carcinomas, classified as type C thymomas according to the WHO classification, are rare epithelial malignancies with marked invasive tendency.
Methods: We report a case of a 57-years old male patient presented with abduens nerve palsy. Brain MRI showed heterogeneous morphology and bone erosion of the clivus. A stereotactic brain biopsy was performed.
Results: Microscopical examination showed anastomosing solid sheets and infiltrating small nests of highly cellular tumour cells with necrosis. The tumour cells were epithelioid with large hyperchromatic nuclei and prominent nucleoli, lying in a desmoplastic stroma containing small lymphocytes. Mitotic figures were frequent. In immunohistochemical staining the tumour cells were positive for: KerAEI/AE3, Ker7, Ker14, Ker5/6, Ker34βE12, Ker19, p63, EMA, pCEA, CD5, CD117, and negative for: vimentin, Ker20, TTF1, CgA, SYP, p16, CDX2, RCC, PAX8, Gata3, β-Catenin, CD34, BerEp4, Tdt, S100, ThG, PTH, p53, MUC5AC. Ki67 proliferation index was approximately 35-40%. Morphology and immunohistochemistry established the diagnosis of metastatic thymic carcinoma
Conclusion: It is extremely rare and only 45 such cases have been reported in the literature, associated with worse prognosis and short survival. We should always consider it in the differential diagnosis of intracranial lesions of unknown primary.

E-PS-15-008
Fatal toxic leukoencephalopathy and bilateral basal ganglia necrosis associated with inhaled heroin and cocaine use: a case report
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Background & objectives: Heroin-associated leukoencephalopathy is a rare complication of heroin fume inhalation. The pathogenesis is poorly understood and the diagnosis challenging. We present a case in a patient with a history of substance abuse and describe the neuropathological findings.

Methods: Detailed coronial autopsy was performed on the patient after a post-mortem interval of 5 days. Histological sampling of the brain was undertaken, and tissue slides were examined using a variety of histochemical stains.
Results: A 32-year-old male with a history of illicit substance abuse presented to the emergency department in status epilepticus. His friends confirmed recent heroin use. CT head showed symmetrical basal ganglia hypodensity with leukoencephalopathy. He was treated with naloxone, anti-epileptics, and antibiotics but failed to improve. He died 9 days after admission. Neuropathological examination showed bilateral symmetrical red necrosis within the globus pallidi. Histology demonstrated extensive demyelination of the central and gyral white matter with axonal sparing. Hair toxicology was consistent with heavy heroin and cocaine use in the 2 months preceding his death. The cause of death was deemed to be toxic leukoencephalopathy secondary to inhalation of heroin and cocaine.
Conclusion: Acute presentations of heroin-induced leukoencephalopathy are rare but should be considered in the context of illicit substance abuse, particularly in view of potential reversibility. We show the presence of axonal sparing suggesting a demyelinating rather than hypoxic process as central to the pathogenesis of acute heroin-induced leukoencephalopathy.

E-PS-15-009
Expression of p53 protein in the hippocampus with increased activity of the adrenal cortex after traumatization of the nasal septum in rats
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Background & objectives: Surgical interventions, provoke neurons apoptosis (AN) activation in the hippocampus(H). Damage to the nasal septum(NS) when modelling septoplasty in rats is of particular importance. Aims: to study expression of p53protein in H with increased corticosterone after traumatization of rats NS.
Methods: NS mucous membrane in 10rats was scarified over its entire length under anaesthesia with zoletil100. The corticosterone concentration was determined and brain sections were stained with mouse antibodies to p53 2,4,6 days after surgery. AN in hippocampal CA1, CA2, CA3 subfield layer was calculated over a length of 574.3±13.5μm and a width of 121.94±31.5μm. The results obtained were compared with a control group(CG,5rats).
Results: In hippocampal CA1, CA2, CA3 subfield at all terms, there were more p53-positive neurons than in the control group (0.98±0.6; 0.86 ±0.28; 0.32±0.08; 8.17±3.08, respectively) ($p<0.001$). The peak of p53 expression in neurons occurred on 4th day in CA1 (9.27±2.63), 2nd&4th days in CA2 (5.5±2.55; 5.6±0.77), and the number of p53-positive neurons in CA3 were consistently high all three days (11.86±3.35; 12.15 ±3.64; 11.5±2.29, respectively). After septoplasty, compared with CG (38.56±2.12ng/ml), corticosterone increased on 2nd day, on 4th day (122.55±5.38ng/ml) & 6th day (118.35±5,69ng/ml) decreased, but retained its stable blood concentration.
Conclusion: Considering the proven presence of mineralocorticoid and glucocorticoid receptors in hippocampal neurons, it can be assumed that the expression of the p53 protein in the cytoplasm of neurons in the pyramidal layer of the hippocampus is closely associated with an increase in the concentration of corticosteroids after surgical trauma of the nasal septum in rats.

E-PS-15-010
Lymphoplasmacytic lymphoma with Waldenström macroglobulinemia: report of a rare entity with a challenging diagnosis
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Background & objectives: Lymphoplasmacytic lymphoma (LPL) is a rare low-grade B-cell lymphoma. Waldenström macroglobulinemia (WM) is found in a substantial subset of patients with LPL. It is defined as an LPL involving the bone marrow with IgM monoclonal paraprotein of any concentration.
Methods: A 64-year-old woman presented with persistent severe headache for a month. Brain MRI revealed a strong and homogenous enhancement with contrast, suggesting a right fronto-parietal osteo-dural meningioma or metastasis. Biopsies were performed.
Results: Histopathological evaluation revealed a diffuse tumour proliferation of small lymphocytes admixed with variable numbers of plasmacytoid lymphocytes and plasma cells. Many mitotic figures were present. Pseudointranuclear (Dutcher bodies) and intracytoplasmic inclusions (Russell bodies) were detected.
Using immunohistochemistry, tumour cells were CD20-positive and CD3-negative. The diagnosis of a non-Hodgkin B cell lymphoma was retained. Furthermore, tumour cells displayed Bcl2 and CD79a positivity. No CD5, CD10 and Bcl6 immunostaining was observed.
Consequently, the final diagnosis was a cerebral infiltration with an LPL/WM with bone extension.
Conclusion: LPL/WM is a rare disease. Its diagnosis can be challenging due to similarities to other small B-cell lymphomas with plasmacytic differentiation and/or with IgM paraproteins. Bone marrow morphology and immunophenotype are important for diagnosis.

E-PS-15-014
Central neurocytoma: experience of a centre in southern Tunisia
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Background & objectives: Central neurocytomas (CN) are rare intraventricular tumours with prominent neuronal differentiation. Few studies have described the clinical and pathological features of these tumours. We report twelve patients with CN and discuss the histological differential diagnosis of these tumours.
Methods: Between 1999 and 2018, 12 patients were diagnosed with CN at our hospital. These tumours were retrospectively analysed with reference to their epidemiological and histopathological features.
Results: The male: female ratio was 2/1 and the mean age at diagnosis was 25 years (10–49 years). Nine tumours occupied the lateral ventricle and three was located in the Fourth ventricle. All patients underwent surgery, with eight undergoing macroscopic total excision and four, partial excision. All tumours consisted of small uniform cells with remarkably round nuclei in a fine fibrillary matrix. Oligodendroglioma-like pattern was found in 2 cases and pseudorosettes in 5 cases. All tumour tissues that were examined showed positive immunoreactivity for synaptophysin and NSE. Four cases were positive for GFAP. No adjuvant radiotherapy was given. Two patients developed tumour recurrence.
Conclusion: The results of this study indicate that CN should be considered in the differential diagnosis of intraventricular brain tumours, particularly those located in the lateral ventricles. CN must be distinguished from other clear cell tumours.

E-PS-15-015
Astrocytomas: a 10-year summary
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Background & objectives: Although radiological imaging has substantially improved, assessment of prognosis by grading astrocytoma has been challenging task for pathologist. We have tried to describe the characteristics of astrocytomas and analyse the most efficient techniques for evaluation.
Methods: We conducted a retrospective descriptive study of patients with astrocytomas seen at our institution between 2011-2020. We divided the astrocytic tumours according to the histopathological grade into low-grade astrocytomas and high-grade astrocytomas. The morphological criteria and role of imaging method were analysed. The data were entered into the SPSS Statistics and were analysed according to demographic and diagnostic parameters.
Results: We identified 117 cases of astrocytic tumours. Most cases identified both histopathologically and by imaging methods - computer tomography or magnetic resonance imaging - were high-grade astrocytomas, 76.07%, respectively 79.2%. We identified a predominance of low-grade astrocytomas over females, 53.57%. High-grade astrocytomas were frequently found in the parietal lobe of right hemisphere (12.94%), while low-grade astrocytomas were found in the temporal lobe of the left hemisphere (18.52%). Given the specific characteristic of high-grade astrocytomas, infiltrativity, the largest tumour diameters were recorded in this category (94.39%).
Conclusion: We noticed that both low-grade and high-grade astrocytomas frequently occur in the sixth decade of life. In terms of imaging, most cases have been described as potentially malignant tumours, without a definite topographic predisposition. In most cases, a concordance of the imaging diagnosis with the histopathological one was observed, this aspect leading to a more accurate assessment of the two astrocytic categories. The results of our study bring new information on the epidemiological data of astrocytomas in the region.

E-PS-15-016
Giant cell glioblastoma: a subtype of glioblastoma with distinct clinicopathological features
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Background & objectives: Giant cell glioblastoma (GCG) is included in the latest World Health Organization classification as an uncommon subtype of glioblastoma (GB), with distinct clinical and biological features. Our aim is to analyse epidemiological, clinical and pathological features of this rare tumour.
Methods: This is a retrospective and descriptive study of 6 cases of GCG registered at the department of pathology of Sfax's university hospital (Tunisia), during a period of 11 years from 2010 to 2020. Clinical, epidemiological and pathological characteristics were retrospectively reviewed.
Results: GCG accounted for 2 % of patients diagnosed with GB. The mean age was 32,6 years (1-60 years). The study included 5 women and 1 man. Temporal lobe was involved in 5 cases and frontal lobe was involved in 1 case. All tumour developed de novo. Surgical resection was performed in 5 patients and stereotactic biopsy in one. Microscopically, there was a highly cellular glial proliferation with predominant pleomorphic multinucleated giant cells. Numerous atypical mitotic figures were present. Pseudo-palisading tumour necrosis was identified in 4 cases. Vascular endothelial proliferation was present in 3 cases. Sarcomatous component was absent. Immunohistochemical analysis performed in 4 cases was positive for GFAP.
Conclusion: GCG is an uncommon tumour accounting for 2-5% of GB. Genetically, GCG is considered a variant of IDH-wild type GB but with high frequency of TP53 mutation and lack of EGFR amplification. Macroscopically it is well limited and histologically it is characterized by the presence of plentiful bizarre multinucleated giant cells. Although their poor prognosis, GCG has a somewhat better outcome than ordinary GB. This can be partially explained by the fact that it occurs most often in younger people.

E-PS-15-017
Atypical meningioma with Arnold Chiari Malformation (ACM) and syringomyelia: a case report
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Background & objectives: Atypical meningiomas are aggressive tumours, composing around 5-15% of all meningiomas. They display mitotic activity with increased cellularity, necrotic foci, and loss of lobular architecture. ACM and syringomyelia can be congenital or infrequently develop following a cranial mass, mostly meningiomas.
Methods: Our case is a 53-year-old woman with a known Diabetes Mellitus Type 2 and hypertension for 15 years. She was later found to have congenital ACM and syringomyelia following its initial scans and was followed for syringomyelia and a meningioma for three years. She was admitted to the hospital for worsening headaches and dizziness for the last three months.
Results: The patient's symptoms were suspected to arise from ACM. Cranial MRI showed ACM type I, syringomyelia, and a meningioma in the right parietal lobe. The patient underwent surgery for both ACM and a meningioma. The mass was fully resected, and posterior fossa decompression was performed for ACM. In the histopathologic examination, the tumour section showed mitotic activity, cellularity prominence, and necrotic foci. The mitotic count was 8 -10/ 10 High-Power Fields (HPF). These findings were compatible with WHO Grade II Atypical meningioma. Subsequently, she received 24-day postoperative radiotherapy. She later developed left side mild muscle weakness and described urgency type urinary incontinence within one year of follow-up.
Conclusion: Atypical meningiomas are uncommon entities of all meningiomas, and accompanying congenital problems can overlap the main symptoms of a space-occupying mass. A long follow-up period is important for patients diagnosed with atypical meningioma considering their aggressive behaviour.

E-PS-15-018
Cervical giant benign notochordal cell tumour in an adult male: a rare entity with an unusual location
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Background & objectives: Of the few cases of benign notochordal cell tumour (BNCT) described in the literature, a minority had a spinal location, mostly being found in the prepontine area, sphenoid sinus, some in the sacrococcigeal region. Distinguishing BNCTs from chordomas is crucial.
Methods: A 29-year-old male admitted to Neurosurgery Department (11/2020) for right-sided cervicobrachialgia, brachial motor deficit. Neuroimaging: T2-hyperintense/T1-hypointense 38/24/38mm lobulated tumour centred on C4, reaching C6, transforaminal (widened foramina), spinal canal 60% narrowed, cord compression, surrounding the vertebral artery (without invasion/stenosis), extension to prevertebral muscles, minor erosions of C5 vertebral body. Intraoperative frozen sections (toluidine blue), paraffin examination (H&E, immunohistochemistry) were performed.
Results: The preoperative diagnosis was of schwannoma/neurofibroma. Intraoperative consultation of the extradural gelatinous mass revealed a proliferation of well-circumscribed cells with clear, bubbly cytoplasm and bland round-to-oval nuclei with mild anisonucleosis (physaliphorous cells of notochordal origin) without atypia, mitotic activity or necrosis. The paraffin microsections (H&E) showed similar aspects and no infiltration or destruction of the adjacent tissue.

Corroborating the histological aspect with the clinical and imagistic aspects, a diagnosis of a chordoid lesion, suggesting BNCT was made.
Immunohistochemical assays showed positivity for S100, AE1/AE3, EMA, CK18, 3% Ki-67 index, strengthening the previous diagnosis.
Postoperative course: diminishing cervicobrachialgia, no additional motor deficit, discharged 8 days later.
Conclusion: Distinguishing BNCTs from their malignant counterpart, chordoma, is of paramount importance and it can be challenging. They are phylogenetically, histologically, and clinically closely related. Contrast enhancement, Ki-67 index, CK18 positivity, CNS involvement are helpful in making the distinction.
While BNCTs are usually asymptomatic, this case shows that these tumours can be large and cause compressive symptoms early in life, requiring surgical treatment. The extradural location of this BNCT shows that it can be isolated to the epidural space, like chordomas.

E-PS-16 | Ophthalmic Pathology E-Posters

E-PS-16-001
Primary intraorbital myxoid (metaplastic) meningioma
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Background & objectives: Meningiomas represent approximately 4% of all intraorbital tumours and can arise from the optic nerve. Myxoid meningioma is a rare histological variant of meningiomas grouped into the subtype of metaplastic meningiomas (World grade I).
Methods: Hereby, we report a case of a myxoid meningioma in a 55-year-old female who presented gradual bulging of the right eye (proptosis) over the past 10 years. Last year optic nerve compression was causing loss of vision. Imaging studies showed a 7x4mm pigmented neoplasm overlying the conjunctiva. The tumour was excised completely.
Results: Histopathology revealed a benign appearing myxoid neoplasm with uniform elongated alcian blue positive cells, without any atypia and a very low mitotic activity.
Immunohistochemical examination was used including these antibodies: CK8/18 (-); CK7 (-); CK20 (-); CK5 (-); S100 (-); HMB45 (-); CD56 (-); Synaptofisin (-); CD68 (-); CD34 (-); P53 (-);CDX2 (-); SMA(-); GFAP (-); EMA (+) Vim (+);CD45 (+)Ki67 –3%;
Immunohistochemical stains showed positivity for vimentin and epithelial membrane antigen confirming the diagnosis of myxoid meningioma.
Conclusion: Myxoid (metaplastic) meningioma is exceptionally rare histological variant of meningiomas arising in intraorbital tumours. Only eight cases of myxoid meningioma have been reported till date in the literature. Intraorbital meningiomas were most frequently of the meningothelial or transitional subtypes none of them was diagnosed as metaplastic variant.

E-PS-16-002
Solitary fibrous tumour of the orbit: a case report and review of the literature on a rare entity
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Background & objectives: The solitary fibrous tumour (SFT) is a rare neoplasm of uncertain histogenesis originally described in the intrathoracic region, but which has been recently described in other sites including unusually in the orbit.
Methods: We report the case of a 53-year-old female with a history of right orbital swelling, ptosis and visual change evolving for 8 months. The CT scan showed an ovoid and lobulated lesion in the superomedial quadrant with 22x22x11mm. The lesion apparently contacted the eyeball, the medial rectus and superior rectus muscles, without signs of invasion. The lesion was removed surgically.
Results: We received an irregular fragment of brownish elastic tissue measuring 25x17x5mm. The histological analysis showed fibroadipose tissue almost completely occupied by a mesenchymal neoplasia consisting of ovoid to fusiform cells, with poorly defined cytoplasmic limits, scarce cytoplasm and small to intermediate-sized hyperchromatic nuclei, sometimes with evident nucleoli and occasional images of nuclear pseudoinclusions. Pleomorphism was mild to moderate. Two mitoses in 10 high-power fields were identified. The cells were distributed in a disorganized manner around a rich vascular network, sometimes with staghorn vessels. The neoplastic cells had strong and diffuse staining with antibodies for CD34 and STAT6 and were focally positive for MDM2. CD45, SOX10 and CAM5.2 were negative.
Conclusion: This case illustrates the main features of this rare orbital entity. The combined WHO score for metastasis risk was low in this case. However, the lesion was incompletely excised. Nearly 1/3 of the solitary fibrous tumours of the orbit have local recurrences. Distant metastasis are uncommon and might only occur after extended periods. Therefore, it is of fundamental value to perform a long-term follow-up of these patients. Currently, our patient remains well, without signs of local or distant disease.

E-PS-16-003
Basaloid follicular hamartoma of the eyelid: a case report and review of the literature on a rare entity
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Background & objectives: Basaloid follicular hamartoma (BFH) is a benign unusual malformative lesion involving the hair follicles, which normally poses challenges in the differential diagnosis with other benign tumours of the follicular infundibulum and infundibulocystic basal cell carcinoma due to significant morphological overlap.
Methods: We report the case of a 53-year-old male who presented with a mass in the upper left eyelid evolving for one year, centred in the cutaneous-conjunctival transition area. The patient had a previous history of total colectomy within the context of familial adenomatous polyposis. The eyelid lesion was biopsied.
Results: We received three fragments, elastic and whitish, between 4 mm and 5 mm. The histological analysis showed fragments with cutaneous-conjunctival lining displaying a subepithelial proliferation of basaloid nests, with peripheral palisade, consistent with primitive hair follicles. There was preservation of their connection to the epithelial lining and images of anastomosis between different basaloid nests. The background stroma had high cellularity and sometimes primitive mesenchymal papillae were evident. The pleomorphism was scant, mitotic figures scarce and necrosis was absent. Most of the nests did not present epithelial-stromal retraction nor mucoid deposits. The initially proposed diagnosis of basaloid follicular hamartoma was later confirmed after the excision of the whole eyelid lesion.
Conclusion: This case illustrates the main features of this rare benign eyelid entity, which is associated with inherited genetic syndromes namely mutations in the patched (PTCH) gene on chromosome band 9q23. The standard medical or surgical approach of these lesions remains to be firmly established. Currently, our patient remains well, without signs of local recurrence.

E-PS-16-004
Case report: choroid metastasis from endometrioid carcinoma
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Background & objectives: To report a case of a uterine endometrioid carcinoma diagnosed in January 2021, metastatic to the eye in February 2021.

Methods: Review of medical record, anatomopathological reports and immunohistochemical study.
Results: Female, 60-year-old, menopause at age 55, seeks medical attention due to large amount of vaginal bleeding, in addition to dysmenorrhea, asthenia and weight loss. She underwent uterine curettage for microscopic evaluation of the endometrium, which showed poorly differentiated endometrioid carcinoma. Immunohistochemical study exhibited positive reaction for CK7, p53 and p16; and negative reaction for hormonal receptors (oestrogen/progesteron) and HER2. After diagnostic confirmation, the patient was admitted for tumour staging with imaging tests that showed lesions suggestive of metastases to the peritoneum, ovaries, and lung. After clinical worsening, the patient died. The patient's corneas were donated, and eyeballs were sent for microscopic analysis, that revealed metastasis to the choroid region.
Conclusion: Endometrial carcinoma metastases usually occur via lymphatic system. Hematogenous metastases are less common, but they can occur; the most common sites are lung, liver, brain, and bone. Choroid metastases from endometrial cancer are extremely rare and there are only very few cases described in the literature.

E-PS-16-005
Intra- and periocular metastatic renal cell carcinoma mimicking choroidal melanoma and presumed keratoacanthoma
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Background & objectives: We aim to show that the eyeball and periocular region are uncommon but known potential metastatic sites of renal cell carcinoma.
Methods: We are presenting three ophthalmologic cases. The lesions presented in different clinical settings and were of unknown origin at the time of diagnosis. The first two cases were thought to be choroidal melanoma based on ultrasound, and the third neoplasm was supposed to be a primary conjunctival neoplasm of epithelial origin. All lesions were removed, the first two required enucleation.
Results: Renal origin was proved by immunohistochemistry and the primary tumour was found.
Conclusion: The cost-benefit ratio of complicated ocular biopsy procedures improves with increasing access to multiple potential treatment options.

E-PS-16-006
Conjunctival myxoma: a rare ocular tumour
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Background & objectives: Conjunctival myxoma (CM) is a rare ocular benign neoplasm, with an incidence ranging from 0.001-0.002% of all conjunctival lesions. The aim of this study is to report an observation about a CM and discuss its differential diagnoses.
Methods: A 54-year-old woman presented with a history of one year gradually progressing, painless, conjunctival swelling, on her left eye. Her medical and family history was unremarkable. A slit-lamp examination of the right eye was unremarkable, in the left eye; it revealed a well-circumscribed, pinkish, conjunctival mass, translucent and freely mobile over the sclera, measuring 5×3mm.
Results: The lesion was clinically diagnosed as a conjunctival cyst, and it was completely excised. Histopathological examination revealed a low-density cellular proliferation; the cells were stellate or fusiform, dispersed in an abundant myxoid stroma. Nuclear atypia and mitotic figure were absent. Few branching vascular structures with thin wall and scattered lymphocytes were also seen. Immunohistochemical study showed strongly positive expression of vimentin. The tumour cells were negative for smooth muscle actin, desmin and PS100. The diagnosis of CM was retained. The patient received extensive cardiac and endocrine evaluation. She had no atypical dermatological findings. After 14 months, the patient remained healthy, with no recurrence of the conjunctival lesion.
Conclusion: Myxomas have common histologic appearance of myxoid ground substance. They are most often found in atrial endocardium and jaw bones. Less commonly, they have been reported in the orbit, cornea, lids and conjunctiva. CM was first described by Magalif in 1913. To our knowledge, only 64 cases of this lesion have been published in the literature. Surgical excision and histopathologic examination of this lesion are necessary. The differential diagnosis of CM includes myxoid neurofibroma, spindle cell lipoma and nodular fasciitis.

E-PS-16-007
Adult patient with malignant intraocular medulloepithelioma: a case report
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Background & objectives: Intraocular medulloepithelioma (IME), which is extremely rare in adults, is a congenital tumour of the non-pigmented ciliary epithelium. Malignant form of IME consists of neuroblastic cells around neuroepithelial rosettes. We present a malignant IME case seen in an adult patient.
Methods: An intraocular mass was detected in a 71-year-old male patient, who was admitted to the hospital with loss of vision in the right eye. Cytological material was taken from the mass intraoperatively and atypical discohesive cells which had brown pigment and prominent nucleoli, were seen in cytological examination. Therefore, malignant melanoma was considered primarily. Whereupon right eye enucleation was performed.
Results: Leukocoria was observed in the macroscopic examination of the enucleation material. When the eyeball is sliced, a black-grey coloured solid lesion, which is filling the anterior chamber and infiltrating iris, ciliary body, and retina was seen. In the microscopic examination, a highly cellular tumour with increased mitotic activity but not mesenchymal differentiation was composed of elongated and round, poorly differentiated and immature cells, which were arranged into solid, trabecular pattern, and retinoblastoma-like rosettes as well. Sclera and cornea infiltration were also present microscopically. Tumour cells were stained with chromogranin, synaptophysin, NSE, and S-100, immunohistochemically. HMB-45 and Melan-A were focally positive and negative, respectively. The patient was diagnosed with malignant IME.
Conclusion: Medulloepithelioma is generally known as a benign childhood tumour. Our case was deemed worthy of presentation, since it is seen in adulthood, the tumour has a malignant course and cytologically mimics malignant melanoma.

E-PS-17 | Other Topics E-Posters

E-PS-17-001
Structural features of suicidal behaviour in central Kazakhstan
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Background & objectives: One of the socially significant problems in modern society is the rising death rates from suicide. The aim is to study changes in the prevalence of suicide methods, analyse the dynamics, structure and social characteristics of suicides in Central Kazakhstan.
Methods: Retrospective analysis of 634 forensic medical examinations carried out on the territory of Central Kazakhstan. The analysis of the dynamics, structure and social characteristics of suicides: place of residence, age, social status, ethnic origins, gender, method of committing suicide from 2016 to 2020. Methods of applied statistical analysis were used to analyse the obtained results.

Results: There was a decrease in the total number of suicides in Central Kazakhstan in 2020 by 13.8% in general, 11% in men, 30% in women. The results of the study showed that in the structure of methods of committing suicides by residents of Central Kazakhstan, regardless of gender, a special place occupied by hanging. The suicide patterns indicate that men use more aggressive methods of suicide. The number of suicides in men increases with age and reaches a maximum in the age groups of 31-40 and 41-50 years old. In women, the number of suicides rises sharply in the age group from 21 to 30 years old.
Conclusion: The summarized data make it possible to form a whole picture of the peculiarities of suicidal behaviour of the population of Central Kazakhstan and are valuable in terms of identifying the most vulnerable age and gender groups. Particular attention should be paid to the growing number of suicides among young men of 25-29 years old. This is a trend in recent years and demonstrates the "rejuvenation" of suicides.

E-PS-17-002
Critical evaluation of the laryngohyoid bone fracture in suicidal hanging
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Background & objectives: Fractures of the larynx in hanged men are one of the most studied and paradoxically controversial topics in forensic pathology. According to the literature sources, the incidence of laryngeal-hyoid bone fractures during hanging varies significantly from 0% to 100%.
Methods: In order to test the diagnostic significance of hanging injuries, we prospectively and sequentially analysed the occurrence of laryngeal-hyoid fractures in a group of 194 suicidal hanging victims depending on the selected variables (age, gender, weight, completeness of suspension of the body and location of the ligature node).
Results: In 141cases of 194 (72.5%) revealed the types of fractures: isolated fracture of the shield-like cartilage in 65 cases (33.7%), combined thyroid fractures in 45 cases (23%), isolated fractures of the hyoid bone in 30 cases (15.7%) and the absence of fractures of the cricoid cartilage or cervical vertebrae. A high frequency of fractures of the laryngeal-hyoid bone was found with collateral hanging. Statistical analysis revealed a significant relationship between the occurrence of fractures of the laryngeal-hyoid bone with the age of the victim ($p = 0.028$), the position of the ligature node on the neck ($p = 0.019$), and the weight of the victim, adjusted for age.
Conclusion: As the results of our research, and the literature analysis as well suggests that, when properly assessed, hanging fractures of the laryngohyoid bone can provide much more diagnostic evidence than just evidence that neck injury has occurred, and can provide research opportunities on a number of issues that need to be analysed and to be explained later.

E-PS-17-003
Inguinal lymphadenopathy: a diagnostic challenge
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Background & objectives: Inguinal nodes are usually benign and regress spontaneously in most patients. They can be caused by a broad spectrum of diseases ranging from infectious diseases, autoimmune diseases to several malignancies. We aim to identify etiologic panel diagnosis's of Inguinal Lymphadenopathies.
Methods: The study was retrospective in a period of five years (2016-2020). We included all cases of nodes dissections and biopsies in guinal lymph nodes. Histopathology reports of 31 were reviewed.
Results: A total of 31 patients was includes. They were diagnosed in 6 men and 25 women with mean age of 36,8±18,64 years.
The size of the inguinal lymph node ranged from 0.4 to 7 cm with a mean size of 2,52±1,35 cm.
We have diagnosed 20 reactive lymphadenitis (64,5 %), 4 cases of Hodgkin Lymphoma (12.90%), one case of follicular lymphoma, one case of diffuse large B cell lymphoma and 2 cases of ganglionar tuberculosis. A lymph node localization of fungoid mycosis was demonstrated in one case and extramedullary haematopoiesis in another one. In one patient, pathological analysis was not possible because the sample was autolyzed due to delayed fixation.
Conclusion: Inguinal lymphadenopathy are generally benign and reactive to infectious or inflammatory diseases which has been confirmed by our study (64.5% of our samples were reactive lymphadenopathies). However, they can be the only way to reveal other pathologies, especially neoplastic ones (22.5% of our patients had lymphomas).Lymph node biopsies are needed to make the diagnosis. A methodological approach to inguinal lymphadenopathy can disclose the accurate diagnosis, enable patients to receive the proper treatment and reduce mortality.

E-PS-17-004
Von-Hippel-Lindau disease: a study of a misleading case
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Background & objectives: Von-Hippel-Lindau disease(VHLd) is a hereditary disorder associating both benign and malignant neoplasms scattered throughout the body. The main causes of morbi-mortality are central nervous system(SNC) hemangioblastomas and clear-cell renal cell carcinoma (CCRC). Pancreatic neuroendocrine tumours (NET) represent an additional risk.
Methods: We report a case of VHL to highlight some of the tumours encountered and emphasize the importance of a thorough pathological examination.
Results: The patient is a 47-year-old female first diagnosed in 1999 with a right-sided pheochromocytoma, then with hemangioblastomas. Lately, CT-scan showed a left-sided adrenal-gland tumour suggesting a pheochromocytoma, a hypervascular right renal lesion seemingly malignant, multiple renal cysts and 2pancreatic lesions: a 10cm cystadenoma and a hypervascular lesion(0.3cm) probably a NET. She underwent surgery. There was well-circumcised brown nodule of the adrenal-gland, microscopically a pheochromocytoma. The renal tumour was encapsulated and yellowish. The renal cysts were smoothly-lined, full of water-like-liquid. All those lesions were CCRCs. The pancreas harboured multiple cysts full of a yellowish fluid. Histologically, they were serous cystadenomas. There was a well-defined fibro-vascular non-tumoral pancreatic nodule, probably the "suspected-NET".
Conclusion: Although no molecular diagnosis is available for this case, a genetic screening for the family members should be done as early-stage identification is key to well managing the disease.

E-PS-17-005
The hidden art of our daily pathology
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Background & objectives: From the normal histological structure to the pathological changes, from the routine to the specific stains, from the immunohistochemical to the molecular tests, from the single slide cases to those with numerous sections and sections, we can discover art.

Methods: Microscopic analysis from the daily routine, the examination of each slide from each case, brings me every working hour, under my eyes, through the lentils a lots of images. HE stain makes me to see pink structures and makes me to analyse them not only from pathological point of view, but from artistic one.
Results: Blood vessels, atypical mitosis, haemorrhage, necrosis, cholesterol crystals, smooth or skeletal muscles, cartilage or bone tissue.
Colonic biopsy, palatine tonsils, cervico-vaginal smear, placenta, ombilical cord, amniotic plate, renal glomerulus.
Skin, melanomas, hair follicles, nevi, placental vili, lithiasis, colonic adenomas.
Parasites, Pacini corpuscles, lymph nodes, spleen, liver, tuberculosis.
Embryonic and foetal structures.
Artefacts.
Conclusion: It is said that the beauty is the eye of the beholder. I say the beauty is the eye of the pathologist. The images on the pathologist's retina can help to relax, to see beyond the histopathological diagnosis. Histology and histopathology provide us a different kind of art. The art of the cells. The art of the tissues and organs. The art inside of human bodies.

E-PS-17-006
Testicular cavernous haemangioma that could lead to diagnostic difficulties among testicular neoplasms; a rare case report
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Background & objectives: Cavernous haemangioma, a benign vascular tumour, is rarely seen in the testis. Before orchiectomy operation, it is difficult to differentiate from other common benign and malign conditions of the testis.
Methods: A 38-year-old male patient had swelling and pain in the scrotum for about one week. Ultrasonographic examination showed an irregularly contoured semi-solid mass with hypervascular characteristics that infiltrate the left testicular parenchyma and cause parenchymal cystic/haemorrhagic degeneration interpreted as a left testicular tumour. Serum levels of tumour markers were normal.
Results: Radical orchiectomy material was sent with a pre-diagnosis of malignancy to our laboratory. Gross examination exhibited a well-circumscribed, 3x2.2x1.9 cm sized intense bleeding lesion, and intact testicular tissue was not observed. Microscopic examination revealed dilated spaces filled with erythrocytes which erased almost all of the testicular tissue. Histopathological examination showed benign vascular proliferation in left testicular tissue, the case was diagnosed with Cavernous Haemangioma.
Conclusion: Cavernous haemangioma is an uncommon tumour among testicular neoplasms. Clinical examination and imaging studies are generally not sufficient for diagnosis. Orchiectomy and then histopathological evaluation are required for definitive diagnosis.

E-PS-17-007
Synchronous clear cell renal cell carcinoma and marginal zone lymphoma: a case presentation
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Background & objectives: During the years there has been an increase in the number of patients who are diagnosed with synchronous primary neoplasms. Here we will present the case of a patient with synchronous renal cell carcinoma and marginal zone lymphoma.
Methods: A 61-year-old man was presented with a random finding of a tumour in the right kidney during an ultrasound examination. The tumour was surgical removed with a partial nephrectomy and sent to our department.
Results: Histological examination revealed the presence of a clear cell renal cell carcinoma, nuclear grade 1-2. The tumour measured 2,5cm in maximum diameter and was confined within the renal parenchyma, without perinephric fat extension (pathological staging pT1aNx). Additionally, the examination of the perinephric fat sections revealed the presence of a diffuse and dense neoplastic lymphoid infiltrate that partly invaded the renal parenchyma. The abnormal lymphocytes had small/medium size, expressed CD20 and focally IgM whereas they were negative for CD5, CD3, cyclinD1, Sox-11 and Lef-1. The morphology and immunophenotyping were consistent with the diagnosis of marginal zone lymphoma.
Conclusion: Coexistence of renal cell carcinoma and Non-Hodgkin B-cell lymphoma is what makes this case unique. Few similar cases were reported, one of which suggests that patients with non-Hodgkin lymphoma have an increased risk for renal cell carcinoma. Therefore, we are looking forward to a future research which could prove the correlation between these two neoplasms or even identifying one as an etiological factor for the other.

E-PS-17-008
A misleading isolated mass of pelvis in a male patient
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Background & objectives: Cystic mass of the pelvis in male patients are challenging diagnostic abnormalities because they are uncommon, and their origin is uncertain. We report a case of an isolated cystic mass of the pelvis in a male patient.
Methods: A 51-year-old man, consulted for a pelvic heaviness-type pain associated with intermittent constipation. Clinical examination did not reveal any abnormalities. An abdominal-pelvic scan detected an isolated well-limited, slightly enhanced central pelvic mass of 32x45 mm, developing at the expense an ileal loop consisting with a gastro-intestinal stromal tumour. On Surgery, there was a non-organ dependent, encapsulated oval, resection was performed.
Results: Macroscopic examination of the surgical specimen showed a cystic renitent mass, thin walled with yellowish membranes, when cut. Microscopy revealed anhist lamellar eosinophilic membranes, which are PAS positive. The diagnosis of hydatid cyst was made. Hydatid serology was positive, thus confirming the diagnosis.
Conclusion: Clinical symptoms of hydatidosis are not specific and the diagnosis may not be evident in some cases despite the contribution of advanced of imaging. The isolated localization of the hydatid cyst in the pelvis is rare and can even mimic a tumour process. Preoperative diagnosis is difficult due to non-specific clinical and radiological features. Therefore, the hydatidosis must always be present in mind when dealing with cyst pelvic formation especially in endemic areas.

E-PS-17-009
Diagnostic challenges in pathology: the value of the second opinion
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Background & objectives: The goal of pathologic examination is to provide accurate and specific diagnoses. However, the diagnosis is not always obvious; the pathologist may seek advice from an expert. The aim of this study was to view the value of second opinion (SO).
Methods: We retrospectively included all SO in the Pathology department of Habib-Thameur hospital over a three-year period. The submitted and matched SO reports were reviewed to extract clinical and pathologic data, the diagnostic hypotheses, and the additional investigations. Each diagnosis was reviewed to determine if there was agreement, minor disagreement, or major disagreement between the original and the SO.

Results: We included 21 consecutive pathology consultation requests. The most common diagnostic categories sent for SO were: lymphoid proliferation (15 cases), inflammatory dermatoses (3 cases), melanomas (1 case), skin tumours (1 case), and undifferentiated tumours (1 case). In 13 cases, further investigations by a panel of antibodies or molecular studies were necessary to establish the diagnosis. In our series, there was an agreement between the initial and the SO in three cases. In 14 cases, there was a difference in diagnostic opinion. Minor disagreements occurred in 10 cases and major disagreements in 4 cases. However, the diagnosis has remained difficult, even for the expert, in four cases.
Conclusion: This study supports the positive impact of SO, especially, in lymphoid pathology and skin proliferations. These tumours are characterized by their polymorphism and complexity. In other cases, the recourse to a SO is justified by a lack of means such as immunohistochemical or molecular studies. However, some rare complex cases remain difficult to interpret even for experts. The SO can be accompanied by a delay of response that should be understandable by both the treating physician and the patient.

E-PS-17-010
Benign lymphoepithelial cyst in retroperitoneal region: a case report
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Background & objectives: Lymphoepithelial cyst is an extremely rare non neoplastic true cyst of unknown pathogenesis.
It is lined by squamous epithelium with underlying abundant lymphoid tissue. A few cases are noted in the literature, most of them in the pancreas.
Methods: We present a rare case of a large lymphoepithelial cyst located in the retroperitoneum. A 64-year-old woman underwent colectomy one year ago. The diagnosis was colorectal adenocarcinoma. During follow up, CT scan revealed a retroperitoneal mass, measuring 6x7x5cm near the pelvic vessels.
Results: Macroscopically the tumour was cystic, round, well demarcated with cheesy keratin-containing material. Under microscope the cyst was lined by squamous epithelium, with a dense band of lymphoid tissue underneath it.
Conclusion: Lymphoepithelial cyst is difficult to diagnose preoperatively. Preoperative fine needle aspiration cytology may help in the diagnosis. Lymphoepithelial cyst does not recur or progress and is not associated with immunosuppression or autoimmune diseases.

E-PS-17-011
Factors affecting turnaround time for cervical biopsy and LEEP for high-grade squamous precursor lesions
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Background & objectives: The objective of this study was to evaluate the impact of age and distance to a tertiary care centre on the turnaround time between preliminary biopsy and definitive management for cervical pre-cancerous lesions.
Methods: Women undergoing LEEP procedures 01/01/17 - 31/12/18 were reviewed (n = 290). Age, patient diagnosis, date of biopsy, surgical date and patient address were collected. Patients were categorized into six Home IDs based on distance to tertiary centre; Turnaround time was calculated using date of biopsy and LEEP procedure. The relationship of age and distance were analysed using linear regression.
Results: 225 patients met criteria. Age plurality was under 30 (93, 41%), the 30-40 years (82, 37%) and over 40 (50, 22%). Mean distance to tertiary care was 60 km and the relationship between distance to a tertiary care and turnaround time was not statistically significant (p=0.535). Age was statistically significant with turnaround time decreasing by 1.36 days for each year of increasing age (p = 0.003). Mean turnaround time of the most populous group (age ≤ 30) was 58 days. Age groups and their respective turnaround times were as follows: 30 ≤ age < 40 = 38.41 days (p = 0.018), age > 40 = 26.53 days (p = 0.001).
Conclusion: There are no guidelines benchmarking turnaround times for cervical biopsy to LEEP follow-up. We must engage clinicians to uncover if this data is meaningful. This is especially important in younger patients as age is highly related to turnaround time. Furthermore, patient-oriented research uncovering the barriers present in the younger population (kids, lack of transportation, inflexible work) would identify variable-specific interventions to improve access for our younger, and most represented population. This could then be reflected in the quality turnaround times.

Funding: University of Saskatchewan Dean's project funding

E-PS-17-012
Cyclic nitroxides as a potential compound for detection of redox state changes in cocaine related intoxication. A basic point in a one future method
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Background & objectives: Cocaine, metabolites norcocaine and norcocaine derivatives play a significant role in cocaine-relited toxicity. The mechanism involves the induction of oxidative stress and generation of reactive oxygen species (ROS). ROS are the main reasons for the induction of irreversible pathological changes.
Methods: We are considering a new potential methodology of ROS determination in patient blood samples by using EPR-X-Band (Bruker ER 116 DS) and 0.1mM, 0.5 mM and 1M solutions of stable cyclic nitroxide: 4-Hydroxy-TEMPO, 4-oxo -TEMPO and 3-Carboxy-PROXYL in oxidase / reduce form. The value of EPR-signal intensity will be measured directly at different time intervals in freshly isolated blood samples.
Results: Characteristic of cocaine intoxication is the formation of an unusual redox pair in the form of nitroxide-hydroxylamine, which is considered the main source of ROS. Aromatic cyclic nitroxides are suitable spin probes for ROS analysis and changes in redox status in vitro after drug intoxication. In order to determine the potential application of nitroxide radicals in the monitoring of drug intoxication, studies with conventional tests to analyse ROS levels will be performed and the results will be compared with EPR analysis.
Conclusion: The reactive oxygen species generation, toxic metabolites formation and oxidative stress play a significant role in cardiovascular, hepatic and neurotoxicity of cocaine. In this review we draw basic points for developing a rapid and effective method for detection of redox state change in a human body in cocaine intoxication cases.

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E-PS-17-013
Are your biohealthcare/biomedical vocational training students aware of the pathology use cases?
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Background & objectives: Pathology is a medical specialty that offers health results in a transversal way between specialties. The objective is to evaluate the degree of knowledge that graduates in branches of Health Sciences have on aspects related to the AP specialty.
Methods: A questionnaire was developed with 20 items. The questionnaire was answered by 223 students who visited the Pathology Unit as

part of their training (186 w, 37 m). The different items were evaluated using a Likert-type scale, based on the consideration that each student had about the item. Statistical analysis was performed with Student's t test.
Results: 19% of those surveyed had previous training on biosanitary laboratories. 48% had heard the word pathology before. 84% had a mother who was not engaged in health activities and 71% a father. 82% of the students did not know how a clinical autopsy differs from a judicial and 73% considered that a coroner and a pathologist perform the same type of autopsy. 19% of the students did not consider AP a specialty at the same level as Cardiology or Family Medicine.
Conclusion: The results obtained must have their implication to make the specialty reach the health field more and better and the students to show the academic and professional excellence of Pathology.

E-PS-17-014
Teach pathology through threshold concepts. Preliminary study
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Background & objectives: A threshold concept (TC) is the fundamental nucleus that endows the student with a lasting, deep and functional knowledge. The objective is to identify and analyse the perception that undergraduate students in Medicine about TC in Pathology.
Methods: Questionnaire with 35 items with 3 three sections was answered. 155 undergraduate students in Medicine, (109 w & 43 m). The different items were evaluated by means of a Likert-type scale (1-5) on their consideration of each CT in pathology. Statistical analysis was performed with Student's t test comparing the values by gender and the differences between the different sections.
Results: The most valued concepts were those in the tissue injury section (4.7 / 5) and biopsy (4.6 / 5). In the section of neoplastic pathology with a score of 4.3 / 5 and clinical autopsy with 3.9 / 5. 60% of the students were unaware of the term TC. 45% of the students did not consider AP as fundamental for the exercise of the medical profession.
Conclusion: The differences observed must be taken into account in the organization in the teaching programming of the Pathology subject and in the entire Medicine degree, to guarantee an autonomous learning process based on specific competencies.

E-PS-17-015
About primary synovial sarcoma of the mediastinum
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Background & objectives: Synovial sarcoma (SS) is mainly located in soft tissues and accounts for 5 to 10% of all sarcomas. Primary mediastinal localization is exceptional. Our aim was to describe the clinical, microscopic and diagnostic characteristics of the primary mediastinal localization.
Methods: we describe a retrospective study of 3 primary synovial sarcomas of the mediastinum diagnosed during a 6 year-period (2006-2021).
Results: We describe the cases of 2 women and 1 man (sex ratio de 1/2) with a mean age of 41.6 years. Chest pain was the most frequent symptom. Radiologic findings consisted in a mediastinal enlargement in all cases. CT-scan revealed a mediastinal mass in all cases evoking a haemangioma in 1 patient. Microscopic diagnosis was performed on a surgical mediastinal biopsy in 2 cases and a pleural biopsy in 1 case. The diagnosis of a monomorphic synovial sarcoma was retained in 2 cases and biphasic synovial sarcoma in 1 case. Cytogenetic findings concluded to the presence of a t(x,18) translocation in all cases.
Conclusion: Primary mediastinal synovial sarcoma is exceptional. Positive diagnosis necessitates the correlation of microscopic and clinical findings in order to rule out other diagnoses consisting mainly in a secondary mediastinal localization of a SS

E-PS-17-016
Sclerosing angiomatoid nodular transformation of the spleen clinically recognized as "splenic haemangioma": a case report
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Background & objectives: Sclerosing angoimatoid transformation of the spleen (SANT) is a rare disease, first introduced by Martel et al.
Less than 200 cases are reported in the literature.
SANT is nodular vascular proliferation of the red pulp without any signs of malignancy.
Methods: We report a case of 57 y.o. female patient, diagnosed clinically with splenic haemangioma by CT.
Abdominal ultrasonography showed heterogeneous formation in upper part of the spleen.
The patient has a past medical history of hysterectomy for uterine leiomyoma.
Laboratory parameters were normal.
Laparoscopic splenectomy was performed. The tissue specimen was submitted for macroscopic and histological evaluation.
Results: A rounded, lobulated mass measuring - 45/55/50 mm in size was identified. It was with focal haemorrhages and harder than surrounding parenchyma.
H&E and VG stains showed fibrotic multinodular formation with central small vessels of different types, focal haemorrhages and scattered inflammatory infiltrate.
By IHC the vascular structures showed different positivity for CD31, CD34 and CD8.
Conclusion: Sclerosing angiomatoid nodular transformation of the spleen (SANT) is rare vascular lesion in most cases without any clinical presentation. SANT is often diagnosed incidentally and mimic other spleen tumours, in particular haemangiomas.
In these cases splenectomy is curative.
Follow-up of the patients with SANT does not show malignant transformation of these vascular lesions.

E-PS-17-018
Retrorectal epidermoid cyst in a pregnant woman: a case report and a review of literature on a rare entity
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Background & objectives: Retrorectal cysts are a rare entity with strong female predominance. Most of retrorectal cysts are congenital developmental cysts (epidermoid, dermoid, and enteric). The rarity of these lesions and their nonspecific clinical presentation often lead to misdiagnoses and inappropriate operations.
Methods: A 33-year-old woman with pelvic pain performed an ultrasound on emergency evaluation context that revealed a twin pregnancy and a retrorectal hypoechoic cystic mass. She then underwent a MRI examination that showed a neoformation compressing the rectus and in close relation with spinal merging nerve roots, suggesting a solid mesenchymal neoplasm. A fine-needle biopsy revealed scant keratin scales.
Results: In multidisciplinary consultation it was decided to wait until the term of pregnancy to perform trans-sacral tumour resection, due to the absence of aggressive features. Then, we received the surgical resection specimen, which consisted of an unilocular cyst with 198g and 8,5x8x6cm with smooth lining containing a whitish soft material. Additionally, we also received the coccyx in continuity with the distal portion of the fifth sacral vertebra. The histopathological examination shows a cystic lesion with fibromuscular wall lined by a bland stratified squamous epithelium with granular layer containing laminated keratin, consistent with the diagnosis of a development cyst, epidermoid-type.
Conclusion: There are no complications resulting from the surgery and the pelvic pain subsided. Retrorectal cysts are a rare entity that can be difficult to diagnose due to nonspecific clinical findings and difficult

radiological differential diagnosis. A malignant degeneration of these tumours was exceptionally described in the literature. The surgical treatment must be performed to treat the symptoms and for a correct diagnosis of the nature of the lesion.

E-PS-17-019

A case report of a tumour-to-tumour metastasis diagnosed on fine needle biopsy

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Background & objectives: A case report documenting tumour-to-tumour metastasis of invasive ductal breast carcinoma in a primary renal neoplasm. A 83 old woman had been admitted to the urology clinic upon computed tomography (CT) imaging of the abdomen and pelvis.
Methods: CT revealed a 7x6 cm solid enhancing mass from the lateral aspect of the r/l kidney, suspicious for renal cell carcinoma (RCC) together with subcutaneous nodular lesions on upper extremities. She was treated 18 years earlier for invasive ductal breast carcinoma and currently was under oncological surveillance.
Results: Using the guided fine needle biopsy (FNB), 3 FNB from renal mass and 2 FNB from subcutaneous nodules were obtained. Pathohistologically, tumour tissue was detected in all samples. In subcutis FNB a metastatic breast cancer, and a clear cell renal cell carcinoma (CC RCC) (ISUP grade 2) was diagnosed in each of 3 samples obtained from the kidney. Simultaneously were also small, histologically distinct tumour areas visible in kidney samples raising suspicion for the presence of another tumour tissue incorporated in CC RCC. Immunohistochemical analysis (ICH) confirmed the suspicion and distinct ICH malignant tumour profiles were determined. Upon these pathohistological findings, the tumour was classified as a collision tumour.
Conclusion: The collision tumours are rare findings; providing important additional information on a particular tumour's biology. Usually, a recipient tumour presents a less aggressive phenotype amplifying the donor tumour re-seeding easily.
In the circumstances when clinical consensus management of primary renal neoplasms indicates, pathological diagnosis is limited by the methodology of acquisition and prone to sampling error. Therefore, we point out that despite applied methodology this rare diagnosis was determined being to our knowledge, the first reported finding of such pathology.

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E-PS-18-002

Congenital high airway obstruction syndrome – report of two foetal autopsies

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Background & objectives: Congenital high airway obstruction syndrome (CHAOS) is a rare and usually lethal malformation, mainly caused by laryngeal atresia. We present the autopsy findings of two 2nd trimester foetuses with CHAOS caused by trachea atresia and severe infraglottic stenosis.
Methods: Foetus A and B were respectively the first and second children of non-consanguineous healthy couples. Both were otherwise uncomplicated pregnancies. Second-trimester ultrasound revealed, in both cases, a hydropic foetus with bilateral enlarged hyperechogenic lungs, prominent bronchial tree and trachea, and inverted diaphragm. The findings were characteristic of CHAOS and after genetic counselling both couples opted for termination of pregnancy.
Results: Foetus A, a 17-weeks male, had micrognathia, low-set ears and bilateral clubfoot. We confirmed hydrops fetalis and the diaphragm inversion. The heart was vertical, entrapped between augmented lungs, histologically diffusely microcystic with an adenomatoid appearance. There was a cul-de-sac interruption immediately below the larynx, and histology sections showed a complete absence of the upper trachea, with downstream segment dilatation.
Foetus B, a 24-weeks female, was unfortunately severely damaged by the extraction, compromising gross examination. We found hypertelorism and nasal hypoplasia. Lungs were heavy, 150% above the normal value. There was a severe luminal narrowing at the infraglottic larynx, confirmed on histology.
Conclusion: CHAOS is typically diagnosed on sonography based on detection of secondary alterations to upper airway obstruction. However, the specific cause of obstruction is not easily determined on imaging. We present two CHAOS cases in which autopsy established the exact obstruction cause: trachea atresia and severe infraglottic stenosis, both rare CHAOS causes. Moreover, autopsy detected anomalies unrelated to airway obstruction, whose reports are necessary to provide a better insight into this unusual malformation.

E-PS-18-003

Malformed foetus due to a genetic disorder-rare case with Ring chromosome 14 syndrome

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Background & objectives: In the majority of cases, the causes of intrauterine death remain unknown despite detailed evaluation. Approximately 25% of neonatal/stillbirths have been attributed to chromosomal abnormalities. Ring 14 chromosome damage is associated with a number of frequent severe signs and symptoms.
Methods: A 35-year-old pregnant women was admitted at the Emergency Department due to premature rupture of the membranes. At the ultrasound there were signs of foetal distress plus multiple abnormalities seen like clinodactyly, polydactyly, craniofacial dysmorphism, multiple and variable malformations (nervous, digestive, cardio-circulatory, genital, renal). Delivery was performed through a caesarean section, with an Apgar score of 3/4.
Results: The baby died after 3 hours from birth due to severe respiratory failure. From the data provided by the mother we found genetic tests were performed with the diagnose of deletion of the long arm of chromosome 14, with major consequences on the nervous system. At the autopsy multiple malformations were noted, in almost every major system: bilateral anophthalmia, large low inserted ears, thin lips with downwardly turned corners of the mouth, high palate, polydactyly and clinodactyly, microcephaly, large anterior fontanelle (4/3 cm), partial hypoplasia of the cerebellar vermis, tetralogy of Fallot, megacolon, imperforated anus, bicornuate uterus, dysplastic right kidney with multiple cysts.
Conclusion: In the case of a foetus with multiple malformations, it is imperative to perform a genetic test to expose the subsequent risks of possible mutations. Ring chromosomes are rare abnormalities, most of the time of de novo origin, presenting a different phenotype according to the loss of genetic material and genetic instability. Clinically, the ring 14 syndrome is characterized by a recognizable phenotype of shortness of stature, distinctive facial appearance, microcephaly and ocular abnormalities.

E-PS-18-004

Tailgut cyst in a child: a very rare case report

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Background & objectives: Tailgut cyst or retrorectal cystic hamartoma (TGC) is a rare congenital anomaly in the presacral space, believed to

arise from the tailgut embryonic remnants. The inconstant anatomical location and the clinical presentation being mostly asymptomatic, make the TGC frequently underdiagnosed.
Methods: We report a case of a 2-year-old girl diagnosed with TCG in the Department of Pathology of the University Hospital of Monastir and we describe its histological features.
Results: A 2-year-old girl presented with a sacral swelling growing for over 6 months. She had no other symptoms. Physical examination and magnetic resonance imaging (MRI) confirmed the presence of a 10 cm cyst in the pre-sacrococcygeal space and a resection was done. Histological examination of the resected specimen concluded to the diagnosis of TGC. It presented as a cyst lined by a mucinous columnar epithelium. The cystic space contain mucinous material. Its wall was composed of disorganized adipocytic tissue and smooth muscle cells surrounded by lymphoid follicles. The postoperative course was uneventful, with no recurrence of the mass on the MRI, performed 6 months after the surgery.
Conclusion: TCG is a congenital lesion usually diagnosed in adult patients and rarely detected in infants. Due to its retrorectal space, the diagnosis can be difficult to distinguish from an inflammatory process or other differential diagnosis such as primary tumours of neurogenic or osteogenic origin. A close follow-up is advisable as TCG could be associated to a malignant tumours that can show disease progression even after surgery.

E-PS-18-005
New-born with left ventricular non-compaction cardiomyopathy
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Background & objectives: Left ventricular non-compaction cardiomyopathy is a persistence of abnormal foetal myocardium and is a rare cause of cardiomyopathy characterised by hypertrabeculation, thin compacted layer, and deep inter-trabecular recesses, commonly hypothesized due to an arrest in compaction during foetal development.
Methods: We present the case of a 35-week-old gestational age newborn with anaemia, thrombocytopenia, gastroschisis and left hypertrophic myocardiopathy, feature that was seen by cardiovascular resonance imaging, and who died one day after because of refractory hypoxemia. We received this new-born in our pathology department as an autopsy.
Results: When we dissected the heart we saw hypertrophy of both ventricles, as well as a lot of trabeculations in myocardium of left ventricle apex. Histologically, we saw many thin muscular trabeculations with deep inter-trabecular recess, with blood between them and with the compact layer separating the muscular trabeculations from the epicardium reduced in thickness.
Because of this features, we made the diagnosis of left ventricule non-compaction cardiomyopathy with hypertrophic myocardiopathy of both ventricles.
Conclusion: Left ventricle non-compaction myocardiopathy is a rare disease with an estimated incidence of 0.12 per 100.000 in children up to 10 years of age, that can be associated with other cardiac abnormalities and diverse syndromes, ordering for genetic counselling. It may present in the neonatal period with cardiac failure or with sudden death, although other cases may not present until later in life. Affected alive individuals are at risk of left ventricular failure, life-threatening arrhythmias and cardio-embolism.

E-PS-18-006
Pentalogy of Cantrell: an autopsy case report of a complete phenotype
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Background & objectives: Pentalogy of Cantrell (POC) is a rare congenital condition classically involving defects of the lower sternum, anterior diaphragm, supraumbilical abdominal wall, pericardium and intracardiac anomalies. Our goal is to report a new case with review of the literature.
Methods: An autopsy from a nonviable 13 weeks' gestation foetus was performed, with previous diagnosis of a large omphalocele with liver protrusion at 11 weeks. External and internal post-mortem examinations, including stereomicroscopic examination for dissection, were conducted. Histological evaluation of tissue sections, analysis of the foetus' skeleton and foetal aneuploidy screening followed by copy number variation (CNV) analysis were performed.
Results: The autopsy showed a male foetus with growth and maturation parameters suitable for gestational age. A lower defect of sternum, anterior diaphragmatic and midline supraumbilical abdominal wall defects, associated to a diaphragmatic pericardial defect, ectopia "cordis" and pulmonary atresia were identified. Exteriorization of abdominal organs (liver, stomach, intestine, pancreas and spleen) was observed across the abdominal defect. Foetal aneuploidy screening and CNV analysis by array comparative genomic hybridization were normal. Placental examination revealed acute deciduitis, morphological aspects suggestive of placenta detachment and hypercoiling of the umbilical cord.
Conclusion: Our case shows a nonviable 13-week-old male foetus with focus on a full expression of the POC, a rare condition of a large spectrum phenotype. With this case we intend to review the POC spectrum condition and reinforce the importance of the autopsy examination for definitive diagnosis.

E-PS-18-007
The importance of histopathology in the diagnosis of a fulminant autoimmune hepatitis of a young child
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Background & objectives: A minority of patients with acute-onset of the autoimmune hepatitis (AIH) present with acute liver failure. Usually, the aetiology is difficult to established. Our objective was to highlight the importance of histopathological examination in the diagnosis of a fulminant AIH.
Methods: We present a case of a 9-month-old girl with complete atrioventricular canal defect (CAVC) and Down syndrome detected during pregnancy. CAVC repair was done at 4 months of age. She presented with persistent fever and acute hepatitis negative for specific autoantibodies and with a fulminant course leading to death less than one month after onset. Total serum gamma-globulins were increased.
Results: Both external and internal autopsy observations were evaluated. The examination of the liver revealed portal mononuclear cell inflammatory infiltrate extending into the lobule (interface hepatitis), centrilobular injury with prominent hepatocellular necrosis and lymphoplasmacytic inflammation. These histopathological features were associated with massive multilobular necrosis and areas of severe piecemeal necrosis. Other examined organs revealed no evident or suggestive pathological features.
Conclusion: The acute-onset AIH can resemble an acute viral or toxic hepatitis. The histopathology is needed for an early diagnosis and an early immunosuppressive therapy. The correct histopathological diagnosis in AIH needs a detailed clinical history, a biopsy request form and a clinicopathological correlation.

E-PS-18-008
Ewing sarcoma displaying extensive ganglioneuroblastomatous differentiation
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Background & objectives: A rare case of Ewing Sarcoma displaying extensive ganglioneuroblastomatous differentiation is presented.

Methods: A nine-year-old female patient presented with back pain and difficulty in walking. MRI revealed a paraspinal mass lesion located at the level of thoracic vertebrae 8. The lesion was completely resected.
Results: The tumour was histopathologically a small round cell tumour however showed extensive ganglioneuroblastomatous differentiation areas. We have given a diagnosis of a ganglioneuroblastoma, intermixed type. Because the tumour did not respond oncologic medical therapy sufficiently, reoperation was performed. The small round cell component was more prominent in this specimen. Immunohistochemically tumour was positive for CD99 and NKX2.2 in the round cell component. Molecular analysis revealed EWSR1/FLI fusion. The pathological diagnosis is renewed as "Ewing Sarcoma Displaying Extensive Ganglioneuroblastomatous Differentiation".
Conclusion: Ganglioneuroblastomatous differentiation in Ewing Sarcoma is exceedingly rare. In this presented case ganglioneuroma component was extensive. Recognition of this phenomenon in Ewing Sarcoma cases may prevent a possible misinterpretation and a failure in oncologic treatment.

E-PS-18-009
Primary pigmented nodular adrenocortical disease: case report and literature review
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Background & objectives: Cushing's syndrome (CS) in paediatric population is adrenocorticotropic hormone (ACTH)-dependent in 80% of cases and ACTH-independent in 20% mostly due to primary hyperplasia or adenomas of the adrenal glands, and very rarely by primary pigmented nodular adrenal disease (PPNAD).
Methods: We present the case of a three-year-old girl that was admitted to our hospital because of obesity, moon-like face, hirsutism and dorsal hump. Nuclear magnetic resonance showed a diffuse thickening with slight nodular appearance in both adrenal glands. Liddle test made evident a paradoxical increase in cortisol. A bilateral adrenalectomy was performed and sent to our pathology department.
Results: On gross examination, adrenal glands were both enlarged and had multiple brown nodules measuring between 2 and 8 mm. All the nodules were located in the adrenal cortex and, microscopically, were composed of large irregular cells with eosinophilic cytoplasm and irregular hyperchromatic nuclei. Some of these cells contained brown pigment compatible with lipofuscin in the cytoplasm. Necrosis, atypical mitotic figures or venous invasion were not found. Nodules showed positivity for synaptophysin, melan A and inhibint, while HMB45 and S100 were negative. These features were consistent with PPNAD.
Conclusion: PPNAD is a rare cause of CS that should be known. PPNAD could be associated with Carney Complex, often accompanied by mutation of the PRKAR1A gene. PPNAD shows infracentimetric multiple nodules in both adrenal glands with atypical cells and brown pigment. The histological differential diagnosis include melanoma and cortical carcinoma. Medical record, imaging and Liddle test together with these histological features are crucial to make the diagnosis of this entity.

E-PS-18-010
Congenital heart malformations (CHM) – a foetal autopsy highlight
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Background & objectives: CHM are an important cause of childhood mortality and the most common congenital abnormality. Foetal heart evaluation is a reproducible exam although with limitations (smallness of the foetal heart, high heart rate and limited foetal access).
Methods: We present an autopsy case report of a 36-week-old female foetus that died in utero. The pregnant was 33 years old, without relevant medical or obstetric background. At 20 weeks, gestational age, there was difficult ultra-sonogram visualization of the foetal heart structures, although apparently normal.
Results: The foetus had anthropometrical parameters compatible with 36-week-old gestation. No external malformations were found. The heart dissection found a 3mm interventricular communication and complex structural cardiac malformations. The pulmonary artery exited from the right ventricle, although, the posterior wall had two ostia which originated the left and right branches and another superior ostium, that communicated with the aortic arch. The aorta emerged and branched as usually till the emerging of the left subclavian artery, where it became atretic and communicated with the pulmonary artery, which turned out to be a systemic vessel and curved down into the remaining thorax and abdomen. No other malformations were described.
Conclusion: CHM are the most common congenital abnormality, either isolated or in association with other foetal anomalies. We present a case report of a foetus with a complex cardiac structural malformation that didn't fit into a syndromic diagnosis and wasn't detected during the pregnancy due to the foetal cardiac ultrasonography limitations. Autopsy still remains an important tool to the final diagnosis, and to clarifying future management into similar cases.

E-PS-18-012
Prune-belly syndrome: an autopsy case report
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Background & objectives: Prune-belly syndrome (PBS) is a rare congenital condition characterized by deficient/ absent abdominal musculature and urinary tract abnormalities, cryptorchidism in males or genital abnormalities in females. Our goal is to report a new case with review of the literature.
Methods: An autopsy from an 18 weeks' pregnancy submitted to termination due to anhydramnios, hydrops and megacystis, was performed. External and internal post-mortem examinations, including stereomicroscopic examination for dissection, were conducted. Histological evaluations of tissue sections, analyses of the foetus' skeleton and genetic testing by array comparative genomic hybridization (aCGH) were performed. The placenta was submitted for examination.
Results: The autopsy showed a male foetus with growth and maturation parameters suitable for gestational age. Hydrops and marked abdominal distension were observed, associated with bladder distention, thin abdominal wall, showing areas of muscle atrophy, bladder neck and distal urethra stenosis. Broad flat nose, low set ears, microretrognathia, clubfeet and pulmonary hypoplasia were identified. Additionally, cardiac examination showed an atrial septal defect (ostium secundum). Testis were located in the abdominal cavity, as expected at this age. aCGH in foetal DNA was normal.
Conclusion: Our autopsy case shows a 18-week-old male foetus with findings consistent with PBS. Cardiovascular malformations as the atrial septal defect and hydrops may also be found in association to PBS, although less frequently. The other features described are secondary to anhydramnios - Potter's sequence – in this context of PBS. With this case we intend to review the PBS condition and reinforce the importance of the autopsy examination for definitive diagnosis.

E-PS-18-013
A fatal extensive plexiform neurofibroma in a new-born
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Background & objectives: Plexiform neurofibroma represents an uncommon variant of Neurofibromatosis type 1 in which neurofibromas arise from multiple nerves as bulging and deforming masses, also involving connective tissue and skin folds. Plexiform neurofibromas have rarely been reported in the neonatal age group.
Methods: We received a 70-day-old infant for diagnostic autopsy. He was born by vaginal delivery at term. The pregnancy was not followed-up. There was no known family history suggestive of neurofibromatosis 1. On neonatal examination, he presents a congenital glaucoma with bilateral exophthalmia and right submandibular mass rapidly growing leading to death.
Results: At autopsy, the infant weighed 3870 grams. His size measured 54cm. His face was deformed by a right parieto-temporo-jugo-mandibular and submaxillary mass measuring 14*6*4cm. The mass was poorly limited. There was not "café au lait" spots. On dissection, the mass infiltrated the meninges, the entire pre-retro-tragian and submandibular zone. It also developed in the posterior mediastinum and compressed the aero-digestive tract. The other organs had no apparent malformations. Histologically, the mass corresponded to a proliferation with plexiform architecture, formed of nodules resembling the nerve sections. It was made of spindle cells without any atypia or mitosis, developing in a myxoid stroma. The tumour cells expressed ps100 and gfap.
Conclusion: Plexiform neurofibromas arise from multiple nerve fascicles and are frequently deep seated, diffuse and infiltrating. The lesions are usually congenital and tend to grow most rapidly during childhood and are common in the head and neck region. Plexiform neurofibromas may compress the airway or spinal cord and can transform into malignant peripheral nerve sheath tumours. Definitive treatment of plexiform neurofibromas is complete surgical removal which can be challenging and difficult due to location of the tumour and frequent recurrence.

E-PS-18-014
Umbilical cord tumour of a new-born
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Background & objectives: Umbilical cord tumours are rare findings. We report a 3 cm measuring umbilical tumour that was surgically excised together with the umbilical cord. The tumour tissue, macroscopically resembling liver tissue, was sent for histological analysis.
Methods: Pathological examination of the tumour was performed according to local standards.
Results: Case of a prenatally diagnosed umbilical tumour of a new-born girl gestational age: 37+1 weeks. Ultrasound revealed a solid mass unrelated to the abdominal cavity except a single vessel leading to the intestine, and an umbilical hernia. A hamartoma was suspected. Histologically the specimen displayed trabecularly arranged hepatoid cells (HepPar1 positive), regular sinusoids (CD31 positive) and disseminated portal fields with CK7 positive bile ducts as well as disseminated hematopoietic foci (GLUT-1 pos, Glycophorin C and MPO pos), concordant with foetal haematopoiesis in foetal liver tissue. Centrally located was oedematous mesenchymal stroma with dilated lymph vessels (D2-40), a prominent blood vessel and encircling bile ducts, resembling a larger oedematous portal field.
Conclusion: Umbilical cord tumours are mainly angiomyxomas and teratomas. Up to now, only 20 cases of iver tissue in the umbilical cord have been published. Some of them describe the complete liver being present within the umbilical cord. Hence in these cases an omphalocele has to be considered as differential diagnosis. But though our case has features of an omphalocele as well, liver tissue was located in the wall of the hernia sac,not within the lumen.

E-PS-18-015
Case of an Ischiopagus-anomaly at the 15th gestational week
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Background & objectives: We present the case of an Ischiopagus-anomaly at the 15th gestational week. The female gemini showed joint lower abdominal organs but separated upper abdominal and thoracal organs. The cause of the intrauterine death was a intervillous hematoma of the placenta.
Methods: Autopsy and histopathology was done according to standard protocols.
Results: The gemini were attached in a 90° angle towards each other. Radiologically they had a commune pelvic bone, two frontally oriented legs and a third rudimentary leg pointing dorsally. Each geminus had only one arm but completely separate vertebral columns and their respective lungs were regularly shaped. One heart showed a single ventricle and tricuspid valve atresia the other was unremarkable. There were seperate stomachs and smaller intestines but a common large bowel. Each foetus showed their own unremarkable kidney-and adrenal pairs plus ureters entering a common urinary bladder. There was also a common liver, pancreas, large bowel, inner genital female organs and anus. Death was related to placental problems.
Conclusion: Conjoined twins are a very rare occurrence without a specific cause of origine. Possible reasons for development are an initially disturbed separation of the embryonic disc or a fusion of initially separate embryonic discs. Ischiopagi – as described here – are the rarest group within the feature of conjoined situations. Typically one of the gemini may show anomalies as was the case here with one foetus presenting with a vitium cordis. Cause of the intrauterine death an placental intervillous hematoma.

E-PS-18-016
Multiple cancers on a family with Li Fraumeni Syndrome: case report
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Background & objectives: Li Fraumeni Syndrome (LFS) is a rare autosomal-dominant familial cancer syndrome characterized by germline TP53 mutations and early-onset cancers. Sarcoma, breast cancer, leukaemia, brain cancer, and adrenocortical carcinoma (ACC) are the most frequently seen cancers in LFS.
Methods: A 14-year-old female patient was diagnosed with Rhabdomyosarcoma (RMS) 12 years ago and was treated for it. The same patient was diagnosed with osteosarcoma of the iliac wing three years ago. Her little brother is a 12-year-old male patient. He was admitted to the hospital with a solid mass in his left abdomen, and he was diagnosed with (ACC).
Results: A female patient who received radiotherapy for bladder-derived embryonal RMS was diagnosed with osteosarcoma eight years later whereas her brother was diagnosed with ACC the same year. The familial genetic analysis was performed germline TP53 mutation was found in both siblings. A year ago in the girl's follow-up, a pulmonary lesion was detected, and her biopsy showed primary pulmonary adenocarcinoma. She received surgical treatment without chemotherapy. Liver and lung metastases that developed within 1 year were detected in the brother who was hospitalized three years ago because of a left abdominal mass and was diagnosed with ACC by biopsy. The boy underwent metastasectomy, and he is currently receiving postoperative chemotherapy.
Conclusion: LFS is a hereditary cancer syndrome that produces disorganized tumour suppressor protein P53. LFS should be evaluated together with family history and approached in a multidisciplinary manner in the presence of more than one tumour.

E-PS-18-017
Childhood eosinophilic esophagitis in children: a report of a case and literature review
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Background & objectives: Eosinophilic esophagitis(EE) is a recent pathology defined by abnormal immune response of the oesophageal mucosa to exogenous allergens, leading to chronic and intense mucosa infiltration by 15 eosinophils per High-Power-Field (Eos/HPF). We report an observation of OE in a child.
Methods: An 8-year-old male child with no notable surgical/ medical history, in particular no known allergies or growth disturbances, has consulted for chronic vomiting without other associated signs. Clinical examination did not reveal any abnormalities. The biological assessment was correct. He underwent an upper gastrointestinal endoscopy which doesn't found any lesions. Systematic, staged oesophageal biopsies were performed.
Results: Histologically, the specimen was lined by squamous, regular epithelium, with morphologically normal nuclei, non-dysplastic or metaplastic, massively infiltrated by numerous eosinophilic polynuclear cells. Thus, the diagnosis of eosinophilic esophagitis was retained.
Conclusion: Few studies have focused on this rare entity, which still poses a diagnostic and therapeutic problem. It seems essential to standardize practices in order to better understand this pathology and improve its management. The place of new diagnostic markers remains to be clarified.

E-PS-18-018
Malignant rhabdoid tumour of the liver - morphological characteristics of biopsy, primary resection and post-chemotherapy specimens in two cases
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Background & objectives: Malignant rhabdoid tumour (MRT) is a very rare hepatic tumour in infants that have an aggressive clinical behaviour. It can create diagnostic problems in tumour biopsy because of its heterogenous histological picture.
Methods: The patho-clinical description with detailed morphological analysis of two hepatic MRT cases are presented. The examined material in case 1 consisted of primary biopsy, surgical biopsy after 1st line chemotherapy and tumour resection after 2nd line chemo, and in case 2- biopsy, and primary tumour resection material. Wide immunophenotyping including INI1 was performed.
Results: In case 1 the biopsy contained the reactive liver tissue made of clear cells and only two fragments of small cell tumour up to 0.5 mm and was erroneously diagnosed as hepatoblastoma foetal type. Post 1st- line chemotherapy surgical biopsy showed MRT made of small cell and more typical rhabdoid pattern. Post 2nd line chemotherapy tumour resection showed pleomorphic focally multinucleated cellular partim myxoid malignancy. In case 2 the biopsy was very limited and inconclusive, the tumour underwent primary resection, showing complex histology with evident rhabdoid population. The immunophenotype was heterogenous with consistent INI1 loss of expression.
Conclusion: MRT of the liver because of its rarity can cause diagnostic difficulties and therapeutic problems. Biopsy material from these infantile tumours can be very limited and non- representative. Post- chemotherapy changes within MRT can show pleomorphic mixed morphology. INI1 loss is the basic marker of this entity in the context of other immunoprofile elements.

E-PS-18-019
Inverted Meckel's diverticulum: an unexpected microscopic diagnosis involving a child
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Background & objectives: Intussusception in children is predominantly idiopathic (90%). In English literature, few paediatric cases have been reported to be caused secondary to Meckel's diverticulum inversion; here we present one such case revealed unexpectedly during microscopic examination.
Methods: A 13-year-old boy experienced recurrent abdominal pain of five-year duration, worsened over the last five months. Ultrasonography showed spontaneously resolved episodes of intussusceptions. The boy underwent exploratory laparoscopy. Intraoperative findings included the identification and reduction of an ileoileal intussusception, 30cm from the ileocecal valve. Segmental enterectomy was performed. An intraluminal mass was palpated and considered to be an ileal polyp.
Results: Grossly, a bulb-shaped polyp of 4x3.5x2.9cm, with a thick, superficially eroded mucosal covering and a fatty core was noted. The base of the polyp was located on the mesenteric side of the intestinal mucosa. No defect of the bowel wall was identified. Macroscopically, a submucosal lipoma was suspected with concern as to the thickness of the mucosa. The microscopic examination of the polyp revealed a central core of mature adipose tissue covered sequentially by ectopic gastric and small bowel mucosa, submucosal and smooth muscle layers. A communication between the mesenterium and the fatty content of the polyp was microscopically obvious. The final diagnosis of an inverted Meckel's diverticulum was made.
Conclusion: This case emphasizes the role of exploratory laparoscopy in paediatric recurrent intussusception. Inverted Meckel's diverticulum should not be overlooked as a lead point of intussusception in children, even when its characteristic features are not identified by imaging techniques and/or macroscopically by the surgeon and pathologist.

E-PS-18-020
Large pulmonary arteriovenous malformation at 25 weeks of gestational age foetus – a case report
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Background & objectives: Pulmonary arteriovenous malformations (PAVs) are rare abnormal communications between pulmonary arteries and veins without capillary-bed complete maturation. Most cases are congenital.
We present a PAV case diagnosed at 23 week gestational (WG) age with subsequent autopsy examination and report.
Methods: Prenatal echocardiography showed PAV in the left lung with increased vascularity of the inferior and medial third of the left hemithorax and cardiomegaly predominantly in the left heart. After medical termination of pregnancy, the autopsy study was consented.
The general complete autopsy observation show well-formed female foetus, only with internal thoracic malformation.
Results: Examination confirms the prenatal evaluation: dilated and large left pulmonary artery and left inferior vein; left lower lobe (LLL) was congestive, with dilated arteries and veins.
On microscope, large vessels have contoured walls and irregular thickness of elastin layers, where artery and vein could be in continuum. LLL tissue shows septal mesenchyme and irregular apposing capillaries (CD31) to airspace epithelial cells (CK7), indicating an incomplete organogenesis: glandular/canalicular phase.
As a first tier genetic study we choose to evaluate the most common causes of Rendu-Osler-Weber Syndrome (ROWS), but the sequencing of genes ENG and ACVRL1 didn't identified any pathogenic or likely pathogenic variant. The sequencing of GDF2 and SMAD4 is ongoing.
Conclusion: PAVs are usually unilateral, affecting inferior lobes, approximately 70% related with ROWS/10-20% sporadic cases. In our case, the two most common causes of ROWS (ENG, ACVRL1) didn't occur. Study is still ongoing because it's important for posterior counselling of the others family members.
Pathological study confirms the diagnosis, shows pulmonary microvascularization and overall architecture and evaluate associated

heart changes. Furthermore, it allows observation of other visceral malformations.
Early detection allows the correct management in prenatal period, preventing those serious situations.

E-PS-18-021
Duodenal duplication cyst masked by intussusception – case report
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Background & objectives: Duodenal duplications are rare congenital malformations that can be found anywhere along the gastrointestinal tract from the mouth to the rectum, but most frequent encountered in the ileum. We present a case of rare duodenal duplication cyst masked by intussusception.
Methods: We present the case of a term born baby, with 1 Apgar index at 37-38 weeks of gestational age. Shortly after birth the infant needed surgery for obstruction caused by a suspected bowel that revealed also the presence of a cyst attached to the duodenal wall. the cyst was submitted to the Pathology Department and analysed by standard methods.
Results: The obstructed symptoms of the baby were caused by intussusception of the jejuno-duodenal portion and the surgical reduction revealed the presence of a cyst attached to the duodenal wall. The pathology report showed the presence of an epithelial layer containing the intestinal mucosa, a smooth muscle layer and the cyst that was closely attached to the duodenal wall and sharing a common wall. The cysts mucosae was ulcerated and ischemic changes are observed. The case was signed as duodenal duplication cyst. Further investigations of the child revealed the presence of a slight ventricular dilatation. Enteric duplications are rare conditions and duodenal even rarer with different and poorly known etiopathogeny.
Conclusion: Even if rare, duplication cyst of the gastro-intestinal tract can produce severe complication that can endanger the life of children so that have to be regarded as possible serious conditions that can also be associated with other malformation/anomalies, often overlooked.

E-PS-18-022
Discordance of the foetuses in cases of monochorionic diamniotic twins reflects placental discordance
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Background & objectives: Selective foetal growth retardation is one of the most common complications of monochorionic twin pregnancy. The aim: to study the histology of the placenta in monochorionic twin pregnancy and assess its role in the formation of selective foetal growth restriction(sFGR).
Methods: Histological study (H&E) on the paraffin-embedded slices of placental samples taken after caesarean section at 28-36 g.a. from 24 patients aged 24-36 yrs old with monochorionic diamniotic twins has been performed. The study group with sFGR consisted of placenta samples from 17 puerperas. Control (without sFGR) placenta samples from 7 ones.
Results: sFGR was detected by ultrasound examination from18–31gestation weeks. The severity of the sFGR depended on the gestational age;the earlier the sFGR was detected, the more pronounced it was at the time of delivery. Moreover sFGR correlated with the severity of placental discordance (asymmetry of development).The area of the placenta adjacent to the foetus with sFGR had a lower blood supply, which is mainly associated with changes in the umbilical cord(marginal,membranous attachment of the umbilical cord($p<0,05$), thinned umbilical cord)($p<0,05$), a greater number of villous tree infarctions, accelerated maturation of the villous tree and an increase in angiogenesis with predominant branching of blood vessels($p<0,05$).In the control group placentas were within gestational age($p<0,05$).
Conclusion: The most pronounced placental changes were present in cases of monochorionic diamniotic twins with discordance of foetal weight more than 25% and depend on the gestation period.

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E-PS-18-023
Report of a "foregut cyst" with oesophageal and bronchogenic features
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Background & objectives: Oesophageal and bronchogenic cysts share their major clinical and radiological features. We present a case with a lesion having coexistent oesophageal and bronchogenic histopathological features.
Methods: A 10-year-old asymptomatic female child had a 6-cm upper pole splenic cyst and a 2-cm cyst posteromedial to hepatic left lobe detected incidentally. Laparoscopic hemisplenectomy and en-bloc removal of the 2-cm cyst in close contact with the intraabdominal oesophagus without any intraluminal connection was performed. The postoperative course was uneventful.
Results: The paraesophageal cyst was lined by ciliated columnar epithelium resembling respiratory epithelium with TTF-1 positivity. The muscularis propria was two-layered and positive with smooth muscle antigen (SMA) as in the gastrointestinal tract. There was no bronchogenic cartilage which is essential for bronchogenic duplication cyst diagnosis. TTF-1 expression in the developing foregut is limited to the respiratory tract. It is known to be expressed in tracheoesophageal fistula indicating that the distal oesophagus is probably a respiratory tract-derived structure. We were not able to make the definite differential diagnosis between oesophageal and bronchogenic cysts, therefore the lesion was reported to be a "foregut cyst".
Conclusion: The histopathological findings of the reported patient support that differentiating between distal oesophageal and bronchogenic lesions is not straightforward. Current data about embryological development of oesophageal and respiratory diverticuli as well as their cystic lesions is insufficient for a thorough definition. We think the term "foregut cyst" is a more appropriate nomenclature for such cysts with indefinite origin.

E-PS-18-025
Right atrial isomerism with biallelic GDF1 variants
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Background & objectives: A primigravida on antenatal ultrasound scan showed foetal cardiac abnormality including unbalanced ventricles and total anomalous pulmonary venous drainage plus exomphalos. Parents were non-consanguineous. No relevant family history. Pregnancy was terminated at 21+5 weeks. Parents' consented to perinatal autopsy.
Methods: Perinatal autopsy confirmed a complex cardiac defect including right atrial isomerism, total anomalous venous drainage and complete atrioventricular septal defect. There were bilateral trilobed lungs. The spleen was absent. The liver showed situs inversus but the intestines were malfixed and partly occupied an exomphalos sac. Following the results of the autopsy the parents were referred to clinical genetics.
Results: Chromosome microarray analysis on foetal skin showed a normal male karyotype. Trio exome sequencing was undertaken and showed

that the foetus was compound heterozygote for pathogenic GDF1 variants. These included a maternally-inherited frameshift variant (c.909dup; p.(Val304ArgfsTer48)), which had been reported previously by Kaasinen et al., 2010 (PMID: 20413652) and a paternally-inherited nonsense variant (c.681C>A; p.(Cys227Ter)) that had been reported previously by Karkera et al., 2007 (PMID: 17924340). Based on these results the couple were counselled a 25% (1 in 4) risk of recurrence in future pregnancies with the option of having diagnostic prenatal testing.
Conclusion: Autosomal recessive forms of right atrial isomerism caused by mutations in GDF1 have been reported infrequently.
Heterozygous loss-of-function variants in GDF1 were previously reported to cause multiple congenital heart defects (Kakera et al., 2007). Jin at al., 2017 (PMID: 28991257) reported one amongst 2,871 probands with congenital heart disease with right atrial isomerism who was compound heterozygous for mutations in the GDF1 gene. Trio exome sequencing is recommended in foetuses with right atrial isomerism to identify monogenic causes.

E-PS-18-026
Zellweger syndrome: 2 case reports and literature review
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Background & objectives: Zellweger syndrome (ZS) is a disorder of peroxisome biogenesis. It is a metabolic disease associating major brain damage, renal and liver lesions and facial dysmorphia. This syndrome is difficult to identify given its clinical and genetic heterogeneity.
Methods: A retrospective study at Pathology department of F. Hached Hospital over a period of 20y, revealed two cases of ZS concerning a 5 days-old boy and a 1-month year-old girl, dying from severe bradycardia. ZS was highly suspected due to parental consanguinity, death in the siblings at neonatal age. Genetic analysis was not available. Autopsy examination was held.
Results: Both new-borns presented a peculiar facial abnormality associating: trigonocephaly, an enlarged anterior fontanelle, a high forehead, hypertelorism, a low located and badly hemmed ears, a small nose with a broad bridge, a highly attenuated philtrum. Characteristic brain lesions were noticed on autopsy examination: focal hypertrophic brain gyration, bulbar olives heterotopias, pseudo-cystic lesions of subependymalgerminolysis. Hematoxylin eosin slides of brain samples highlighted subcortical neuronal heterotopias and astrocytic gliosis of white matter. Both kidney and liver showed respectively renal microcysts and remodelling oh the hepatic ductal plate enlarged by inflammatory fibrosis.
Conclusion: ZS is a rare congenital disease with fatal evolution. The aim of this work is to warn and remind physicians about the role of autopsy examination for clinical diagnosis, in peculiar because of great difficulties of genetic diagnosis.

E-PS-18-027
Primary adrenal teratoma in childhood: a rare case report
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Background & objectives: Teratomas usually occur in the ovaries and testes, however, they can arise in a variety of locations. Paediatric adrenal teratomas are extremely rare neoplasms. We report a case of a 2-year-old girl with adrenal mature cystic teratoma.
Methods: A 2-year-old girl is brought to the hospital by her parents after she falls from the stairs. Therefore, a mass is detected in the region of left adrenal gland in the abdominal ultrasound. Magnetic resonance imaging showed a 93x88x58 mm heterogeneous mass in the left adrenal gland area. The patient underwent mass excision.
Results: At the operation, it was observed that the mass expanded the renal vein and its blood poured into the renal vein. Macroscopic examination of the surgical specimen showed a 11 cm soft and roundish mass with well-defined margins. The cut surface of the mass was fatty and heterogeneous with solid and cystic areas along with focal cartilaginous areas. Histopathological examinations revealed a mature cystic teratoma with no malignant features. No normal adrenal gland was seen. The mass included organized mature adipocytes, intestinal mucosa, respiratory mucosa, mature glial tissue, nerves and ganglion cells, cartilage, bone, muscle fibres, lymphoid tissue, skin and hair shafts.
Conclusion: Paediatric adrenal teratomas are uncommon neoplasms, representing 5% of all paediatric teratomas. Radiologic imaging such as ultrasonography, CT and MRI is helpful in the pre-operative diagnosis. However, the gold standard of managing adrenal teratoma is surgical resection and histopathological examination to differentiate them from similar characteristic retroperitoneal lesions.

E-PS-18-028
The early debut of an inflammatory myofibroblastic tumour of the gastrointestinal tract – a case report
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Background & objectives: An inflammatory myofibroblastic tumour (IMT) can occur in any location, more frequently in the lung and mesentery of children and young adults. IMT is thought to be a borderline malignancy, with a tendency to recur locally, but can rarely metastasize.
Methods: A 3 months old boy was admitted with a 10 days debut of a subocclusive syndrome. Abdominal ultrasonography illustrates a tumour in the right iliac fossa, which measured 54/35/31 mm. Emergency surgery was performed and intraoperative examination revealed a tumour adherent to the terminal ileum, jejunum, cecum, and ascending colon. The excision specimen was sent for gross and microscopic examination.
Results: Gross examination revealed a white, firm-elastic tumour, without necrosis, infiltrating the ileum and colonic wall, but with intact colonic mucosa. Microscopic examination illustrates a tumour proliferation with moderate cellularity formed by spindle cells of moderate atypia, with vesicular nuclei and small nucleoli, on a pleomorphic inflammatory background with lymphocytes, plasma cells, eosinophils, and neutrophils; without necrosis or perineural invasion and with 8 mitosis/10 HPF. Immunohistochemistry showed positivity for Calponin, AE1-AE3, Actin, Desmin, CD34, as well as ALK, and negativity for EMA, Myogenin. There was a proliferation index of 25% with Ki-67. All these features were consistent with a diagnosis of Inflammatory Myofibroblastic Tumour.
Conclusion: This particular case highlights the early onset of the IMT, in a 3 months old boy, with a sudden debut of a subocclusive syndrome. There must be made a differential diagnosis with other sarcomatous and inflammatory entities. Usually, immunohistochemistry illustrates the more aggressive variants, with ALK-negative staining. Due to the fact this tumour can recur and metastasize, one has to always follow up with the patient after excision and, in rare cases, to continue the treatment with adjuvant therapy.

E-PS-18-029
Renal rhabdoid tumour: two cases report and review of the literature
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Background & objectives: Renal rhabdoid tumour is an uncommon entity and one of the most aggressive and lethal malignancies in children. We describe two cases (the only ones in our department over the last 20 years) and we have reviewed the literature.
Methods: There are two cases of renal rhabdoid tumour in our hospital: two young male and female children, in the third and fifth month of life,

with a big left and right renal mass, respectively. They were identified in ultrasound examination in the context of mild urologic symptomatology after a well-controlled pregnancy.
Results: Macroscopically, both nephrectomies showed a big renal mass (8,5x7,5 and 9,5x7 cm) occupying practically all its size. They had greyish-white and necrotic reddish cut surface and soft consistency. The microscopic study showed large ovoid to epithelioid cells that have abundant eosinophilic cytoplasm with the characteristic dense hyaline inclusion and a large vesicular nucleus with prominent nucleolus. In the first case, the tumour infiltrated into adjacent renal parenchyma and blood vessels. Both of them showed cancer-free resection margins and regional lymph nodes, being staged as stage II. The immunohistochemical profile showed negative muscle markers with vimentin and EMA positive. The study of INI1 showed loss of staining of tumour cell nuclei.
Conclusion: Paediatric renal rhabdoid tumour is an uncommon and highly aggressive malignancy found in young children, diagnosed mainly during the first 2 years of life. Because of the advanced stage at the time of presentation, his early detection and diagnosis are critical to ensure proper therapeutic management. Our first patient, 6 years later was in complete remission of symptoms after chemotherapy treatment and the second one, 3 months following diagnosis, responds well to chemoradiotherapy treatment.

E-PS-18-030
Characteristics of paediatric tumours of the genitourinary system and retroperitoneal space in children of the industrial region
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Background & objectives: Paediatric malignant tumours compared with adult malignancies are relatively rare pathologies. Although modern methods of diagnosis and treatment have allowed a positive prognosis of the outcome of treatment for paediatric patients, cancer remains a main cause of children's death.
Methods: A retrospective review of paediatric malignant tumours of the genitourinary system and retroperitoneal space in 75 children over a twelve-year period was made. The incidence of such paediatric neoplasms in Lugansk region, Ukraine was studied. Tumours morphological characteristics and the aetiology evaluated and analysed.
Results: Seventy-five cases of paediatric malignant tumours of the genitourinary system and retroperitoneal space were retrospectively reviewed. Nephroblastic neoplasms (Wilms tumours) had the highest incidence - 27 cases (36%); retroperitoneal tumours were in the second place in incidence - 19 cases (22%). A histological study of nephroblastomas revealed a typical tumour structure in 24 cases, and epithelial-type Wilms tumours in 1 case. The five-year disease-free life expectancy was 91%. The second large group consisted of tumours of the retroperitoneal space. Malignant soft tissue neoplasms were presented with liposarcoma-2 cases, infantile fibrosarcoma-1, angiosarcoma- 1, undifferentiated sarcoma – 2. Lymphoid neoplasms included 8 malignant lymphomas. Five cases were paediatric neuroblastomas.
Conclusion: Modern surgical techniques, adequate postoperative chemotherapy and radiation resulted in improved children survival rate. In present study five-year event-free life expectancy was 91% after Wilms tumours surgery and 13% in cases of the soft tissue tumours. Increasing knowledge about paediatric malignancies, cooperation of pathologists and oncologists create the possibility for complex investigations in this area. Many issues related to the study of the prevalence, tumorigenesis and pathology of children malignant tumours require further research.

E-PS-18-031
Intrauterine COVID-19 infection
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Background & objectives: One of the most important and disputable issues of COVID-19 is intrauterine infection. In spite of detection of SARS-CoVi2 in placenta and stillborn tissues by several investigators there are still no detailed descriptions of histological changes related to it.
Methods: Detailed clinic-pathological correlations, macro- and histological study of autopsy material of the mother, placenta and stillborn with COVID-19 infection proven by PCR, including immunohistochemical revealing of spike protein SARS-Covi2.
Results: .N.ZH., 34 y., pregnant at 37 w, got ill with respiratory symptoms, died on 11th day of disease due to viral pneumonia with ARDS. SARS-CoVi12+ on life time and postmortem. After death a stillborn boy was removed by caesarean section. Swabs for SARS-COvi2 from lungs and trachea were positive. Was diagnosed antenatal asphyxia with aspiration. Histologically proliferative overgrowths of bronchial epithelium and macrophages. In all organs endothelial cells with enlarged light nuclei. Similar changes in adrenals, pancreas, brain meninges. Moderate mononuclear infiltration in liver and kidney, more expressed around pancreas ducts. During IHC virus antigen in spleen, pancreas, brain, adrenals. Viral placentitis with chronic insufficiency and acute decompensation.
Conclusion: We confirm the possibility of intrauterine transplacental challenge of the foetus. In lungs are notes proliferative changes similar with observed in adults, but without signs of ARDS. We can also postulate the development of generalized infection with involvement of brain, kidney, pancreas, heart, adrenals and probably other organs. Histologically special attention has to be attracted to nuclear changes. Hematogenous viral dissemination is supported by typical for new coronavirus infection endothelial changes.

E-PS-19 | Pulmonary Pathology E-Posters

E-PS-19-001
Solitary pulmonary capillary haemangioma mimicking early lung cancer: a case report
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Background & objectives: Solitary pulmonary capillary haemangioma (SPCH) is a rare benign lung tumour. It is a capillary derived mesenchymal neoplasm that typically presents as pure or part-solid ground-glass nodules on computed tomography, mimicking early lung cancer or precancerous lesions of the lung.
Methods: A 54-year-old female with heart failure presenting with dyspnoea, fatigue and chest pain, with a previous history of smoking, showed a ground-glass opacity with 4mm diameter in the left inferior lobe of the lung in a computed tomography showed. FDG-PET didn't reveal hypermetabolic lesions. Clinically the nodule was suspicious for malignancy and an atypical lung resection was performed.
Results: On gross examination, the nodule was 4mm in diameter, round and reddish. Histological sections on hematoxylin and eosin revealed a well-defined nodule with thickened alveolar septa which had multiple proliferated capillary lumens. The proliferated lumens varied in size and were filled with blood cells and lined with single layers of flat cells. No atypical cells were found in the lesion. Immunohistochemical study revealed that the flat cells that lined the lumens were positive for CD34. The additional lung parenchyma had mild septal fibrosis and lymphoid aggregates foci. There were no additional hemangiomatous lesions in the resected specimen. The patient was diagnosed as having SPCH.
Conclusion: Lung vascular tumours are extremely rare. SPCH is even a rarer benign vascular tumour, with only 33 cases reported in literature until 2020. It tends to present as a single small lesion, located in the lower lobe. Localized capillary haemangioma manifests as a cystic lesion or focal ground-glass opacity nodule in a CT scan and can be easily misinterpreted by radiology as a malignant lesion. Therefore, it is important for pathologists to be aware of this entity for accurate diagnosis.

E-PS-19-002

Pleuroparenchymal fibroelastosis in young adults with pneumothoraces

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Background & objectives: Pleuroparenchymal fibroelastosis (PPFE) was recognized in 2013 as a distinct and rare pulmonary fibrotic disease but is still a poorly characterized entity. We report the clinicopathological findings of PPFE in three non-smoker young adults on apical lung resection after pneumothoraces.
Methods: Patient A, a 21-years-old "marfanoid" male with mitral valve prolapse without Marfan syndrome genetic confirmation, presented spontaneous pneumothorax with bronchopleural fistula.
Patient B, a 20-years-old slender asthmatic male who has had a spontaneous pneumothorax two months before, had another pneumothorax.
Patient C, a 16-years-old male with irritable bowel syndrome, had the third pneumothorax in a 2-year-period.
All patients were non-smokers.
Results: All three patients were submitted to apical lung resection. On histopathological examination, all cases were similar, presenting with pleural blebs and globally maintained lung parenchyma lobular architecture. There were also various small triangular subpleural scars and alveolar septal fibro-elastosis that also extended into interlobular septae. Parenchyma away from the pleura was sparsed. There were focal fibroblastic foci, mild inflammation, and alveolar haemorrhage in some bronchial axes. These findings met the diagnosis requirements for PPFE, then described in the pathological reports.
Conclusion: To the best of our knowledge, these three PPFE patients are the youngest reported. They illustrate that PPFE is probably more common than previously believed and should be purposely searched in specific clinicopathological settings, as pneumothorax events, even in very young patients. Our patients had specific clinical settings that can function as underlying disease-associated factors for PPFE. It is therefore essential to better characterize PPFE clinical framing, particularly because it might have prognostic significance.

E-PS-19-003

Primary pulmonary EWSR1-negative myoepithelial carcinoma in a 13-years-old girl: a case report

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Background & objectives: We report a case of primary myoepithelial carcinoma of the right lung in a 13-year-old girl. Primary myoepithelial carcinoma of the lung is an extremely rare entity with only a few reported cases in the literature.
Methods: A 13-year-old girl presented with one year history of chronic cough diagnosed initially as tuberculosis. Her chest CT showed tumour conglomerate 51x43x45 mm at the root of the right lung. Bronchoscopic biopsy diagnosis was epithelioid malignant peripheral nerve sheath tumour (with diffuse S100-protein and SOX10 immunoreactivity but retained INI1 expression). She underwent right lung extended pneumoectomy after neoadjuvant chemotherapy.
Results: Histology showed predominantly epithelioid cell malignant tumour, identical to the previous bronchoscopic biopsy material with marked nuclear atypia, significant pleomorphism, increased mitoses, areas of geographical necrosis, and infiltrative growth. The tumour cells were positive for S-100, SOX10, INI-1, EMA, Cytokeratin(CAM 5.2), MCK (AE1/AE3), p63, whilst Calponin, CD34, CK 7, Desmin, GFAP, HMB-45, MelanA, SMA, SMMS1 were negative. No EWSR1 gene alterations were detected in the FISH assays, but EWSR1 gene rearrangements in myoepithelial tumours identified only in about 50% of cases according to WHO 2021 Classification of Thoracic tumours. The patient died from postoperative complications a month after the surgery.
Conclusion: Thoracic myoepithelial tumours are very rare, most often occurring in adults, but significant number of cases arise in children under 10 years old with higher incidence of malignancy (myoepithelial carcinoma) in this age group. In our case, exclusion of the bronchoscopic biopsy diagnosis was necessary and was performed with a immunohistochemical study assessing the presence of neoplastic cells with a myoepithelial immunophenotype. Awareness of the characteristic epidemiology, morphologic features of this tumour and mimics is warranted for its correct diagnosis.

E-PS-19-004

Solitary tracheobronchial papilloma: a rare entity involving the respiratory tract

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Background & objectives: Solitary tracheobronchial papillomas are rare benign tumours of the respiratory tract, accounting for approximately 0.38% of all lung tumours.
The aim of this study was to present clinicopathological characteristics of these rare tumours with literature review.
Methods: We report a retrospective study of 8 cases of trachea bronchial papillomas diagnosed at our department of pathology between 2004 and 2020.
Results: There were 4 male and 2 female aged between 52 and 89 years with mean of 69. All patients presented with respiratory symptoms. Fibroscopy revealed polypoid endoluminal lesion located in the bronchus in 6 cases and in the trachea in 2 cases. A biopsy was performed in all cases. Microscopically, there were 4 cases of squamous papillomas and 4 cases of glandular papillomas. The squamous papilloma was lined by squamous epithelium with acanthosis and keratinization of the surface, whereas the glandular papilloma was lined by glandular epithelium consisting of ciliated columnar cells.
Conclusion: Tracheobronchial papillomas are rare benign lesions. The course of the disease is unpredictable. It may regress spontaneously, but in other instances it may lead to serious complications ranging from airway obstruction up to malignant transformation.

E-PS-19-005

Cheek mass revealing lung adenocarcinoma

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Background & objectives: Primary lung cancers commonly involve other structures by direct extension or metastasis. Facial metastasis has rarely been reported and is even more unusual as the initial presentation. Here we report a case of lung adenocarcinoma metastasising to the cheek.
Methods: A 61-year-old man, smoking, presented for evaluation of a rapidly expanding mass on his right cheek dating since two months associated to ulceration of the lining of the inner side of the right cheek. A biopsy of the lesion was done.
Results: we received a biopsy of 1cm. Microscopic examination showed an invasive carcinomatous proliferation poorly differentiated made of solid sheets. The tumour cells presented a marked cytonuclear atypia and several mitoses. The stroma was fibrous of moderate abundance with a polymorphic inflammatory infiltrate. There were images of endovascular tumour embolism. The tumour cells were positive to TTF-1 and negative to P40. Therefore, the diagnosis of cheek metastasis of lung adenocarcinoma was made. Chest X-ray and computed tomography revealed an expansive process in the right lung and mediastinal

lymphadenopathy. The patient was referred to the department of oncology for further treatment.
Conclusion: Metastases in face may be the first sign of lung cancer. Although rare appearing, we should raise suspicion in cases of atypical lesions in the skin not only of the smokers, but also of the non-smokers. Facial metastases from poorly differentiated adenocarcinoma are a poor prognostic indicator. It's appearance with other internal metastases shorten the survival time. A high index of suspicion is necessary for the early detection of facial cutaneous metastases. Appropriate treatment may prolong patient survival.

E-PS-19-006
ROS1 translocated lung adenocarcinoma with paired osteoclastic-like microenvironment reaction
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Background & objectives: 56-year-old woman presented complaining of shortness of breath. Cardiac tamponade due to pericardial effusion was diagnosed. Imaging studies showed a lung mass with multiple visceral metastases. Core needle biopsy of the suspected primary lesion was performed.
Methods: It showed irregular clusters of neoplastic cells intermixed with a singular tumour microenvironment. It consisted of densely packed multinucleated, osteoclastic-like cells. Immunophenotype revealed TTF1 and CK7 positivity. Napsin A was negative within the tumour. Since the patient suffered stage IV disease, NSCLC (non-small cell lung cancer) biomarker panel (EGFR, ROS1, ALK, BRAF, KRAS and PDL1) was conducted.
Results: ROS1 immunohistochemistry was positive. FISH test showed, using the specific probe XL ROS1-GOPC BA, one fusion signal and one green single signal. The patient was considered for targeted therapy. PD-L1 expression reached 70%. ROS1 translocated adenocarcinomas have been previously associated with high PDL1 expression. However, its link with specific tumour microenvironment has not been deeply explored.
Conclusion: We present a case of ROS1 translocated adenocarcinoma. It harbours both an uncommon FISH positivity pattern and a singular tumour microenvironment. Association among such features remains unknown.

E-PS-19-007
EGFR mutation and a ROS1 fusion gene detected by FISH and IHC in pulmonary adenocarcinoma – case report
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Background & objectives: Chromosomal rearrangements involving ROS proto-oncogene 1 receptor tyrosine kinase gene (ROS1) define distinct molecular subset of bronchial-pulmonary carcinoma with sensitivity to ROS1 inhibitors. This case report visualizes the co-existence of EGFR activating mutation and ROS1 positive fusion by FISH.
Methods: A 73-year-old female presented with an Pulmonary Adenocarcinoma in the transthoracic biopsy, Molecular Pathology was performed for testing EGFR Idylla™ EGFR Mutation Test (CE-IVD, Idylla™), ALK SPEC ALK-Dual Colour Probe (ZytoVision), ROS1 FISH and immunohistochemistry (IHC), by applying a SPEC ROS1-Dual Colour Probe (ZytoVision) and a ROS1 antibody Clone D4D6 (Cell Signalling Technology), respectively.
Results: The observed transthoracic biopsy represented a primary pulmonary adenocarcinoma mixed type, with acinar pattern where mucinous producing cells, PAS-D + were demonstrated in between cylindrical cells; CK7 and TTF1 were expressed in all tumoral cells and vimentin was present in less than 50% of tumoral cells; PD-L1 22C3 DAKO was negative – 0%. EGFR activating mutation deletion exon 19, ROS1 translocation with aberrant signals in 20% tumoral nuclei in FISH analysis and cytoplasmic positive ROS1 protein expression were also demonstrated. ALK fusion gene tested by FISH was negative.
Conclusion: ROS1 is an exclusive driver in published studies. EGFR – exon 19 deletion and ROS1 can co-exist in the same sample. This coexistence has been reported in previous studies with very remote occurrence.
Concurrent driver mutations might be confirmed through, other testing methodology to confirm molecular diagnosis before proceeding with targeted therapy. Tumour biopsy specimens' limitations correlate with either tumour and metastatic tumour heterogeneity.
This case report highlights mucin production and vimentin expression to associate with molecular results.

E-PS-19-008
SMAD4 mutation in bronchial – pulmonary carcinomas: a challenge for immunotherapy and potential new target
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Background & objectives: SMAD4 encoded protein mediates transduction signal TGF-ß/BMP superfamilies, on transcriptional activation of target genes and pathways: WNT/ß-catenin, MAPK and PI3K/AKT, enhancing EMT/stroma/tumour progression.
SMAD4 mutations often found in pancreas, colorectal, oesophagus and stomach neoplasias, are less reported in other tumours.
Methods: Paraffin block microdissections of three adenocarcinomas (biopsy, surgical specimen – two independent tumours in different lobes) and one NST carcinoma (biopsy) were prepared for DNA-extraction and Next Generation Sequencing in Ion PGM. Library followed Ion AmpliSeqTM Colon and Lung Cancer Research Panel v2 procedures. Analysis results of Torrent Server/Ion Reporter and Catalogue of Somatic Mutations in Cancer (COSMIC) were reported.
Results: Bifocal solid/micropapillary adenocarcinomas under 3cm diameter each had CK7/TTF1 expression and PD-L1 22C3 DAKO 100%, mucinous adenocarcinoma CK7/TTF1/Vim expression and 22C3 DAKO 5%; CK7+ TTF1/CK5.6- NST carcinoma with PD-L1 90%. Proliferative index Ki67 was over 30%.
The missense mutation SMAD4 (exon 6) c.767A>T;p.(Gln256Leu), not reported in ClinVar, was represented in the four samples submitted to NGS. Complete separation between malignant epithelial cells and stroma components was tried. It means, sequencing was performed on extracted DNA theoretically enriched for malignant epithelial compartment with residual representation of tumoral stroma, as usually performed in Pathology for molecular pathology studies on FFPE tissue, based on Hematoxylin-Eosin tumour representativeness selection.
Conclusion: DNA/RNA sequencing for target therapy in bronchial-pulmonary carcinomas is raising knowledge about tumoral mutational status, without rigorous distinction between malignant epithelial and stroma components.
TGF-ß/SMAD4 signalling pathway/expression in tumoral extracellular matrix, proliferation, differentiation, apoptosis, cell adhesion and progression through E-cad/vimentin, after initiation and progression, indicates SMAD4 c.767A>T;p.(Gln256Leu) missense mutation relevant for personalized therapy interpretation (R Wan 2020/ A Todisco 2019).
Loss of SMAD4 function is being correlated with reduction of T cell anti-tumour immunity due to MYC/SMAD4 independent function impairment.

E-PS-19-009

Malignant solitary fibrous tumour (SFT) in extralobar pulmonary sequestration in an adult

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Background & objectives: Extralobar pulmonary sequestration (EPS) is a rare congenital anomaly of extrapulmonary lung tissue with own blood supply and pleural covering within thorax, diaphragm or abdomen1. Malignancy within EPS is rarely reported mostly carcinomas, but SFT has not been reported before.
Methods: A 55-year-old asymptomatic man was referred to cardiothoracic department with incidental finding of a left chest mass on radiology. A moderately PET avid mass was found in the left hemithorax, extending to chest wall with arterial supply from pulmonary artery. Mass was not biopsied due to high vascularity but surgically resected with a small uninflatable left lower lobe2&3.
Results: Macroscopy showed a solid greyish mass 230 gm and 230 mm maximum dimension with lung tissue at one edge. The left lower lung lobe appeared hypoplastic and oedematous with no lesion on sectioning. Left upper lobe was not resected. Microscopy showed a plump spindle cell proliferation with marked atypia and mitoses 7/10 HPF. Stroma was dense, collagenous, myxoid and cystic, mostly patternless and focally storiform. The tumour and attached lung were totally invested by pleura with no bronchial connection to the tracheobronchial tree. The tumour was strongly positive for Vimentin, STAT6, focally S100 and negative for Calretinin, AE1/3, EMA, CD34 and Desmin, consistent with malignant solitary fibrous tumour in EPS.
Conclusion: There are very few reported cases of malignancy in extralobar lung sequestration including Adenocarcinoma, Squamous carcinoma, mesothelioma and carcinoid tumour. We present a case of Malignant Solitary Fibrous tumour in extralobar lung sequestration in an adult, a triple rarity. Carful and microscopic examination with clinical and radiological correlation is crucial to reach the correct diagnosis. The patient remains well and symptom free 7 months after resection.

E-PS-19-010

Acute interstitial organising pneumonia in SARS-Cov-2 infection - a case report

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Background & objectives: COVID-19 is a multi-organic systemic disease that can lead to death by pulmonary compromise, its most commonly affected site. Histopathological patterns have been described for the staging of the pulmonary infection.
Methods: An Asian 53-year-old non-smoking man, living in Portugal for the last five years, was admitted to the Hospital with a history of dyspnoea and cough that had started 2 days before. An x-ray showed bilateral opacities and SARS-Cov-2 infection was confirmed by RT-PCR testing. Subsequently, pneumothorax was diagnosed with the need for pleurodesis and a surgical biopsy was performed.
Results: Histopathological diagnosis was performed in a right upper lobe fragment measuring 5x3,5x3,7cm, as well as visceral and parietal pleural fragments.
The histomorphological study of the pulmonary tissue biopsy exhibited oedema, dense septal and alveolar inflammatory infiltrate, primarily composed of macrophages, some multinucleated, thickened walled blood vessels and fibroblastic proliferation. A peripheral infarct was identified with an organizing hematoma with fibrin deposition. The pleura showed chronic pleuritis features with marked angiogenesis and collagenization. Acute interstitial organizing pneumonia (AIOP) was characterized by a discrete presence of fibrin and predominance of myofibroblastic inflammatory polyps and type II pneumocytes hyperplasia.
Conclusion: Histopathological characterization of COVID-19 has been fundamental to establish the mechanisms by which SARS-Cov-2 pulmonary infection progresses and reaches repair, shedding light to the pathophysiology of this new disease.
The findings in this case report were compatible with a late phase, after the stage of exudative diffuse alveolar damage and before the organizing phase, according with Hans Bösmüller et al (2021) and Emanuela Barisione et al (2021).

E-PS-19-011

One centre experience in evaluation of PD-L1 immunohistochemistry staining in patients with non-small cell lung cancer

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Background & objectives: Experience of Institute for Pathology, Medical School, University of Belgrade in applying and evaluation of PD-L1 immunohistochemistry in patients with Non-Small Cell Lung Cancer (NSCLC) during 2018.
Methods: Material used is bronchoscopic and surgical samples of NSCLC stage III/IV. A qualitative IHC test with monoclonal mice antibodies is used (Dako, clone 22C3). PD-L1 expression is defined as tumour proportion score (TPS) which has to have a minimum of 100 viable tumour cells. Given TPS score is reported as one of tree-cut system: TPS<1%; TPS 1-49%; TPS ≥ 50%.
Results: During 2018 a total of 120 NSCLC samples were reviewed of which 102 were eligible for PD-L1 evaluation. There were 44 female and 58 male patients, age 65±14. In 3,9% (4/102) of samples TPS was <1%; 50,0% of samples (51/102) expressed PD-L1 with a TPS of 1%–49% and 46,1% (47/102) with a TPS of >50%. A statistically significant difference in PD-L1 immunopositivity was associated to adenocarcinomas.
Conclusion: Our immunohistochemical laboratory is a centralized centre for PD-L1 testing. Results obtained in our centre during 2018 regarding PDL-1 testing have been in correlation with other reference centres. Patients with PD- TPS ≥ 50% in their samples have been considered as eligible for first-line immunotherapy with remarkable effect on survival rate.

E-PS-19-012

"Pseudomeostheliomatous" carinoma: clinicopathological study of 4 cases

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Background & objectives: Pseudomesotheliomatous carcinoma (PCL) was the name given to a lung cancer with pleural growth-pattern. This tumour has a clinical and histological resemblance to diffuse malignant pleural mesothelioma but retaining histological, immunohistochemical and molecular characteristics of pulmonary adenocaricnoma.
Methods: We report 4 cases of Pseudomesotheliomatous carcinoma. Two patients were men and two were women, ranging in age from 42-80 years. None had a history of asbestos exposure, nor they were smokers. All patients had chest pain, pleural effusion and pleural thickening. CT scan showed an advanced stage at diagnosis with multiple swelling of mediastinal lymph nodes in all patients.
Results: Microscopically, the tumours grow with a diffuse or solid pattern and had large polygonal cells with sharply defined borders. Nests of neoplastic cells were limited by trabecules of connective tissue with many lymphocytes. The tumour cells in all cases strongly reacted for thyroid transcription factor-1 (TTF-1), podoplanin, pan-cytokeratin, Ber-EP-4, epithelial membrane antigen (EMA). None of the cases stained for mesothelial marker calretinin or WT-1. Immunohistochemistry provides enough sensitivity and specificity for distinguishing lung adenocarcinoma from epithelioid mesothelioma, and our results of

immunohistochemistry are unequivocal for diagnosis of adenocarcinoma. EGFR wt cases were died before ten months, but EGFR mutated was live 79 months.
Conclusion: PCLs are uncommon and pathologically heterogeneous tumours. Immunohistochemistry plays an effective role in distinguishing adenocarcinoma from epithelioid subtype malignant mesothelioma. Calretinin has been demonstrated to be a highly discriminant marker between mesothelioma and adenocarcinoma with high sensitivity and specificity for mesothelioma. Most importantly, PCLs have a dismal prognosis; however, further studies would be necessary to find out if these patients may benefit from the treatment with inhibitors of the EGFR tyrosin kinase.

E-PS-19-013
Diffuse alveolar septal type pulmonary amyloidosis: case report and literature review
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Background & objectives: Amyloid is a form of fibrillary protein that is deposited in the extracellular matrix and has characteristic physical, ultrastructural, immunophenotypic, and tictorial properties. Pulmonary amyloidosis can taken a variety of forms: nodular, tracheobronchial, and diffuse alveolar sept forms.
Methods: A 52-year-old woman, ex-smoker and with a history of breast cancer treated with conservative surgery and radiotherapy, consulted for dyspnoea of one year of evolution. She had no cough, chest pain, or wheezing on auscultation. A CT scan of the chest showed multiple symmetrical and bilateral, thin-walled air cysts. The hemogram showed no alterations and the autoimmunity studies were negative.
Results: Histologically the alveolar septa showed diffusely and extensive eosinophilic deposits. At higher magnification, the eosinophilic material was distributed in thick an thin hyalinized bundles in a lamellar arrangement. The hyalinized bundles showed a concentric arrangement around small blood vessels. Occasional cluster of mononuclear cells that included focally abundant plasma cells and a minor background population of small lymphocytes separated the eosinophilic deposits. This deposit showed positive staining for Congo Red but multiples stains form amyloid AA, light chains Kappa and Lambda were negative. It was diagnoses as compatible with pulmonary amyloidosis type diffuse septal alveolar (ADSAP).
Conclusion: This entity is extremely rare and lung limited. Main radiological differential diagnosis is linfangioleiomiomatosis or Langerhans cells histiocytosis and both were descarted. ADSAP is a rare mixed entity related to AL amyloidosis and usually underlying collagen disease. Literature review demonstrate that incidental pulmonary amyloid are unrelated to systemic amyloidosis or plasma cell myeloma. However, marginal zone lymphomas with amyloid deposits must be careful excluded.

E-PS-19-014
Clinical case of lung NUT carcinoma
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Background & objectives: NUT (nuclear protein in testis) carcinoma is very rare but extremely aggressive high-grade carcinoma characterized by the presence of a fusion NUT gene. It is also called midline carcinoma because it affects the structures in this location- head, neck, lungs.
Methods: We report a case of 27-year-old woman with lung NUT carcinoma, diagnosed by bronchoscopic fibro-punch biopsy.
Results: The histological examination showed massive infiltration of bronchial wall of predominantly spindle-shaped neoplastic cells with unclear cytoplasmic borders. In some areas there were groups of rounded cells with clearly visible nucleoli and high mitotic rate. Foci with necrosis were also found. Immunohistochemistry showed positive expression of cytokeratin, p63, CD56 and NUT antibodies and negative reaction for TTF1 and chromogranin A in neoplastic cells. The proliferative activity of tumour cells was very high (over 70%).
Conclusion: Immunohistoshemical study of NUT expression is mandatory in cases with poorly differentiated lung tumours, with predominantly midline mass.

E-PS-19-015
Comparison of E1L3N and SP263 clones of PD-L1 in non-small cell lung carcinoma (NSCLC): may it be associated with cut-off value?
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Background & objectives: PD-L1 immunohistochemistry has become an important tool for targeted therapy in lung cancer. PD-L1 status as a predictor of treatment response has led to development of different clones. Our aim is to compare diagnostic performances of SP263 and E1L3N clones.
Methods: Consecutive sections were taken from paraffin blocks with tumour tissue from 102 NSCLCs. PD-L1 staining performed with SP263 and E1L3N clones. After samples were randomized, staining evaluation performed by one pathologist blindly. PD-L1 protein expression was reported as tumour proportion score(TPS) which was ranging from 0% to 100% and, scored as positive or negative by using cut-off ≥1% and ≥50%.
Results: The mean age was 63.25 and 81.4% of the cases were male. Sample types in order of frequency were small biopsy (n=47), resection (n=37) and cytology (n=7).
The distributions of SP263 and E1L3N expression were as the following: negative n=15/18, weak positive n=31/45 and high positive n=56/39. Using the TPS ≥1% cut-off to define cases as 'positive,' there was 94,3% sensitivity, 86,7% specificity, 93,1% accuracy, 93.8% positive predictive value and 96% negative predictive value, with five false-negative and two false-positive results. Using the TPS ≥50% cut-off to define cases as 'positive,' there was 74,7% sensitivity, 86,7% specificity, 76,5% accuracy, 97% PPV, and 37,1% NPV, with 22 false-negative and two false-positive results.
Conclusion: In this study of 102 NSCLC tumour samples, when ≥1% cut-off was used for positivity a high level of concordance was observed among SP263 and E1L3N clones of PD-L1. E1L3N clone seems to have difficulties comparing SP263 because of either examination of weak stained tissues or staining protocol problems causing weak positivity.

E-PS-19-016
Immunohistochemical study of the anti-inflammatory activity of apigenin in experimental model of acute pancreatitis
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Background & objectives: Acute pancreatitis is an inflammatory disease that causes pancreatic damage via complicated molecular mechanisms. Among other complications, it can lead to ARDS. We aimed to evaluate the anti-inflammatory activity of apigenin in lungs after surgically causing acute pancreatitis in mice.
Methods: 126 pulmonary tissue specimens of Wistar mice were divided in three groups: S: virtual surgery, C: surgically caused AP, A: surgically caused AP while Apigenin was induced. Groups C and A were separated in subgroups 12h, 24h, 48h and 72h according to the time point of mice euthanasia. Then, the expression of the inflammatory biomarkers HSP-60 and HSP-70 was evaluated.

Results: We observed that HSP-60 and HSP-70 expression was higher ($p<0.01$) in group A compared to the other groups at 12h and 24h. This result remained the same at 48h as far HSP-60 expression is concerned, while there was no statistically significant difference of HSP-70 expression among the groups. Last, HSP-60 and HSP-70 expression were higher with statistical significance in group C at 72h compared to groups A and S.
Conclusion: It is encouraging to see that apigenin may have a protecting role against pulmonary damage due to acute pancreatitis. However, more experiments are in need to reach more secure conclusions so apigenin can be used as an anti-inflammatory agent in prevention and treatment of acute pancreatitis in the future.

E-PS-19-017
Acute fibrinous and organizing pneumonia (AFOP) and desquamative interstitial pneumonia (DIP): diagnosis in transthoracic pulmonary biopsies - two case reports
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Background & objectives: AFOP and DIP are rarely diagnosed and difficult to recognize in transthoracic pulmonary biopsies due to sampling. Two cases of alveolar filling, clinically interpreted as pneumonia, were characterized for differential diagnoses and to highlight interstitial diseases classification.
Methods: Non-smoker 72-years-old man complaining of cough, fever and headache, presenting occupational risk exposure to paints, lead and textile particles and with medical history of asthmatic bronchitis and hypertension, presented diffuse ground glass opacities in the right upper and middle lobes in computerized tomography scan. Smoker 42-years-old man presented with thoracic pain and right upper lobe diffuse lesion in chest x-ray.
Results: Transthoracic needle biopsy with fibrin balls partially organized with fibroblasts, macrophages and eosinophils in myxoid matrix in alveolar lumina characterized AFOP for the first patient diagnosis. Round massive groups of macrophages occupying the alveoli spaces and also present in the alveolar septa fulfilled the criteria for DIP diagnosis in the second case. The association between occupational risk exposure and AFOP in the first case and between DIP and tobacco exposure in the second case are commonly recognized and as primary/idiopathic patterns in the classification of interstitial diseases.
Conclusion: AFOP, characterized by deposits of intra-alveolar fibrin balls and associated organizing pneumonia within the alveolar ducts and bronchioles, was achieved in biopsy representative tissue. Overlap with diffuse alveolar damage, cryptogenic organizing pneumonia and eosinophilic lung may be possible for final diagnosis with scarcely represented in biopsies. DIP and AFOP keep in common alveolar filling with different cellular representation. Morphological criteria of these distinct entities allowed differential diagnosis, important due to different outcomes and clinical dealing for patient's treatment and counselling.

E-PS-19-018
The use of p16 in association with TTF1 and CD56 may be extremely helpful in establishing the correct diagnosis of small cell lung carcinoma on small biopsy specimens: report of two challenging cases
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Background & objectives: Small cell lung carcinoma (SCLC) can usually be diagnosed based on the morphological evaluation on routine haematoxylin-eosin stain. However, immunohistochemistry may be extremely helpful and necessary in problematic cases, such as small biopsy specimens with extensive crush artifacts.
Methods: We report the cases of two patients (72 years old male and 53 years old female) admitted to the hospital for cough, difficulty in breathing and dyspnoea. Lung tumour was suspected. Bronchoscopy was performed and the biopsy specimens were submitted to the Department of Pathology for pathological examination. Due to small size of the specimen the interpretation was challenging.
Results: Both the examined biopsies showed a tumoral proliferation with crushing artifact, consisting of small cells with diffuse growth pattern and also nesting architecture. Cells presented low cytoplasm, irregular pleomorphus nuclei, with indistinct cell boundaries. Apoptotic bodies and numerous mitosis were present. Immunohistochemically, both tumours stained positive for TTF1 and negative on p40. CD56 staining revealed a fine, membranous expression that was diffuse in one case and focal in another one. The Ki67 proliferation index was high in both tumours. P16 labelling revealed intense and diffuse positive nuclear staining in both tumour cells. Based on the morphological features and the immunohistochemical profile of the tumours, a diagnosis of SCLC was set.
Conclusion: For lung biopsies, especially in case of small amount of material, the histopathological diagnosis is challenging and cannot only rely on morphological features. The triple marker, composed of p16, TTF1 and CD56 may be useful in establishing the correct diagnosis of SCLC.

E-PS-19-019
Malignant mesothelioma of the pleura: relevance of a multidisciplinary concertation
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Background & objectives: The diagnosis of malignant pleural mesothelioma is suspected based on clinical features but positive diagnosis is microscopic. Our aim was to describe the clinical and microscopic features of MPM through a single institution experience.
Methods: We conducted a retrospective study about 30 MPM diagnosed over a 20-year-period (1995-2015). We included only patients with complete records including clinical, radiologic and microscopic features. All the microscopic diagnoses were reviewed by 2 pathologists. A mean of 12 slides per case was reviewed. The diagnosis was based on the 2015 WHO classification.
Results: The mean age of the patients was 61 years. The sex ratio was 6,5. The most frequent symptoms was chest pain reported in 25 cases. The microscopic exam concluded to an EM in 17 cases, sarcomatoid mesothelioma (SM) in 4 cases and biphasic mesothelioma (BM) in 9 cases. Immunohistochemical technique was repeated in 15 cases and the most used antibodies were the anti-calretinin and the TTF1. Surgical resection was possible in 2 patients. 15 patients were lost of view after a mean follow-up period of 3 months. Thirteen patients died before or during the follow-up.
Conclusion: In this work, the major limits faced were the incomplete databases, the small number of patients included. Microscopic positive diagnosis necessitates a degree of expertise and every laboratory has to determine the most valuable antibodies through its experience in order to optimize the diagnosis and to reduce the delay of diagnosis.

E-PS-19-020
Synchronous lung adenocarcinoma and diffuse idiopathic pulmonary neuroendocrine hyperplasia (DIPNECH) – a case report
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Background & objectives: DIPNECH is characterized by widespread hyperplasia of pulmonary neuroendocrine cells that may be confined to the mucosa of airway, invade locally to form tumourlets or carcinoid tumours. We present a case of DIPNECH that was diagnosed synchronously with lung adenocarcinoma.

Methods: A 57-yr-old female with history of asthma and heavy smoking presented with cough, dyspnoea, and haemoptysis. CT revealed 3cm mass in the left upper lobe, in addition to multifocal air-trapping and mosaic perfusion pattern in both lungs. Transbronchial biopsy from the mass showed adenocarcinoma confirmed by positive immunohistochemical stains for CK7 and TTF1 in atypical cells. A lobectomy was performed.
Results: On gross examination, a tan-white solid mass measuring 3cm with stellate border was present. In addition, serial sections of the uninvolved pulmonary parenchyma revealed multiple small grey-white nodules measuring up to 0.5cm. Microscopic examination of the mass showed acinar adenocarcinoma. The small nodules were composed of uniform cells arranged in nests. These cells showed round to oval nuclei, eosinophilic cytoplasm and salt and pepper chromatin. In addition, spindle cell features were also present. Immunohistochemical stains for chromogranin and synaptophysin were positive in these nodules, confirming them as neuroendocrine tumourlets. In addition, the airway mucosa at several sections including the surgical margin demonstrated intramucosal hyperplasia of neuroendocrine cells.
Conclusion: DIPNECH is a rare phenomenon. The synchronous presentation of DIPNECH with primary lung adenocarcinoma is an exceedingly rare scenario.

E-PS-19-021
Pulmonary mucous gland adenoma. A case report
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Background & objectives: Pulmonary mucous gland adenoma (PMGA) is a rare tumour, arising from tracheobronchial seromucinous glands and ducts, classified as lung adenoma in WHO classification. Diagnosis is challenging due to microscopic similarity with benign and malignant entities and surgical excision is required.
Methods: We report the case of a 32-year-old asymptomatic female patient who was admitted to our hospital with an incidentally found bulla in the right lower pulmonary lobe observed in chest X-ray and measuring 8.3x7x6.5cm. The patient underwent right lower lobectomy due to high suspicion of malignancy.
Results: On cut surface we found a well-circumscribed multi-space cystic lesion containing numerous mucin-filled smaller cysts. Microscopic examination revealed exophytic nodules above the cartilaginous plates of the bronchial wall consisting of neoplastic mucous glands, lined by a single layer of tall columnar cells with basally oriented nuclei and abundant mucous-filled supranuclear cytoplasm. Cytologic atypia, infiltrative pattern, mitoses, necrosis and pleomorphism were not detected, excluding low-grade mucoepidermoid carcinoma as well as pulmonary adenocarcinoma scenarios. Immunohistochemistry demonstrated similar staining to non-neoplastic bronchial glands [EMA(+), CEA(+), CK7(+), TTF-1(-), Napsin-A(-) and Ki-67(+) with rare positivity]. TTF-1 negativity along with topography, size and morphology helped us exclude papillary adenoma, mucinous cystadenoma and alveolar cell adenoma.
Conclusion: Experienced pathologists should keep PGMA in mind since its differential diagnosis includes both benign and malignant entities. The collaboration of radiologists, pneumonologists and pathologists along with thorough sampling and immunohistochemical assays is mandatory for the accurate pathological diagnosis and appropriate therapy of the patient.

E-PS-19-022
The value of TTF-1 and Napsin-A biomarkers in primary lung adenocarcinomas
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Background & objectives: Adenocarcinoma (AC) represents the dominant subtype of lung cancer. Differential-diagnosis of primary from metastatic lung AC requires immunohistochemical assays. According to literature, the sensitivity and specificity of Napsin-A (84.9/93.8%, respectively) and TTF-1 (84.4/83.9%, respectively) for primary lung AC are high.
Methods: We reviewed 215 cases of primary pulmonary ACs in lobectomy specimens diagnosed in the year 2020 from the archives of Pathology Department of General Hospital of Thoracic Diseases of Athens "Sotiria". Fifty-six of the cases were poorly differentiated ACs. The remaining 159 were well/moderately differentiated ACs. We performed immunohistochemical examination of all 215 cases with Napsin-A and TTF-1 biomarkers.
Results: Among the 159 cases of well and moderately differentiated ACs, 146/159 cases were TTF-1(+) (92%) and 129/159 were Napsin-A(+) (81%). Additionally, 54/159 cases were TTF-1(-) and Napsin-A(+) (34%) whereas 46/159 cases were TTF-1(+) and Napsin-A(-) (29%). Out of 56 poorly differentiated ACs, 20 cases were TTF-1(+) (36%), while 36 were Napsin-A(+) (64%), leading to the assumption that Napsin-A performed better than TTF-1 in poorly differentiated ACs.
Conclusion: According to our findings, the combination of positive immunostaining for TTF-1 and Napsin-A biomarkers is mandatory for the accurate diagnosis of primary lung ACs and improves the diagnostic accuracy, as recorded in the current literature. The findings of our survey also confirm the remarkable contribution of Napsin-A in poorly differentiated primary pulmonary ACs.

E-PS-19-023
Granular cell tumour of the trachea bronchial tree: a report of 4 cases
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Background & objectives: Granular cell tumour (GCT) is a rare benign tumour, commonly found in the head and neck region. Tracheobronchial GCT remains an exceptional site. The aim of our study is to describe clinical and pathological features of this rare entity.
Methods: We report here a retrospective study of 4 granular cell tumour diagnosed at our department of Pathology from January 1998 to December 2020.
Results: Patients were all males aged from 45 to 85 years with a mean of 52.5. Presenting symptoms includes cough, chest pain, wheezing, haemoptysis and dyspnoea. Bronchoscopy revealed endoluminal tumour obstructing trachea in 3 cases and bronchus in one case. A biopsy was made in the 4 cases. It showed a population of polygonal large neoplastic cells with eosinophilic coarse granules and small nuclei with mild atypia. They were arranged in nests, bands, or cords, separated by thin fibrous tissue. On immunohistochemistry, the tumour cell expressed CD56, S100 and CD68 and were negative for Cytokeratin. The histopathological findings were consistent with GCT. All the patients were treated by bronchoscopic resection.
Conclusion: The diagnosis of granular cell tumour of the tracheobronchial tree is based on histology with the contribution of immunohistochemistry. The prognosis is good following surgical or endobronchial resection.

E-PS-19-024
Primary mediastinal leiomyoma: an exceptional tumour
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Background & objectives: Benign mesenchymal tumours of the mediastinum are rare and primary leiomyomas are even rarer with less than 20 cases reported in the English literature. Our objective is to to clarify histological features and discuss histogenesis of primary mediastinal leiomyoma.
Methods: A 78-year-old man admitted in cardiovascular surgery department after fortuitous discovery of a giant mediastinal mass during the preoperative assessment for a gallbladder lithiasis. The thoracic computed tomography scan showed a middle mediastinal mass measuring 14.6x14x9cm compressing the oesophagus, the left atrium and the pulmonary inferior veine. The tumour was enucleated by thoracotomy and was not related to the oesophagus.
Results: Gross examination showed a large tumour measuring 14×10×5 cm. It was firm multilobular with myxoid areas. Histologically, it was composed of monomorphic spindle cells forming intersecting fascicles. No nuclear atypia, mitoses or necrosis were observed. Immunohistochemical stain revealed strong positivity for smooth muscle actin and desmin compatible with benign leiomyoma.
Conclusion: Primary mediastinal leiomyomas are rare, representing 1 to 6% of all mediastinal masses. They are seen in middle-aged women. They develop from small vessels in the soft tissue of the mediastinum wall. Although leiomyoma's pathogenesis is obscure, oestrogen and traumatic theories were suggested. Leiomyomas are usually slow-growing tumours and often detected incidentally on chest radiographs. It should be considered in the differential diagnosis of mediastinal tumours. The definitive diagnosis is achieved by histology.

E-PS-19-025
Wegener's granulomatosis: a histopathological study of 14 cases
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Background & objectives: Wegener granulomatosis (WG) is a multisystem disease related to the presence of circulating antineutrophil cytoplasmic antibodies (ANCAs). It is characterized by a necrotizing granulomatous vasculitis affecting predominantly the upper and lower respiratory tract and lungs.
Methods: This retrospective study was performed on 14 cases of WG selected from pathology department from 2001 to 2020.
Results: There were 7 men and 7 women (mean age 45,6; range 3-64). The diagnosis was made by thoracoscopy biopsies in 9 cases and surgical resection of pulmonary nodules in 5 cases. Histopathological analysis found parenchymal necrosis in 9 cases as neutrophilic micro-abscesses or as areas of geographic necrosis. Granulomatous lesions consisted of microabscesses surrounded by giant cells in 13 cases. Vasculitis were identified in 13 cases. Fibrinoid necrosis was relatively uncommon (1 case).
Conclusion: On microscopic findings, pulmonary WG is characterized by a necrotizing vasculitis affecting blood vessels of all sizes. More than 90% of patients with WG respond to cytotoxic and immunosuppressant medications and nodules may regress without scarring in almost cases. However, they may recur on treatment or after a period of complete disease remission; in this context, the cavitary nodules may occasionally become infected tending to be thick-walled with irregular inner margins.

E-PS-19-026
Pleomorphic carcinoma of the lung – distinct sarcomatoid component and cystic papillary adenocarcinoma
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Background & objectives: Pleomorphic carcinoma of lung is rare and presents with aggressive course, representing 0,1%-0,4% of pulmonary carcinomas. Sarcomatoid pattern may be predominant over unusual cavitated/cystic papillary adenocarcinoma component: a "cyst" was not interpreted as neoplastic in HRTC.
Methods: A smoker 58-year-old man, in follow up due to left pulmonary tumour after transthoracic inconclusive biopsy with 54mm –necrotic tumoral tissue, performed PET scan where persistent discrete uptake was observed. Patient was submitted to lobectomy and lymphadenectomy. Pulmonary left lower lobe (LLL) exhibited two continuous lesions: upper solid mass with 7cm diameter and cystic/cavitated lesion with 5cm diameter.
Results: LLL (280g/22x17x6,5) - 6x7x3cm well-defined white, soft, extensively necrotic tumour measuring 6x7x3cm presented a neighbour a 5,5x4x3,7cm cavitated lesion twinned with adjacent 2x2x1,5cm "cystic" lesion. Microscopy: solid compound with peripheral preserved fusiform cells rim eosinophilic cytoplasm and elongated nuclei, interspersed giant cells with anisokaryosis and atypical mitotic figures; positivity for EMA, CD10, CD56, NSE, Vimentin, TTF1 and HHF35. The "cysts" were predominant papillary adenocarcinoma with micropapillary and focal acinar patterns. CK7, TTF1, Cam 5.2 and Vimentin contrasted with NSE and CD56 negativity. Lymphadenectomy comprised 14/21 hilar lymph nodes metastasis with both tumoral components. PD-L1 (22C3DAKI) expression was 90% and 40%, respectively.
Conclusion: LLL pleomorphic carcinoma with cystic papillary/micropapillary/acinar adenocarcinoma and sarcomatoid carcinoma with neuro-endocrine differentiation was reported. Necrosis is associated with high proliferative index and poor prognosis becomes worse due to lymph node metastasis Large sampling was essential to characterize heterogeneity and morphological variety, in this case. Correlation with smoke/particular smoking type was expressed in smoking lung and BALT hyperplasia in pulmonary parenchyma.

E-PS-19-027
Extra-skeletal osteoid osteoma of the lung, a rare case
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Background & objectives: Osteoid osteomas are very rare benign bone tumours (3%) and the extra-skeletal osteoid osteoma in the lung is even rarer. Lung tumours with osseous elements have been described (hamartoma, amyloid tumour, reactive lesions - osseous metaplasia).
Methods: Osteoid osteomas are benign tumours and require distinction from other benign lesions. We present a 77-years-old woman admitted to our hospital with a productive cough two months. Lung CT showed a solitary well-circumscribed tumour up to 2,5cm in diameter in the right upper lobe. The patient underwent VATS resection.
Results: On microscopic examination, the lesion comprised mainly of amorphous material resembling immature osteoid with the a few osteocytes, while at the periphery osteoclasts were identified. Scattered spaces with Havers structure were present. The cell proliferation index (Ki-67) was <1%.
Conclusion: Extra-skeletal osteoid osteoma of the lung is an extremely rare entity that may be associated with Gardner syndrome (presence of multiple polyps of the colon or carcinoma of the colon, in combination with extra-intestinal lesions such as desmoid tumours, osteomas, epidermoid cysts or fibromatosis).

E-PS-19-028
Pleomorphic epithelioid leiomyosarcoma of the lung
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Background & objectives: Lung sarcomas are rare neoplasms, comprising only 0.2-0.5% of all lung malignancies. Leiomyosarcomas are the most common and their diagnosis is a challenge for the pathologist.

Methods: We present the case of a 70-year-old female, who underwent surgical resection (VATS) for a lung mass. On gross examination of the pulmonary parenchyma, a white circumscribed tumour up to 2.5cm. in greatest diameter was found.
Results: On microscopic examination the tumour was composed of mesenchymal epithelioid cells with marked nuclear pleomorphism, nuclear inclusions, presence of multinucleated giant cells, and increased mitotic activity. Immunohistochemistry was performed: SMA, HHF-35, Calponin, Desmin, EMA, CKAE1 / AE3, CK7, CK8 / 18, which confirmed the morphological findings. Primary lung leiomyosarcomas (PPLs) are rare, rapidly growing tumours with slow rate of metastasis. They are differentiated in relation to their origin: from the pulmonary parenchyma, the bronchial tree, and the pulmonary artery.
Conclusion: The morphological and immunohistochemical findings, in combination with the absence of a known history of leiomyosarcoma from the gynaecological tract are in favour of the pleomorphic epithelioid PPL, parenchymal type. Valid screening offers appropriate treatment and the possibility of improving the prognosis. The indicated therapeutic approach is surgical removal with adjuvant chemotherapy or radiotherapy.

E-PS-19-029
Pulmonary hamartoma - ten-year single centre study
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Background & objectives: Pulmonary hamartoma is common benign neoplasm composed of cartilage, connective tissue, smooth-muscle and fat tissue. For pathologists, diagnosis is routinely easy, unless hamartoma is composed of the cells of only one origin.
Methods: We analysed 168 pulmonary hamartomas regarding their gender and age distribution, their size, growth pattern and morphology, diagnosed last ten-year period, from 2011. to 2020.
Results: Pulmonary hamartomas were diagnosed in 81(48.2%) females and 87(51.8%) males. Average age was $\dot{X}$=58.7 (Mdn=64), ranged from 24- to 74-year-old. The average measure of the greatest diameter of hamartoma was $\dot{X}$=20.3mm (Mdn=17mm), ranged from 8mm to 100mm. The great majority were localized intrapulmonary. Endoluminal growth pattern was found in 4 patients (2.4%). Monomorphic feature of pulmonary hamartoma were diagnosed: five leiomyoma-, 4 lipoma-, one fibroma- and chondroma-like hamartoma. Pulmonary hamartoma was accidental finding associated with 9 lung tumours (4 adenocarcinoma, 4 squamous cell carcinomas, 1 MALToma), one interstitial lung disease (NSIP), 3 tuberculomas and one with thymoma.
Conclusion: Absence of nuclear polymorphism and mitoses distinguish metastatic mesenchymal tumours from monomorphic pulmonary hamartoma. Pulmonary hamartoma could be accidental finding, associated with the other thoracic tumours. Diagnosis of pulmonary hamartoma eliminates surgeons' suspicion of metastatic tumour in the lungs according to their radiological findings.

E-PS-19-030
A modular approach to the study of the morphogenesis of atelectasis in radio-induced lung injury
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Background & objectives: Among the morphofunctional systems of humans and animals, the lungs, due to the implementation of the oxygen effect, are the most sensitive to ionizing radiation. Radiation pneumonitis, atelectasis, lung fibrosis may develop approximately in 30% of cases after radiation exposure.
Methods: A total of 258 experimental animals (white non-linear male rats aged 14-18 weeks, weighing 200-220 grams) were used in the experiments. Radio-induced exposure was simulated on 216. The control group consisted of 42 animals, which were simulated by the irradiation procedure and used to assess the total content of surfactant and its fractions in accordance with the timing of the experiment.
Results: The dynamics of changes in the morphological substrate of the pulmonary parenchyma is presented in the form of peculiar modules-blocks, morphologically complete in quantitative and qualitative terms of complexes of changes that are realized in the lungs. In total, 6 modules were identified: the formation of initial (background) preatelelectatic changes in the lung tissue; implementation of radial alterations in the subpleural parts of the lung, the formation of subpleural mono-factorial atelectasis; implementation of radial alterations in the intrapulmonary parts of the lung, the formation of intrapulmonary multifactor atelectasis; persistence, transformation and modification atelectasis; permission and/or organization of atelectasis, complete (restitution) or incomplete (substitution) restoration of lung tissue.
Conclusion: The development of subpleural atelectasis was associated with a decrease of pulmonary surfactant in the fluid of the bronchoalveolar lavage, intrapulmonary atelectasis - the attachment of the obstructive mechanism. Given the defining nature of surfactant deficiency in the onset and development of lung atelectasis, it seems appropriate to use it for prophylactic purposes, immediately after radiation exposure in order to eliminate losses as a result of radiolysis of phospholipids and other surfactant components under the action of ionizing radiation.

E-PS-20 | Soft Tissue and Bone Pathology E-Posters

E-PS-20-001
Cellular angiofibroma: unusual presentation
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Background & objectives: Cellular angiofibroma (CA) is a rare, benign, cellular, and highly vascularized fibroblastic neoplasm. This tumour occurs mainly in the vulvar region in females and in the inguinoscrotal region in males. The tumour is equally affecting males and females.
Methods: We herein present a case of 45-year-old gentleman who was found to have a lesion occupying the subcutaneous compartment of right buttock. This case was difficult to diagnose on core biopsy. Therefore, it was recommended to be resected entirely with adequate margins to reach a final diagnosis.
Results: The histologic appearance was deceiving and showed similarities among different tumours (to name some; mammary type myofibroblastoma, angiomyofibroblastoma, aggressive angiomyxoma) which hampered revealing the definitive diagnosis. Therefore, the immunohistochemical studies have been helpful in differentiating this tumour from other entities. By reviewing the histology along with the immunohistochemical studies, a diagnosis of cellular angiofibroma was yielded.
Conclusion: CA represents a distinct benign neoplasm with a broad anatomic distribution even if it is mainly localized in the vulvo-perineal and inguinoscrotal area. This lesion may exhibit some variations in its phenotypic features, as well as atypia and morphologic features of sarcomatous transformation but these characteristics seem not to predispose to a malignant transformation or recurrences. For these reasons, a treatment of simple local excision appears to be adequate and effective to avoid recurrences and injuries to surrounding tissues.

E-PS-20-004
Malignant gastrointestinal neuroectodermal tumour: a case report
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Background & objectives: Malignant gastrointestinal neuroectodermal tumour (GNET) is an uncommon mesenchymal neoplasm of the gastrointestinal tract with less than 100 cases reported in literature. This entity has distinctive clinical, histologic, immunophenotypic and molecular features, and represents an aggressive form of neuroectodermal tumour.
Methods: 35-year-old male with abdominal pain, bilious vomiting, melena, fatigue and weight loss. Endoscopic evaluation detected no abnormalities. Abdominal CT-scan revealed various collapsed jejunal loops and lymphadenopathies in the mesentery. Surgical excision was performed. The resected segment of small bowel showed a 3.6x3.5cm ulcerative neoplasia with raised margins, invading serosa and configuring an adherent process to the bowel loops.
Results: Histology showed high grade malignant neoplasm in the muscularis propria of the intestine with mucosal ulceration and adipose tissue invasion. Neoplastic cells were epithelioid with eosinophilic cytoplasm, arranged in sheets and small aggregates. Scattered osteoclast-like multinucleated giant cells were seen. Pleomorphism was moderate, mitotic rate was high and necrosis was absent. Immunohistochemistry showed diffuse expression for S100 and SOX10 and negativity for HMB45, Melan A, GFAP, CD34, CD117, DOG1, SMA, desmin, EMA, cytokeratins, synaptophysin and chromogranin A. H3K27me3 and INI1 were retained. EWSR1 gene rearrangement was detected by FISH, allowing a diagnosis of GNET. Patient underwent chemotherapy and surgical resection of jejunal recurrence. A year after diagnosis, he is alive.
Conclusion: Previously considered a "clear cell sarcoma-like tumour of the gastrointestinal tract", GNET has recently been described as a different entity with its own morphological, immunohistochemistry and genetic features. Due to its rarity it can easily be misdiagnosed by the pathologist. Immunohistochemical studies with epithelial, neural and melanocytic markers and genetic testing are required for a correct diagnosis. More studies are needed in order to better understand the pathogenesis and prognosis.

E-PS-20-005
A rare case of pseudomyogenic haemangioendothelioma with unicentric involvement
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Background & objectives: Pseudomyogenic haemangioendothelioma (PMH) is a very rare, low-grade vascular tumour, with approximately 130 cases described in the literature. PMH is often presented as a multifocal disease, with involvement of the bone in only 14% of all cases.
Methods: A 17-year-old boy presented with a 5-month history of lateral lower leg pain, initially of low-intensity and triggered by effort, later of high intensity and continuous, radiating into the lower back and heel. The boy underwent several radiologic investigations, which demonstrated a well-defined lytic lesion measuring 1,8/0,8 cm, involving the left proximal fibular epiphysis. Surgical treatment was performed.
Results: Histologic examination showed woven bone and fibro-adipose tissue with infiltrating sheets of epithelioid and spindled cells with abundant eosinophilic cytoplasm, round nuclei with prominent nucleoli and scarce mitotic activity. At immunohistochemical examination, the tumour cells showed diffuse expression of AE1/AE3, vimentin, FLI1, INI1, ERG, with a low ki67 proliferation index of 6% and the diagnosis of PMH was made. Follow up computed tomography (CT) with multiplaner reconstruction (MPR) and 3D CT, 8 months after resection, showed post-surgical modifications, without evidence of tumour recurrence.
Conclusion: Although PMH was recognizes recently as a distinctive entity with indolent behaviour, the correct recognition is very important because is a locally recurrent and rarely metastasizing tumour. Even though PMH is usually located in cutaneous and subcutaneous tissue, the probability of bone involvement must not be omitted. Considering its absence of vascular differentiation characteristics on hematoxylin-eosin stain, the diagnosis of PMH can be easily mistaken, and interpreted as other lesion with different treatment and prognosis.

E-PS-20-006
Aggressive angiomyxoma of the left buttock: a case report
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Background & objectives: Aggressive angiomyxoma is a rare and benign mesenchymal tumour that most commonly arises in the lower genital tract, perineum and pelvis of women. The aim of the study is to discuss clinicopathological features of this disease.
Methods: A 54-year-old female was presented with a 14 cm, slowly growing, and painless mass of the left buttock. There is no familiar or personal history. An excision of the mass was practiced.
Results: We received a well-circumscribed, blue grey and myxoid mass. Its size was about 14.5 cm. The histological examination revealed locally infiltrative and hypocellular mass composed of spindle to stellate cells and dilated capillaries. The tumour cells have scanty cytoplasm and bland chromatin with small nucleoli. Mitosis was rare. There is no necrosis. At immunohistochemistry, the tumour cells were positive for oestrogen receptor (ER), progesterone receptor (PR), smooth muscle actin (SMA), Desmin and CD34 but were negative for MDM2. The patient was rapidly recovered without any recurrence.
Conclusion: Aggressive angiomyxoma is a rare tumour of the soft tissue. It mainly occurs on the vagina, vulva, pelvic cavity, perineum and hips in reproductive female aging from 30 to 40 years old. It is a hypocellular myxoid tumour with bland spindle cells and prominent variably sized vessels. Overexpression of HMGA2 in immunohistochemistry confirms the diagnosis. This tumour is aggressive due to its nature of local infiltration and recurrence. Distant metastasis and death are exceptional.

E-PS-20-007
Chordoma: a report of six cases and a literature review
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Background & objectives: Chordoma is an uncommon malignant tumour. It accounts for 1% of intracranial tumours and 4% of all primary bone tumours. It is classified into conventional, dedifferentiated and chondroid chordoma.
Our aim is to highlight clinical and pathological features of chordoma.
Methods: We report 6 cases of chordoma collected over a period of 8 years (2013-2021) in the department of pathology of the university hospital of Monastir. All histological types were included.
Results: Patient's ages ranged from 45 to 82 years with sex ratio = 2/1.Chordoma was located in the cervical vertebra in one patient and in the skull base in two patients. Two chordomas arised in the sacrococcygeal area whereas one arised in the pelvic region. Microscopically, 4 cases of chordomas were of conventional type and two of chondroid type. Tumour shows lobular architecture. Tumour cells were arranged in cords and nests with mixed epithelioid and physaliphorus features. Mild nuclear atypia was found in three of cases. The stroma was either myxoid or chondromyxoid. In immunohistochemistry, tumour cells stained positively for keratin, epithelial membrane antigen and S100 protein.
Conclusion: Chordoma is a malignant tumour that mainly involves bones of axial skeleton but may arise in extra axial areas. It is characterized by a slow progression with local aggressive character. The chondroid variant accounts for 4% of chordoma cases with a better prognosis than other chordoma variants.
Treatment dilemma leads to a high rate of local relapse and distant metastases. Molecular targeted therapy is an option for advanced chordoma, but its therapeutic efficacy and safety have not been investigated systematically.

E-PS-20-008

Osseous hydatid disease - case report

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Background & objectives: Echinococcosis (hydatidosis) is a parasitic and zoonotic disease of animals and humans, prevalent throughout much of the world. The cause is Echinococcus granuloses. Almost all organs and systems can be involvement. The incidence of bone echinococcosis is low (3%).
Methods: A 53-year-old construction painter was referred with complaints of pain in the right knee, with progressive oedema, without fever and unresponsive to analgesic therapy.
The TAC and RMN images showed, at the distal femur, a multicystic lesion, without hydro-air levels and heterogeneous contrast uptake. It caused cortical disruption extending to the soft tissues, raising the possibility of osteosarcoma.
Results: A 19x10 x 9 cm distal femur segment, circumferentially covered with muscle and adipose tissues, was received. A cut section showed an area of ill-defined limits, 15x7x7 cm, consisting of multiple cavitated and yellowish areas, some with a peripheral gelatinous membrane, which were distributed in the bone marrow, bone cortex and adjacent soft tissues.
Microscopically, an extensive granulomatous reaction was observed, related to abundant hyaline cellular lamellar structures (ectocysts), often with necrotic proliferating membranes. Representations of rare scolices were also identified. The lesion invaded the periosseous, muscle and adipose tissues and also the cortical and medullary bone. The lesion was intersected by the surgical margins.
Conclusion: Osseous hydatidosis is a rare occurrence of hydatid disease. Clinically it does not present distinctive symptoms and specific characteristics on x ray or CT which are similar to other entities. Because of the poor results with medical treatment, osseous hydatidosis must be treated by a radical operation with wide excision, adapted to each localization. Complete surgical eradication is rarely possible. The prognosis and treatment of osseous hydatidosis is similar to a locally malignant lesion.

E-PS-20-009

High-grade chondrosarcoma arising in a preexisting enchondroma: a case report

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Background & objectives: Chondrosarcoma is a malignant cartilaginous tumour, which may arise from a pre-existing atypical cartilaginous tumour (ACT). The aim of this study is to present a case of conventional high-grade chondrosarcoma developed on a previously diagnosed enchondroma.
Methods: A 73-year-old female patient was admitted at "Foisor" Orthopaedics Hospital for 3-year-long lasting pain and loss of function in the right knee. Ten years before, patient was discovered with a 4 cm tumour mass in the right distal femur, which was treated with intralesional curettage and bone cement reconstruction. The lesion was diagnosed microscopically as an enchondroma.
Results: After ten years, imaging findings revealed an expansile tumour mass of 13/7/4 cm, localized in the distal femur, with ill-defined margins, extending into adjacent soft tissue, associated with pathologic fracture. The patient underwent surgical treatment with "en bloc" resection of the distal femur and tumour prosthesis. Macroscopically, the neoplasm was filling the entire medullary cavity with cortical destruction and soft tissue invasion. Microscopic examination showed a cartilaginous tumour, with infiltrative growth pattern and cytologic atypia, corresponding to high-grade chondrosarcoma. Revising the initial slides, no cytologic atypia or features of invasion could contradict the initial diagnosis of enchondroma.
Conclusion: There is a significant histologic overlap between enchondromas and atypical cartilaginous tumours, therefore radiographic and clinical data, such as dull continuous pain, are highly suggestive of malignant transformation. Clinical history and evolution of the case indicate that the initial tumour could have been an ACT, misdiagnosed due to lack of invasive features on the excisional biopsy. Even if solitary enchondromas have a very low risk of malignant transformation, benign cartilaginous tumours arising in older individuals should be carefully managed.

E-PS-20-010

Dedifferentiated chordoma of thoracic spinal region: case report of a rare entity

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Background & objectives: Chordomas are tumours of notochordal origin and are localized in axial skeleton. Dedifferentiated chordomas are biphasic tumours, rare subtype of chordomas , consisting of high grade sarcomatous components and conventional chordoma areas. We present a case of such morphologic appearance.
Methods: 74-year-old-male with back pain was referred to our neurosurgery clinic, whom had a history of posterior thoracic instrumentation surgery at 2016, due to pathological fracture at T12. MR imaging demonstrated a 78x70 mm mass lesion at T11-T12, extending to neural foramen from right side of vertebral body which exhibited hyperintensity at T2 weighted images. Removal of lesion was performed.
Results: Fragmented resection material was 6x5x3 cm in total size, consisting of solid areas of tan/white colour with haemorrhage. Upon histopathological examination; conventional chordoid areas consisting of chords/sheets of cells of physaliphorous morphology arranged in lobules interspaced with chondromyxoid matrix were seen. Mixed with such areas, multiple sarcomatoid foci of various morphologies (consisting of spindle cells, epithelioid cells, lipoid cells) were present. Invasion of bone, muscle and connective tissue by tumour cells was observed. Mitotic count was 6 mitoses/10 HPF. Small foci of necrosis (%5) was present. Pancytokeratin, EMA, S100 immunohistochemistry showed focal positivity in chordoid areas. Diagnosis of dedifferentiated chordoma was established.
Conclusion: Chordomas are slowly growing tumours with relatively good clinical behaviour, while dedifferentiated chordomas are tumours with aggressive clinical behaviour and high metastasis potential. It is important to recognise this rare entity which can cause diagnostic challenges, especially in small biopsy specimens due to its broad morphologic and immunophenotypic spectrum of findings.

E-PS-20-012

DOG1 positive leiomyosarcoma of the mesentery

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Background & objectives: Mesenteric leiomyosarcoma is a malignant mesenchymal tumour showing differentiation towards smooth muscle. It occurs very rarely, less than 20 having been reported so far. We herewith report one case of leiomyosarcoma of the mesentery showing positive staining for DOG1.
Methods: A 43-year-old female was admitted to our hospital due to a sizeable mesenteric mass discovered during a uterine myomectomy procedure. CT showed the 5.5cm large tumour to be well-circumscribed, with pushing borders. The tumour was resected with adequate margins. On gross examination, the tumour was well-circumscribed, with a solid cut surface.
Results: On microscopic examination, the tumour consisted of atypical spindle cells arranged in fascicles with moderate pleomorphism and up to

5 mitoses per 10 high power fields. Necrosis was not observed. Tumour cells were immunostained for SMA, desmin, and DOG-1 and negative for CD34, CD117(C-KIT) and S100. Molecular analysis of KIT and PDGFRA genes showed no mutation. Based on histological, immunohistochemical and molecular findings, our diagnosis was malignant mesenchymal tumour consistent with low-grade leiomyosarcoma of the mesentery.
Conclusion: Mesenteric LMS is an infrequent entity. The principal differential diagnosis is gastrointestinal stromal tumour (GIST), the most common mesenchymal tumour of the digestive tract. Precise diagnosis is essential since treatment and prognosis differ. CD117 and DOG1 positivity are considered to be the gold standard for GIST diagnosis. As evidenced by the case we present, molecular analysis is necessary to make the correct diagnosis in case morphological and immunohistochemical findings are inconclusive.

E-PS-20-013
The many shapes of schwannoma: a morphological study
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Background & objectives: Schwannoma is a benign nerve sheath tumour of differentiated schwann cells. The World Health Organization defines several subtypes, including ancient, cellular, plexiform, epithelioid and microcystic schwannoma. We present a unique case which simultaneously displays many different morphologies and compare them.
Methods: The patient is a 39-year-old male with no prior medical history of interest. He was referred to our institution because of a pelvic tumefaction. A computed tomography scan revealed the presence of a well-defined pelvic tumour, measuring up to 14cm, exhibiting signs of haemorrhage and no evidence of invasion. The lesion was excised and sent to the pathology department.
Results: Two lobulated and encapsulated nodules were received. Microscopically, an epithelial neoplasm with pushing borders and variable cellularity was found. The tumour was comprised of spindle cells, with wavy or oval and vesicular nuclei, arranged in variable sized fascicles, with a surrounding stroma partly fibrillary and partly myxoid. Areas with centrally hyalinized rosetoid aggregates and pseudoglandular spaces were identified. Focally, mononuclear inflammatory infiltrate, haemorrhage, thrombosis, calcification, hyaline degeneration and ischemic necrosis could be observed. Immunostaining was positive for S100, SOX10, GFAP, EMA, CD10, CD34 and CD99. INI1 retained expression. A diagnosis of ancient schwannoma was rendered, strikingly displaying large concomitant areas of pseudoglandular, neuroblastoma-like, plexiform and microcystic schwannoma.
Conclusion: The array of patterns and cytologic features schwannomas can exhibit is astounding, and is quite peculiar to find so many in a single case. It is of the utmost importance to recognize these findings as still within the spectrum, since differential diagnosis includes malignancies such as spindle cell sarcoma and malignant peripheral nerve sheath tumour. Although malignization of schwannoma is exceedingly rare, the presence of foci of malignant peripheral nerve sheath tumour, angiosarcoma and rhabdomyosarcoma may occur.

E-PS-20-014
Early resected extra skeletal osteosarcoma of the vocal cord
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Background & objectives: Laryngeal sarcomas constitute an extremely rare entity in the head and neck oncology field. Furthermore, most are histologically chondrosarcomas and the osteogenic form remains a true rarity.
Methods: Our patient, a 73-year-old Japanese man, presented with hoarseness. Laryngoscopy showed a solid tumour of the right vocal cord. Biopsy of this lesion was undertaken, yielding a histological diagnosis of atypical cellular proliferation, suggesting a sarcoma or squamous cell carcinoma with sarcomatoid changes. Computed tomography revealed a right laryngeal nodule, 10x8 mm in size, with no evidence of metastasis.
Results: Tumourectomy via direct laryngoscopy was performed. The cut surface of the excised specimen contained a relatively well-circumscribed, greyish-white, solid tumour, measuring 15x13x11 mm. This lesion was histopathologically composed of short-spindle atypical cells, with irregularly shaped, hyperchromatic nuclei. Ten mitotic figures were detected per 10HPF. Osteoid formation was occasionally observed, accompanied by focal calcium deposition. Immunohistochemical examinations revealed neoplastic cells to be positive for vimentin and SMARCB1/INI1 (BAF47), focally reactive for p63, and negative for p40, cytokeratin 5/6, AE1/AE3, CAM5.2, S-100, MDM2, CDK4, D34, CD68, STAT6, α-SMA and desmin. The Ki67 (MIB-1) labelling index was 51.2%, and p53 showed a random pattern. Based on these pathological findings, we diagnosed extra skeletal osteosarcoma.
Conclusion: Vocal cord enlargement surgery was subsequently performed, and the absence of residual cancer was confirmed histologically. The patient remains alive and well, with neither recurrence nor metastasis, 10 months after surgery. Osteosarcoma of the larynx is typically an extremely aggressive neoplasm that metastasizes early, has a propensity for hematogenous spread and also has a marked tendency to recur. Fortunately, our current patient presented with trachyphonia and was recognized in the early stage, allowing a complete remission to be achieved.

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E-PS-20-015
Low grade osteosarcoma associated with fibrous dysplasia: a case report
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Background & objectives: Osteosarcoma, the most common primary malignant tumour of bone, usually occurs in the second decade of life and in long bones of upper or lower extremities. Rarely, it may arise in the jaw and in older patients.
Methods: Here, a young male patient with maxillary osteosarcoma is presented.
Results: A 42-year-old male presented with a maxillary mass which was diagnosed as fibrous dysplasia 3 years ago. The bone destructing, hard palate-invading mass in the right maxillary sinus was excised in the second year of the follow-up. The tumour was reported to bear histopathological features of fibrous dysplasia with areas suspicious of a low-grade osteosarcoma. Six months later, maxillectomy was performed due to recurrence. Macroscopic examination revealed an 8.8 cm, tan-yellowish tumour. The tumour was mainly composed of spindle cells with osteoid formation and areas reminiscent of fibrous dysplasia. Immunohistochemically, tumour cells were positive for CDK4 with a Ki67 index of 15%. A diagnosis of low-grade osteosarcoma was made.
Conclusion: Osteosarcoma of the maxilla is a rare entity and may occasionally be preceded and/or accompanied by lesions such as fibrous dysplasia. In some cases, distinguishing between fibrous dysplasia and low-grade osteosarcoma may be challenging which may require application of MDM2 and/or CDK4 immunohistochemistry, and their positivity indicates a diagnosis of low grade osteosarcoma.

E-PS-20-016
Periosteal osteosarcoma with diffuse bilateral pulmonary metastasis: A case report
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Background & objectives: Periosteal osteosarcoma is a rare malignant bone tumour arising from the bone cortical surface which is seen in mostly 20 to 30 of age person. Periosteal osteosarcoma is a rare malignant bone tumour arising from the bone cortical surface.
Methods: Our case is a 47-year-old woman who presenting with a mass in the posterior of right thigh for 3 months. In the pathological analysis of the resected mass, sclerotic-looking areas are seen in the central region of the tumour. A lesion compatible with well-circumscribed parosteal osteosarcoma showing development the bone surface was detected on knee radiograph an MRI.
Results: The tumour was fully resected and prothesis was planted in the proximal tibia. In the histologic examination, the mass with an osteoblastic appearance invading the striated muscle is detected in the periphery of the tumour. The resected tumour mass was in chondroblastic character and endochondral ossification areas were detected. Following the operation developed prosthesis infection. Bilateral lung metastases and residue metastatic areas lymph node were detected in the patient after tumour resection.
Periosteal osteosarcomas are treated with wide excision. Their prognosis is better than that of high-grade intramedullary or high-grade surface osteosarcomas but worse than that of parosteal osteosarcomas.
Conclusion: Periosteal osteosarcomas are a malignancy with a long life expectancy, unlike classical osteosarcomas, with its early stage and treatment. Patients with bilateral lung metastases have a worse prognosis unlike parosteal osteosarcomas. The factors that significantly affect the prognosis in typical low-grade osteosarcomas are infection secondary to the prosthesis and diffuse metastases. The risk of developing osteomyelitis is high in patients with prosthetic site infection despite repetitive debridements.

E-PS-20-017
Spinal osteosarcoma: a rare localization
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Background & objectives: Although osteosarcoma represents the second most common primary bone tumour, spinal involvement is rare, accounting for 3%–5% of all osteosarcomas. The objective of this report is to emphasize the diagnostic problem.
Methods: It was about a 56-year-old man, complaining from a low back pain, radiating to the left lower limb and associated to a spinal stiffness. It was evolving for two months. He underwent a spinal MRI showing an osteolytic, exophytic mass of L5 left vertebrae and extended to soft tissue.
Results: Pathological examination of the biopsy, showed a malignant tumour. The neoplastic cells were compressed and trapped in an osteoid matrix associated to multi-nucleated cells. These cells showed irregular hyperchromatic nuclei with increased mitotic activity. Some calcifications were noted. After a confrontation with the radiological data, we retained the diagnosis of L5 osteosarcoma.
Conclusion: Osteosarcoma of the spine accounts for 3 to 5% of primary spinal tumours. It is distinguished by a peak of incidence located in the fifth decade, unlike the other localizations. Pathological diagnostic may be difficult on small biopsy specimens. The diagnosis of vertebral spinal osteosarcoma is based on the different microscopic aspects. However, the confrontation for this localization, both radiological and pathological, is essential.

E-PS-20-018
Epithelioid inflammatory myofibroblastic sarcoma: report of a new case of a rare entity with challenging diagnosis
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Background & objectives: Epithelioid inflammatory myofibroblastic sarcoma(EIMS) is a rare and recently defined neoplasm as an aggressive subtype of inflammatory myofibroblastic tumour (IMT) which has distinctive morphological features. It can be missed because of the lack of familiarity of pathologists with this entity.
Methods: A 43-year-old man presented with chest pain and productive cough. The thoraco-abdomino-pelvic CT revealed right pleurisy with pulmonary, hepatic and splenic metastasis. These features were consisting with the diagnosis of mesothelioma. Parenchymal biopsies of the middle and upper lobes of the right lung were performed.
Results: On microscopic examination, the tumour was composed predominantly of large round to epithelioid cells with vesicular nuclei, prominent nucleoli and eosinophilic cytoplasm. Tumour cells were arranged in clusters or sheets embedded in a myxoid stroma containing prominent neutrophils and lymphocytes. The plasma cells were absent. Mitotic figures were multiple with atypical forms. A minor component of spindle cells was present in focal areas. Immunohistochemical study was performed. Tumour cells were positive for anaplastic lymphoma kinase (ALK) with a nuclear membrane pattern, desmin, vimentin and INI-1 and focally positive for EMA. Pan-cytokeratin, melan-A, HMB45, ACE, WT1, calretinin, CD45, CK7, CK20, CK5/6 and D2-40 were negative. Thus, the diagnostic of EIMS was retained.
Conclusion: EIMS can be diagnosed in combination with morphologic features and an appropriate immunohistochemical panel. The striking feature of EIMS is the presence of obvious inflammatory infiltrates frequently composed of neutrophils. All tumours almost contained a small amount of spindle cell component. On immunohistochemistry, this tumour is characterized by distinctive nuclear membrane or perinuclear ALK staining. Accurate diagnosis is crucial not only for prognostic reasons but also because of the potential for treatment with targeted therapies such as ALK inhibitors.

E-PS-20-019
Soft tissue leiomyosarcoma: a clinical-pathological study of six cases from southern Tunisia with literature review
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Background & objectives: Leiomyosarcoma (LMS) is a malignant neoplasm composed of cells showing smooth muscle differentiation. The most common location is the retroperitoneum, soft tissue sites are less common. The aim is to analyse the epidemiological and histopathological characteristics of this entity.
Methods: Six cases were identified as LMS of soft tissue at our department over a period of 11 years (2009-2020). Their demographical and pathological characteristics were retrospectively reviewed.
Results: Mean age of patients was 62,33 years old (extreme: 39-91). Sex ratio: 0,5 (2men/4women). Different locations were: lower limbs (4cases), upper limbs (1case), and paravertebral (1case). Anatomopathological study is comparable in all patients: Macroscopically, mean tumour size was 6 cm (extreme: 3-12,8 cm). It was an indurated whorled yellowish mass, with necrotic and haemorrhagic changes. Histologically: This is a moderate to high density proliferation of entangled bundles of spindle cells with large atypical nuclei. Mitoses were numerous with focal necrosis. Immunohistochemical study showed positivity for AML and h-caldesmon in all cases, and desmin in 3 cases. FNCLCC grade was 2 in 4 cases and 3 in 2 cases.
Conclusion: LMS is a rare subtype of soft tissue sarcoma, can occur in almost any part of the body. Common locations include the abdomen, retroperitoneum, larger blood vessels, and the uterus. LMS is less common in the extremities compared with other sarcoma subtypes, accounting for 10% to 15% of limb sarcomas. The incidence increases with age. Histologic grade, tumour size, and tumour depth are the three major clinic pathologic prognostic factors.

E-PS-20-020

Rhabdomyosarcoma of soft tissue: a retrospective study of 15 cases from southern Tunisia

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Background & objectives: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma of children and represents a high-grade neoplasm. It is not limited to skeletal muscle, and show diverse clinical presentations, usually related to mass effect. Histologic features of RMS are variable.
Methods: The histological and immunohistochemical features of 15 cases of RMS were described with a review of the related literature. These cases were diagnosed in our department of pathology between 1995 and 2021.
Results: Patients were aged between 2 and 84 years (mean age: 45 years). The study included 9 men and 6 women (SR= 1,5). The most affected site was thigh (4 cases) followed by leg (3 cases). The most frequent subtype was pleomorphic (6 cases) followed by embryonal (4 cases) then alveolar (3 cases). Pleomorphic RMS affects older patients. While embryonal subtype affects young patients. Immunohistochemical study was performed to help make the diagnosis. Desmine and myogenin were positive in all cases, while vimentin was positive in 12 cases. Only two patients had metastases, one of spinal localization the other multiple metastases of pulmonary and retroperitoneal localization.
Conclusion: RMS is a malignant neoplasm in which tumour cells have a propensity for myogenic differentiation. The two major RMS subtypes are: alveolar and embryonal. Various classification systems including age, stage, and tumour site have been used in risk stratification. Histologic subtype has been a key variable, and patients with alveolar RMS were considered higher risk than those with embryonal RMS. New histologic and molecular subtypes such as MYOD1-mutated RMS can lead to a better prognostic classification of RMS.

E-PS-20-021

Primary leiomyosarcoma of bone: a rare diagnostically challenging bone tumour

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Background & objectives: Leiomyosarcoma is a malignant smooth muscle neoplasm that usually arises from uterus and soft tissue. Its occurrence as primary bone tumour is extremely rare event. It can be difficult to differentiate from other primary bone neoplasms with spindle cell morphology.
Methods: We describe a 29-year-old female patient who presented with right knee swelling and pain for 2 months duration and found to have a bone tumour by imaging studies. We discuss the radiologic and histopathologic features of the tumour. A panel of immunohistochemical stains were performed on the tru-cut biopsy to determine the line of differentiation of the tumour.
Results: MRI revealed 8.5 cm intramedullary mass arising from the metaphysis of right distal femur. Tru-cut biopsy was taken, which revealed low grade spindle cell neoplasm arranged in fascicles and infiltrating into bone trabeculae and bone marrow spaces. No malignant osteoid formation was seen. The tumour cells were immunoreactive for smooth muscle actin, muscle specific actin and calponin but negative for CKAE1/AE3, S100, CD31, CD34 and Desmin. No uterine or soft tissue masses were detected by imaging studies. The diagnosis of primary leiomyosarcoma of bone was rendered. Wide local excision was performed. No local recurrence or distant metastasis were detected upon follow-up by imaging studies for 2 years.
Conclusion: Primary leiomyosarcoma of bone is an entity that bears diagnostic difficulty. It is essential to differentiate from other aggressive primary bone tumours with spindle cell morphology to prevent potential unnecessary overtreatment.

E-PS-20-022

The clinical significance of EPH-A1, -A2, -A4, -A5 and -A6 expression in gastrointestinal stromal tumours

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Background & objectives: Erythropoietin-producing human hepatocellular receptors (EPHs), members of the receptor protein-tyrosine kinase (RTK) superfamily, are implicated in embryonic development and multiple physiological procedures, including cancer. The clinical significance of EPH A subgroup members expression in Gastrointestinal Stromal Tumours (GISTs) was evaluated.
Methods: The expression of EPH-A1, -A2, -A4, -A5 and -A6 was assessed immunohistochemically on formalin-fixed, paraffin-embedded tissue sections obtained from 43 GIST patients (27 males, 16 females; age 41-90 years). The association between EPHAs positivity and expression as histoscore (HSC, staining intensity and percentage of positive tumour cells) was correlated with patients' clinicopathological parameters.
Results: EPH-A1, -A2, -A4 and -A6 were expressed in 41 (95%), 43(100%), 41(95%), and 25(58%) out of 43 cases, respectively, exhibiting both cytoplasmic and nuclear staining, except for EPH-A6 (only nuclear staining). EPH-A5 was not expressed. EPH-A1 nuclear positivity correlated with epithelioid tumour cell morphology (p=0.021), while high cytoplasmic HSC associated with high mitotic rate (p=0.012) and advanced prognostic group (p=0.03). EPH-A2 had the dominating effect on GIST clinical profile, as nuclear positivity inversely associated with stage, mitotic rate and prognostic group (p=0.007, p=0.037 and p=0.026, respectively). Moreover, EPH-A2 nuclear HSC inversely correlated with stage (p=0.03) and prognostic group (p=0.048). Lastly, EPHA4 cytoplasmic positivity correlated with spindle cell morphology (p=0.013).
Conclusion: Our results suggest an association between EPH subgroup A members expression and GIST histological and clinical profile, which not only reveals their role in the development of the aforementioned tumours, but also renders them potential prognostic markers and therapeutic targets.

E-PS-20-023

A rare case of a soft tissue angiofibroma with GAB1/ABL1 gene fusion in a 13-year-old patient with associated right-hemibody anomalies

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Background & objectives: Soft tissue angiofibroma was recently defined as a new tumour type that presents as a slow-growing painless mass. In 60-80% of tumours, a NCOA2 rearrangement or fusion is present and in single cases the GAB1/ABL1 fusion was also described.
Methods: A 13-year-old patient presents with an asymptomatic slow-growing mass of the right thigh and associated cutaneous and mood anomalies. The magnetic-resonance-imaging highlights an intramuscular well-demarcated tumour measuring 11x5,5x13 cm, raising the suspicion of a rhabdomyosarcoma. A guided surgical biopsy was performed. The sample was analysed in the pathology department by standard histology, immunohistochemistry, and RNA-sequencing.
Results: The microscopic examination reveals a moderately cellular proliferation consisting of spindle cells with inconspicuous elongated nuclei and eosinophilic cytoplasm. The tumour stroma is fibrous, and the vascularization consists of a rich network of small-size capillaries. The tumour has the following immunohistochemical profile: Actine-, Desmine-, Caldesmone-, Myogenine-, MyoD1-, PS100-, SOX10-, GFAP-, EMA-, STAT6-, ALK1-, ROS1-, NTRK-, MDM2-, SATB2-, BRG1+, INI+, BCOR-, CD34-, CD31-, MUC4-. Ki-67 proliferation index was 5%. The RNA sequencing using exploratory bioinformatics analysis with a combination of different specialized gene fusions software identified the GAB1/ABL1 gene fusion.

Integrating the morphology, immunohistochemical and molecular profiles the diagnosis of soft tissue angiofibroma was made.
Conclusion: We present an unusual case of a soft tissue angiofibroma in a 13-year-old patient. Conventional histology and immunohistochemistry were not enough to characterize the tumour. Further RNA sequencing identified the GAB1/ABL1 gene fusion, previously described in very rare cases of benign paediatric soft tissue tumours including solitary fibrous tumour, perineurinoma and soft tissue angiofibroma. The unusual association of this soft tissue tumour with dermatological and neurological anomalies highlights the need for a genetics follow-up for this patient.

E-PS-20-024
Classical non-proximal type epithelioid sarcoma of the fingers: 3 cases
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Background & objectives: The aim of study is determine the relation between pathological features and clinical course of classical non-proximal type epithelioid sarcoma of the fingers.
Methods: A review of histological picture, IHC (INI-1, EMA, CD99, CD56, CD34, Cytokeratin 8/18, p63, Cytokeratin 5/6, Cytokeratin HMW, GFAP, Desmin, Myogenin, Melan A, HMB45, MITF, S-100, TLE-1, CD117, DOG1, SOX10) from 2 females, 50 and 67 y.o., and 37 y.o. male was carried. Localization: middle phalanx of 2-nd finger; stump of 5th finger - local recurrence of sarcoma; 2-nd finger.
Results: size of tumors:1 - 3x2.5x1.5cm; 2 - local recurrence of epithelioid sarcoma, excised 3 years ago - 7x6x4 cm with ulceration, bone destruction, metastases in axillary lymph nodes. 3- 4x2.5x2.5 cm, skin ulcer 5 mm. Bone destruction 30x3x3 mm. Histological picture varied: 1 - extensive zones of coagulation necrosis, abscesses, small fusiform cells. 2 - spindle and epithelioid cells, collagen deposits, 45 mf/10hpf . 3 - spindle and epithelioid cells, with pseudo-granulomatous structures with central necrosis, osteoid-like stromal collagen, up to 6 mf/1 hpf, 23 mf/10 hpf. Loss of INI-1 nuclear expression, Cytokeratin 8/18, Cytokeratin 5/6, Cytokeratin HMW, EMA positive in all cases, focal CD34, GFAP, Desmin - in 1.
Conclusion: Large size of the tumour, high mitotic activity and the absence of necrosis and granulomas were associated with a more aggressive clinical course with local recurrence and metastases to the lymph nodes.

E-PS-20-025
Rhabdomyomatous mesenchymal hamartoma: a review of the literature regarding a case
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Background & objectives: Rhabdomyomatous Mesenchymal Hamartoma (RHM) is a rare and usually congenital lesion developed in dermis and soft tissues. We report a case to aid in the description of specific clinical-pathological criteria towards correctly characterizing this rare entity.
Methods: Formalin-fixed and paraffin-embedded material was evaluated with 3-micron sections and hematoxylin-eosin staining. An immunohistochemical panel was performed including vascular (CD31, CD34) and muscle (muscle specific actin, desmin, caldesmon) markers.
Results: We describe a 70-year-old patient with a poorly defined 3 cm lipomatous nodule in the left nasolabial fold, with perilesional erythema which had been previously diagnosed with rosacea and venous malformation / intramuscular haemangioma by microscopic evaluation. Facial MRI and angiography suggested a vascular tumour or vascular malformation. No deep tissue infiltration was observed.
We identified a dermal lesion composed of striated muscle fibres at different levels, arranged in a perpendicular disposition to the epidermal surface, interspersed with abundant blood vessels, mature adipocytes, immature follicle-sebaceous units, and nervous fibres. It expressed muscle (actin HHF35 and desmin), and vascular markers (CD34 and CD31) and had a negative S100 and HMB45 expression.
Conclusion: HMR is a rare hamartomatous lesion, associated with polymalfomative syndromes, with very few cases described. It usually occurs in the facial and perineal area of children, although it can develop in adults, as in this case. Diagnostic criteria is based on its congenital nature, typical location and characteristic arrangement of the striated muscle. An adnexal component, with immature follicle-sebaceous units, prominent vasculature, and nerve fibres, was seen in our case, making it more complex than those described so far.

E-PS-20-026
Parachordoma/myoepithelioma of soft tissue at posterior mediastinum
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Background & objectives: Parachordoma/Myoepithelioma of soft tissue is a rare tumour localizes mostly at extremities but also in trunk and head and neck region. Apart from our case there are only two cases located in mediastinum in the English literature. ...
Methods: ...Histologically tumours show great variety both between cases and in different locations of a single case. Grossly tumours are mostly well circumscribed but not encapsulated solid masses. Histologically, these tumours consist of any composition of spindle, epithelioid, or vacuolized cells. Immunohistochemically, they show variable staining patterns with cytokeratins and myoepithelial markers. Mostly seen genetic changes include fusions with EWSR1 gene.
Results: We represent the case of a 62-years-old woman with a well-demarcated cystic mass of 5x4.5x3cm in the left posterior mediastinum. Resection material was reported as "mesenchymal tumour" in another centre and paraffin blocks were sent to our laboratory for re-evaluation. Microscopically we've seen a well circumscribed cystic tumoral lesion in a myxoid background, enveloping an area of haemorrhage. Tumour cells showed mild atypia, some of them showed an epithelioid or spindled morphology with eosinophilic cytoplasm, vesicular nuclei and inconspicuous nucleoli; others had vacuolized cytoplasms reminiscent of physaliphorous cells. Immunohistochemically, tumour stained diffusely with S100 and vimentin, also focally with EMA and CK8/18. Brachyury was negative. Myoepithelial markers (p63,SMA,GFAP and calponin) were negative.
Conclusion: Differential diagnosis of parachordoma/myoepithelioma of soft tissue, especially if it develops at an unexpected localization, like our case, may be difficult. It is also important to take into account the wide spectrum of histomorphological and immunohistochemical findings, especially the brachyury stain, for this rare entity.

E-PS-20-027
An unusual case of retroperitoneal cellular schwannoma masquerading as renal cyst
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Background & objectives: A 71-year-old woman presented with fever and a history of chronic left-sided back pain. Renal ultrasound and MRI showed a large renal cystic lesion measuring 18 cm. The patient underwent surgery, and the specimen was sent for pathological evaluation.
Methods: We received a specimen of left total nephrectomy presenting an encapsulated cystic lesion measuring 18x15x6 cm with variable thickness of the wall (max diameter 3 cm), attached to the kidney. The tissue was fixed in 10% buffered formalin, routinely processed and embedded in paraffin; 2–4μm thick sections were stained with hematoxylin and eosin and immunohistochemistry was performed.

Results: Histological examination revealed a cellular neoplasm presumably of mesenchymal origin, totally encapsulated, with extensive cystic degeneration. The tumour was, mostly, composed of uniform spindle cells of schwannian origin, without significant atypia, embedded in a collagenous stroma (Antoni A areas). Vessels with thick hyalinized wall were also apparent. Mitotic activity was absent.
During immunohistochemistry, tumour cells were S100 strongly and diffusely positive, Vimentin (+), SOX10 (+), p16 (+) and retained INI-1 expression. The rest of the markers (Desmin, SMA, STAT-6, Melan-A, HMB-45, CD31, CD34, AE1/AE3, EMA, HK27me3) were negative.
Conclusion: Morphological and immunohistochemical evaluation favoured the diagnosis of cellular schwannoma with extensive cystic degeneration, which mimic a renal cyst, clinically.
Cellular schwannomas are rare (6%), slow growing benign retroperitoneal tumours, usually found incidentally, with peak incidence from 4th to 6th decade. Total resection is sufficient and recurrence is extremely rare.

E-PS-20-028

Malignant peripheral nerve sheath tumour (MPNST) arising in plexiform neurofibroma in a neurofibromatosis type I (NF1) patient

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Background & objectives: NF1 is a genetic disorder predisposing to the development of Peripheral Nerve Sheath Tumours. These are neoplasms of Schwann cell origin, benign (neurofibroma, schwannoma) or malignant (MPNST). Plexiform Neurofibromas may undergo malignant dedifferentiation and progress to atypical neurofibromas and MPNSTs.
Methods: A 44-year old woman diagnosed with NF1, presented with a bulky tumour localized at the anterior mediastinum. Surgery was performed and we received three tumour masses measuring 2,5 to 8,8cm in maximum diameter. Tumour was partially encapsulated, had a white-tan appearance and a firm-solid texture. Due to its size, we proceeded to extensive sampling of the mass.
Results: Histological examination revealed a spindle cell neoplasm arranged in a fascicular pattern of mixed cellularity with areas of myxoid appearance. Tumour cells were variably pleiomorphic with hyperchromatic nuclei and high atypia. Mitoses were abundant. Immunohistochemical analysis showed patchy expression of SOX10 and S100, aberrant expression of p53 and loss of p16. Ki67 proliferation index was 70%. Peripheral sections showed a different histological pattern of a benign neoplasm with uniform bland spindle cells without atypia or mitoses. Immunohistochemical analysis in these sections demonstrated strong-diffuse expression of S100, absence of p53, retainment of p16 and very low Ki67 expression. Morphology and immunophenotypic analysis confirm the diagnosis of MPNST arising in Plexiform Neurofibroma.
Conclusion: MPNSTs arise either de novo or from malignant transformation of benign Nerve Sheath Tumours in NF1 patients. In this setting, MPNSTs affects younger individuals and represent the leading cause of death associated with NF1. Plexiform neurofibromas are very common in NF1 patients and are considered as MPNST precursors because a subset of them (especially deep) undergoes transformation to MPNSTs. The malignant transformation is a dynamic process and the differential diagnosis between an atypical neurofibromatous tumour and MPNST is challenging.

E-PS-20-029

Angiomatoid fibrous histiocytoma – rare, molecularly defined tumour of soft tissue

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Background & objectives: Angiomatoid fibrous histiocytoma (AFH) is a rare neoplasm with intermediate malignant potential (local recurrence rate 15%, distant metastases up to 5%, single reports of AFH-related deaths). AFH is a genetically defined lesion with *EWSR1-CREB1* (>90%) or less common *EWSR1-ATF1* fusion.
Methods: We present a 46-year-old female with a 3.5cm diameter, well-circumscribed tumour localized in the cubital fossa area's soft tissue. In the biopsy, low-grade sarcoma was diagnosed, and the surgical resection was performed. The neoplasm was lobulated, surrounded by an incomplete fibrous pseudocapsule, and composed of epithelioid cells with bland, vesicular nuclei and a scant amount of cytoplasm.
Results: The further evaluation revealed rare mitoses (up to 5 mitoses/10HPF) and no necrosis. In the stroma, there were areas with myxoid change and multifocal blood-filled pseudoangiomatous spaces and haemorrhages. We did not observe the surrounding lymphoplasmacytic infiltrate or cuff of B- and T-cells. Immunohistochemically, the tumour cells were: CD99(+) weakly, Desmin(-/+) only single positive cells, SMA(-), S100(-), SOX10(-), CD34(-), ERG(-), MDM2(-), CKAE1/AE3(-), PD-L1(-) positive control in macrophages, Ki67(+) in 5-7% of nuclei. The microscopic resection margins were radical (R0). In the extended NGS sarcoma panel assessment (FusionPlex Expanded Sarcoma Kit for Illumina, ArcherDx), we found *EWSR1-CREB1* fusion and no additional mutations. The final diagnosis of angiomatoid fibrous histiocytoma was made.
Conclusion: In conclusion, our case was diagnostically challenging because of myxoid features, lack of pericapsular rim of lymphoplasmacytic cells with germinal centres, immunohistochemically weak desmin, and CD99 expression. According to the latest report, nearly 60% of AFH shows PD-L1 expression, although our case lacked PD-L1 expression. Since treatment options for unresectable and/or metastatic tumours are limited, the immunotherapy with PD1/PD-L1 inhibitors may be worth further investigations.

E-PS-20-030

Primary osteosarcoma originating of the kidney – a differential diagnosis with sarcomatoid renal cell carcinoma with osseous metaplasia

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Background & objectives: Extra skeletal osteosarcoma (OS) makes up <1% of all soft tissue sarcomas and 4% of all OS. Mainly it originates in the dermis/subcutis and is located in the thigh (~50% of cases); other sites include the buttock, shoulder, trunk, and retroperitoneum.
Methods: We present a 55-year-old male with a tumour with a 20cm diameter localized in the left retroperitoneal space. In January 2020 patient underwent radical nephrectomy, adrenalectomy, and splenectomy outside our hospital. In March 2020, computed tomography revealed the local abdominal recurrence (16.4x21.8x26.4cm) and multifocal liver metastases (4.2x4.4x5.8cm and 3.6x3.3x3cm). The consultation of histopathological material was performed.
Results: The tumour measuring 22x18x15cm was replacing nearly the entire kidney and focally infiltrating the spleen on gross examination. Microscopically, the neoplasm was highly cellular, composed of spindle cells with moderate/high atypia, mitotic activity up to 6 mitoses/10HPF, with necrosis and multiple haemorrhages, and numerous multinucleated

giant cells. In the stroma, abundant osteoid formation and lace-like ossification fields were seen. The resection margins were R1 and Immunohistochemically, the tumour cells were: SATB2(+) strongly positive, SMA(+/-), Desmin(-), CD34(-), MDM2(-), p53(-), H3F3A(-), H3F3B(-), CKAE1/AE3(-), PanCK(-). The tumour was examined in several sections and did not show renal cell carcinoma (RCC) architecture. The patient was qualified for palliative chemotherapy with anthracyclines (CyADIC scheme).
Conclusion: In conclusion, the primary osteogenic OS of the kidney is extremely rare. Up-to-date, only 28 cases have been reported, which characterize high local recurrence rate and distant metastatic potential. The differential diagnosis with sarcomatoid RCC requires extended sampling and immunohistochemical assessment. Nevertheless, the prognosis is dismal in both entities.

E-PS-20-031
A case of leiomyosarcoma with high tumour mutation burden, microsatellite instability, mismatch repair deficiency and significant PD-L1 expression
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Background & objectives: Microsatellite instability (MSI) or mismatch repair deficiency is extremely rare in sarcomas with an incidence of 2.2% in a recent study. We report a case of a 55-year-old man with metastatic abdominal wall leiomyosarcoma that is microsatellite unstable.
Methods: Histological and immunohistochemical (IHC) assessment was performed to arrive at the diagnosis of leiomyosarcoma. Tumour tissue was subsequently sent for molecular profiling via FoundationOne CDx which includes testing for MSI status and tumour mutation burden. MSI PCR and IHC for mismatch repair (MMR) proteins and PD-L1 (22C3 clone) were also performed.
Results: Histology showed a FNCLCC grade 3 spindle cell sarcoma in keeping with a leiomyosarcoma. Tumour infiltrating lymphocytes and plasma cells were noted within the tumour and at the tumour edge. FoundationOne CDx showed MSI high status and tumour mutation burden of 11.35/megabase. Somatic alterations included TP53, BCL2 and MLL2, along with truncating mutations in RB1, MSH3 and MSH6. MSI PCR showed shifts in microsatellite markers confirming MSI-high status. There was loss of MSH6 on MMR IHC while PD-L1 stained positive with Tumour Proportion Score of 40% and Combined Positive Score of 45. Clinically, the patient demonstrated primary resistance to 2 lines of chemotherapy and was subsequently treated with checkpoint immunotherapy.
Conclusion: We report a rare case of leiomyosarcoma with MSI-high status, high TMB (>10/megabase), MMR protein loss and significant PD-L1 expression. The presence of a significant number of tumour infiltrating lymphocytes within the tumour and at the periphery may be a histologic clue to MSI high status. However, more study is needed. There is good correlation between MSI status, TMB, MMR and PD-L1 expression in this case.

E-PS-20-032
Recurrent metastatic granular cell tumour: a case report
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Background & objectives: Malignant granular cell tumour is an exceedingly rare Schwann cell-related sarcoma with aggressive behaviour and poor clinical outcome. Prediction of malignant behaviour based on morphologic and immunohistochemical features remains a challenge, with metastases being considered the definitive criterion for malignancy.
Methods: A 52-year-old man presented with a 6-month history of rapidly growing painless mass in the posteromedial aspect of the proximal upper arm. Ultrasound examinations revealed a 3 x 2 cm well-defined, firm, subcutaneous mass with heterogeneous echo pattern and fascial contact. Computed tomography showed no evidence of metastatic disease.
Results: Core-needle biopsy revealed a granular cell tumour with uncertain malignant potential. The excised lesion measured 5.4 cm in the direction of maximum dimension and had infiltrative borders. The neoplastic cells were PAS-positive with diastase-resistant cytoplasmic granules and showed S-100 and SOX10 immunoreactivity. Unfavorable histological features were noted, such as increased cellularity, prominent spindling, focal pleomorphism, vesicular nuclei with conspicuous nucleoli and increased mitotic activity. The margins were positive. After three months, a wide re-excision showed local recurrence measuring 2.7 mm in maximum diameter. Six months later, the patient presented local recurrence and metastatic disease in axillary lymph nodes.
Conclusion: The tumour met five out of six Fanburg-Smith criteria for classification as malignant. The treatment of choice was wide excision, with careful assessment of surgical margins. Although the diagnosis of a granular cell tumour is straightforward, the process for making the distinction between benign and malignant is controversial, but its accuracy is of paramount importance, as the clinical behaviour and prognosis differ greatly. Patient follow-up for development of metastases is essential, regardless of the histologic criteria for malignancy.

E-PS-21 | Thymic and Mediastinal Pathology E-Posters

E-PS-21-001
Combined thymic carcinoma developing in the lung; a rare case report
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Background & objectives: Combined thymic carcinoma is a relatively rare malignant neoplasm of the thymus composed of thymic carcinoma and any type of thymoma that was recently added to the 4th edition of the World Health Organization (WHO) classification of thymic tumours.
Methods: Our case is a 32-year-old female patient diagnosed with type B2 thymoma (including those with type B3) in 2015. Therefore, the patient, who was treated with chemotherapy and radiotherapy, had respiratory distress for 2 months. Following the symptoms, a 16x11 mm nodular lesion with increased FDG uptake was detected in the right lung, and lower lobe wedge resection was performed.
Results: In resection material, a tumoral infiltration forming solid islets of different sizes containing extensive bleeding and fibrotic areas adjacent to the lung parenchyma was observed. Histopathological findings showed a presence of two separate components, squamous cell carcinoma, and thymoma. The immunohistochemical examination showed diffuse positive staining for PanCK and CD19, slight positivity in some cells with TdT and CD20, negative staining was detected in CD1a and PAX8 leading to a diagnosis of combined thymic squamous cell carcinoma and type B3 thymoma,
Conclusion: The combined thymic carcinoma is a rare entity with an ambiguous etiological background. However, the presence of thymoma in patients could be demonstrated as a predisposing risk factor for further development of thymic carcinoma. In conclusion, histopathological examination and clinical management of these tumours should be executed carefully because these lesions may co-exist in the spectrum of differentiation and regional or distant recurrence may occur.

E-PS-21-002
Inflammaging: the silicates definitely accelerate involution of thymus
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Background & objectives: Earlier we proved that the water-soluble silicon intake with the bottled, tap and distillate drinking water accelerated the thymus involution in male outbred rats. Will the response of murine thymus be similar to the rat's one after the silicon intake?
Methods: During 9-month white outbred male 5 rats and 3 mice received ad libitum bottled drinking water; 5 rats and 3 mice received the same water supplemented with sodium metasilicate (10 mg/l). After the animals were sacrificed the liver were isolated, fixed in 10% formalin, embedded in paraffin, cut and stained with hematoxylin and eosin.
Results: After 3 months, the histological slides of hematoxylin and eosin-stained thymus of the mice treated with silica was different from the thymus of untreated mice. The cortical septa are expanded, the appearance of adipocytes is observed in them. A similar picture was observed in the thymus of rabbits. After 9 months we noted the full-depletion in lymphocytes the cortex and medulla of the thymus of mice treated by silica. The thymus of treated mice was totally replaced by the adipose tissue while the thymus of untreated mice conserved the islands of lymphocytes.
Conclusion: Thus, the reaction of the thymus of mice after 9 months of silicon intake with drinking water is similar to the reaction of the thymus of rats. This fact proved that the intake of silica with drinking water accelerates the involution of thymus.

E-PS-21-003
A case report: micronodular thymoma with lymphoid stroma, and thymic cysts
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Background & objectives: Micronodular thymoma with lymphoid stroma (MTWLS) is a rare thymoma type that consists of multiple small tumour islands composed of spindle or oval cells that are surrounded by epithelial cell-free lymphoid stroma.
Methods: A 54-year-old woman who had undergone an endovascular abdominal aneurysm repair presented to the cardiothoracic surgery (CTS) clinic for postoperative 3-month follow-up. CT revealed a mass with a diameter of 3.4 cm at the anterior mediastinum. The patient has undergone a mediastinal mass excision. Gross examination showed two cysts and a 5 cm diameter solid mass in the fragmented material.
Results: Microscopic examination revealed a thymoma that had invaded the pericapsular connective tissue. The thymoma consisted of tumour islands composed of short spindle to oval cells without mitoses and a lymphoid stroma that was free of epithelial cells and contained lymphoid follicles with germinal centres, while only a few lymphocytes were scattered within the tumour islands. Immunohistochemically the tumour islands were Cytokeratin19(+), p63(+), PAX8(+), and CD117(-) within CD5(+) few scattered lymphocytes. There was an accompanying cyst lined by a single layer of flattened cuboidal epithelium. The case was diagnosed as WHO pT2 and Masaoka stage IIa MTWLS and thymic cysts. The patient is in a close follow-up by the CTS clinic.
Conclusion: Micronodular thymoma with lymphoid stroma is a very rare type of thymoma showing a similar pattern but varied morphology and immunophenotype of tumour cells. Although it is known to be associate with a favourable outcome, more cases and longer follow-up periods are needed.

E-PS-21-004
Thymic carcinoma in a patient with concurrent breast cancer
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Background & objectives: Thymic neoplasms are rare tumours, ranging from indolent thymomas to aggressive thymic carcinomas. Patients with thymic neoplasms have increased chances of developing a second or third neoplasm. We present a case of thymic carcinoma with concurrent breast carcinoma.
Methods: A 57-year-old female with a history of grade II, stage T1cN1Mx breast ductal (NOS) carcinoma under chemotherapy-hormonotherapy demonstrated at post-surgery imaging examination an upper-anterior mediastinal mass of 8cm. The patient underwent surgical abscission of the mediastinal tumour, 10 months after the first operation (mastectomy).
Results: Histopathologic examination revealed a thymic neoplasm with regular contours and multi-nodular, compact configuration consisting of atypical, polymorphous, non-keratinized cells and giant cells. There was brisk mitotic activity and foci of necrosis. The neoplasm had areas with more bland morphology, like a B3-thymoma and was accompanied by lymphoplasmacytic stroma organized in lymph nodules. Residual thymic tissue was observed. The neoplasm was surrounded by a rudimentary capsule focally infiltrated. Immunohistochemical analysis revealed positivity for: CKAE1AE3, CK5/6, p63, CD117, MUC1, CD5 and negativity for GATA-3, ER, PgR, HER-2. The two neoplasms (of the breast and mediastinum) were morphologically and immunohistochemically independent.
Conclusion: Thymic carcinoma accounts for 0,06% of thymic malignancies. These patients can develop other tumours (mostly lymphomas, sarcomas and gastrointestinal cancers). Co-existence of thymic carcinoma and breast carcinoma is exceedingly rare. Our case refers to thymic carcinoma with characteristics of lymphoepithelial carcinoma, arising from a thymoma, which possibly pre-existed the breast tumour. 20% of thymomas may be transformed to thymic carcinomas. Extra-thymic neoplasms are much more common in patients with thymoma and can appear before, simultaneously or after the thymoma diagnosis.

E-PS-21-005
A case of mucin producing type AB thymoma
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Background & objectives: Thymomas show morphological heterogeneity. According to WHO classification, a thymoma showing both lymphocyte-poor spindle cell and lymphocyte-rich components is called AB-thymoma. Microcystic changes, rosettes, papillary areas, whorls can be observed in type-A areas. However, mucin production is not expected.
Methods: A 44x33 mm mass with lobulated contours located in the anterior mediastinum was found on the thorax CT in a 68 years-old male, who was admitted with suspicion of COVID. SUVmax was 3.77 on the PET-CT. On gross examination, an encapsulated tumour measuring 5x4x2.5 cm, with a pinkish-white cut surface was observed.
Results: On histological examination the tumour was consistent with an AB thymoma. CD3, Tdt, CD1a were found to be positive at lymphoid cells, while spindle cells were positive with cytokeratin and p63. Chromogranin A and synaptophysin were negative. In one section, mucin-rich columnar epithelium was observed. The presence of mucin was shown with PAS-AB and mucicarmine stains.
Conclusion: A case of otherwise typical type AB thymoma with focal mucinous epithelium is presented. Mucin production can be observed in thymic adenocarcinomas. The present tumour was a typical thymoma and mucin production did not create any diagnostic problems. We cannot comment on the prognostic impact of this morphological finding. However, this case shows that mucin producing epithelium should be added to the wide spectrum of morphological findings, that can be observed in thymomas.

E-PS-21-006
A classic case of NUT carcinoma
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Background & objectives: A 25-year-old male, with no smoking habits or relevant medical history, presented to the hospital with one-month evolution of productive cough. He had no other symptoms and clinical examination was innocent.
Methods: Chest radiography evidenced a superior mediastinal enlargement; chest CT revealed an infra-carinal mediastinal mass of 64x50mm. Endobronchial endoscopy with bronchial biopsies and adenopathy aspiration cytology were performed.
Bronchial biopsies revealed a neoplasia with solid to trabecular pattern, consisting of small, cuboidal cells with granular chromatin and generally absent nucleoli, with scant eosinophilic cytoplasm. Keratin pearls and necrosis were observed.
Results: Immunohistochemistry was positive for p40, p63, CK5, CK34ß12 and CD56.
The differential diagnosis was between basaloid squamous cell carcinoma and NUT Carcinoma. Immunohistochemistry for nuclear carcinoma of the testis protein (NUT) revealed strong and diffuse expression in more than 50% of the neoplastic cells.
Diagnosis of NUT carcinoma was made.
Global evaluation, including PET scan, revealed pulmonary parenchyma involvement, regional adenopathies; hepatic lesion; right adrenal gland nodule; osteomedullary lesions and was staged IVB, with probable primary neoplasm of the mediastinum, with lung invasion and several metastases.
Conclusion: NUT carcinoma is a rare, aggressive carcinoma defined by rearrangement of the NUTM1 gene. The histologic features are unspecific: it is poorly differentiated, with or without squamous differentiation with a monomorphic, clonal appearance. It is under-recognized by most pathologists, consequently it is commonly undiagnosed, or misdiagnosed, most often as squamous cell carcinoma.
Immunohistochemistry for NUT expression easy diagnoses it, so it should be recommended in all poorly differentiated non-cutaneous carcinomas, with or without squamous differentiation, that have a monomorphic appearance.

E-PS-21-007
Germ cell mediastinal tumour associated with a presumable acute megacaryocytic leukaemia
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Background & objectives: The association between mediastinal germ cell tumours and haematological malignancies is very rare, with only 26 cases reported in the last 7 decades. We present here the case of a 26-year-old patient with an undifferentiated mediastinal tumour.
Methods: An autopsy was performed in order to establish the diagnosis. Formalin-fixed, paraffin embedded tissue samples harvested from the mediastinal tumour were processed by means of standard HE and special stains (VGE, PAS-alcian, Gomori). IHC was performed on semi-thin sections according to the manufacturer specifications for the following antibodies: AE1-AE3, SMA, desmin, ER, Vim, Ki-67.
Results: Grossly, a large mediastinal tumour was found, along with massive peritumoral hematoma and paraneoplastic bilateral pleural effusion. Bronchopneumonia and acute transmural myocardial infarction were also found as subsequent complications. Microscopically , the tumour cells were arranged in gland-like or tubular structures with areas of necrosis and haemorrhage, accompanied by a proliferation of elongated spindle cells with hyperchromatic nuclei. AE1-AE3 was positive in the epithelial component, with a Ki-67 proliferation index of 40-50%. The mesenchymal component stained positive to SMA, desmin and vimentin in the spindle cells. ER was negative.
Conclusion: The diagnosis of a non-seminomatous mediastinal germ cell tumour with a mature teratoma component, associated with areas of adenocarcinoma and sarcomatous proliferation with muscular differentiation was made, accompanied by a possible acute megacaryocytic leukaemia. Nonseminomatous germ cell tumours in association with AML are a rare combination of two malignancies that affect the young male patients and have a poor prognosis.

E-PS-22 | Uropathology E-Posters

E-PS-22-001
Cavernous haemangioma of the bladder: a case report of a rare lesion and literature review
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Background & objectives: Haemangioma is a benign vascular tumour. Although frequently diagnosed on skin, these lesions are extremely rare in the bladder, accounting for only approximately 0,6% of primary tumours. Nonetheless, haematuria is a clinical manifestation that overlaps with that of epithelial malignancies.
Methods: We report the case of a 86-year-old man, with history of prostatic adenocarcinoma diagnosed 16 years before, who presented with haematuria and weak urine flow. The disease had been staged as cT1c N0 M0 and treated with hormone therapy, external radiotherapy and brachytherapy, with no evidence of relapse. An urethrocystoscopy was now performed.
Results: A large intravesical clot and a suspicious erythematous lesion in the left lateral bladder wall were detected, along with a stricture of the bulbo-membranous urethra. A transurethral resection of the bladder tumour was performed. Microscopically, diffuse haemorrhage associated to large cystically dilated vessels with thin walls, without cytological atypia in the endothelial lining, were identified. The diagnosis of cavernous haemangioma of the bladder was made. Fibrosis and reactive features of both stromal fibroblasts and urothelium were present and considered as radiation therapy effect. No evidence of epithelial dysplasia or neoplasia was found, supported by cytokeratin 20 and Ki-67 immunostaining.
Conclusion: History of malignancy should increase the suspicion for tumour-related causes of haematuria. Haemangiomas are extremely rare bladder lesions but should be considered in the differential diagnosis. Endoscopic features may be highly suggestive of a vascular lesion, and microscopic analysis allows for the definitive diagnosis. As in our case, hemangiomas are generally of cavernous type and diagnosed in male adults. This is the second case reported in a patient after radiotherapy, but no etiologic factors have been established.

E-PS-22-002
Paratesticular inflammatory myofibroblastic tumour: a benign entity with a very rare location
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Background & objectives: Inflammatory myofibroblastic tumour is a benign entity originating in the soft tissues, with unknown aetiology. Its treatment consists only in complete surgical excision. Genito-urinary localization, and especially the testicular/paratesticular one, is particularly rare, being reported in less than 10 cases.
Methods: We present the case of a 57-year-old male patient, who presented for scrotal pain and swelling of the right testicle, with palpation of a hardened area, for about 4 months, which did not remit after clinical treatment. The right orchiectomy revealed a normal testicular parenchyma and a poorly defined lesion of 2 /1.5cm, adjacent to the epididymis, affecting the tunica vaginalis.

Results: Microscopic examination identifies a mesenchymal tumour composed of a proliferation of fusiform cells, with elongated nuclei, without atypia, arranged in bundles and associated with a diffuse inflammatory infiltrate. The highlighted aspects indicate an inflammatory myofibroblastic tumour of the testicular vagina and immunohistochemical tests were mandatory in order to establish the final diagnosis. Immunohistochemical examination revealed fusiform cell positivity in SMA, and in Vimentin, negativity in the epithelial marker AE1 / AE3, S100 and Desmin. For the evaluation of inflammatory cells, CD3 was positively intensified in lymphocytes and CD68 was positive in macrophage cells. The final diagnosis was paratesticular inflammatory myofibroblastic tumour (tunica vaginalis). Patient was followed without any further treatment.
Conclusion: Histopathological examination, in correlation with proteomic evaluation, established the biological potential of the paratesticular lesion, benign in this case, despite the noisy clinical appearance and suspicion for malignancy, important aspects in establishing therapeutic behaviour. It is also a diagnosis that must be considered in the differential diagnosis of paratesticular lesions.

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E-PS-22-003
Chromophobe renal cell carcinoma presenting as a renal cyst
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Background & objectives: Chromophobe renal cell carcinoma (ChRCC) is a rare subtype of RCC. Cystic RCC are rare among all RCC subtypes and cystic ChRCC are even a more uncommon presentation. We describe here a ChRCC presenting as predominantly cystic renal mass.
Methods: We report a rare case of ChRCC presenting as a unilocular renal cystic mass. It is about a 69-year-old man presented with a history of right lumbar abdominal pain and discomfort. Computed tomography showed a solid with prominent cystic mass measuring 2,5 cm×2 cm arising from the lower pole of the right kidney. A partial nephrectomy was performed.
Results: Gross pathological examination of the surgical specimen revealed a 2,5 cm cystic mass. The wall thickness of the cyst was 0.4 cm. The surrounding renal parenchymal tissue was normal. Histological examination of the cystic mass showed solid nests, tubules and papillae of tumour cells in the lumen. These cells were polygonal with distinct borders, nuclei were wrinkled, angulated, and with perinuclear halos in a background of abundant pale eosinophilic cytoplasm. The cystic wall was lined by a layer of tumour cells. There was no perinephric tissues invasion. Surgical margins were negative.
By immunohistochemistry, the tumour cells were diffusely positive for CK7, focally positive for c-kit and negative for CD10.
Conclusion: Cystic renal neoplasm varies from benign to malignant. Cystic RCC is frequently misdiagnosed as a benign renal cyst because it shares similar clinical manifestations and imaging characteristics. Cystic presentation of ChRCC is believed to account for 4% of all morphological variants of chromophobe RCC.
Because of the rarity of this entity and the limited number of patients reported in the literature, additional research is needed to further show diagnostic and prognostic implications.

E-PS-22-004
Carcinoma cuniculatum of the penis – a case report
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Background & objectives: Carcinoma cuniculatum is a low-grade squamous cell carcinoma, first described in the plantar skin and extremely rare in the penis (less than 1% of penile carcinoma). We report a case of verrucous carcinoma of the penis with extensive cuniculatum component.
Methods: A 70-year-old patient underwent a partial penectomy due to a slow-growing penile tumour. Macroscopically, the lesion had 6x5,6x4,1 cm, with an exoendophytic growth, involving the glans and extending into the distal third of the shaft, without foreskin involvement; the exophytic component comprised two verrucous lesions in the skin. The tumour was mobile relatively to the surrounding tissues.
Results: The morphology showed a well-differentiated carcinoma with prominent acanthosis and keratinization with a sinus-like endophytic burrowing growth pattern. The tumour was well-delimitated with pushing borders accompanied by a chronic inflammatory infiltrate. The glans and corpus spongiosum were infiltrated but the corpora cavernosa were spared and completely compressed; it was not possible to evaluate urethral invasion at the tumour site although it appeared tumour-free at the surgical margin. Fistulisation to the skin was observed which translated into two verrucous lesions at the outer penile surface. Immunohistochemical staining for p16 was negative. Considering these morphologic characteristics, particularly its unique endophytic growth pattern, the diagnosis of penile carcinoma cuniculatum was established.
Conclusion: We present this case of carcinoma cuniculatum given the rarity of this entity in this location, with only 9 cases reported in literature to date. Its recognition is important given its excellent prognosis due to its usual absence of vascular and perineural invasion and regional metastasis, as was the case with our patient.

E-PS-22-005
Rare case; desmoid fibromatosis in the spermatic cord
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Background & objectives: Desmoid fibromatosis(DF) is a monoclonal, locally aggressive lesion with infiltrative growth and categorized as a non-metastatic, fibroblastic/myofibroblastic neoplasm. The tumour is most commonly located in the extremity, followed by the abdominal wall, retroperitoneum, and chest wall. Spermatic cord-located DF in literature is extremely rare.
Methods: 28-year-old male patient presented with complaint of left scrotal swelling for 1.5 years. On physical examination, two firm, interconnected nodules associated with left epididymis were observed. Imaging methods revealed scrotal hernia and nodular mass lesions. Largest was 5cm in diameter and orchiectomy was planned. Gross examination of orchiectomy revealed two interconnected nodular lesions, reaching 8x5.5x5cm in total size, associated with spermatic cord.
Results: The cross-sectional surface of the nodules was solid, cream-white in colour. Long fascicular proliferation of spindle cells with bland nuclei and eosinophilic cytoplasm were observed in hematoxylin and eosin sections of samples taken from the lesion. In some of the samples, there were rough hyalinized collagenization areas between spindle cells. Tumour cells showed immunohistochemically negative reactions with CD34, S100 and desmin, and positive reaction with SMA and beta catenin. The mutation c.121A>G (p.Thr41Ala) was detected in the CTNNB1 gene (NM_001904.4) after bioinformatic analysis with the new generation sequence method. Our case was diagnosed with desmoid fibromatosis located in the spermatic cord. No recurrence was observed in the 2-year clinical follow-up of the case.
Conclusion: Desmoid fibromatosis is a rare locally aggressive tumour. Spermatic cord-located DF has been reported in only a few case reports in literature. Here, a spermatic cord DF case is presented with its clinical, radiological, histopathological and genetic features due to it's extremely rare localization.

E-PS-22-006

Relevance intraoperative diagnosis of fibrous pseudotumour paratesticular: challenge for sparing testis

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Background & objectives: Paratesticular fibrous pseudotumours are rare pathologies with quite wide and variable topographic-morphological features. It is difficult to distinguish from malignant masses. Treatment can be done by resection of the mass subject to a diagnosis of histological proof.
Methods: A 34-year-old man presented with a painless palpable mass in the right scrotum. Scrotal ultrasound revealed a normal testicle and hyperechoic lesion adjacent to the right testis. The levels of testicular tumour markers were normal. We planned tumour biopsy combined with intraoperative rapid diagnosis.
Results: Scrotal incision was performed to explore the scrotum, and paratesticular white lobular mass is observed at the tunica vaginalis. The maximum size was approximately 35 mm. Frozen section assessment was performed, and intraoperative rapid diagnosis suggested a fibrous pseudotumor without malignancy. We excised the paratesticular white mass and successfully performed testicular-sparing surgery. Pathological findings revealed the proliferation of typical fibroblasts that were distributed in multidirectional bundles of dissociated collagen fibres. Lymphocyte infiltration including immunoglobulin G4 positive plasma cells was observed.
Conclusion: If a scrotal tumour is detected in patients with normal tumour markers, and its relation with the testis cannot be determined, these patients might have a fibrous pseudotumour, using frozen section analysis during surgery, an organ-sparing strategy can be pursued in these patients.

E-PS-22-007

Para-testicular genital-type rhabdomyoma: a case report

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Background & objectives: Extracardiac rhabdomyomas are relatively rare benign tumours of striated muscles that can be classified into foetal, adult and genital types. Genital rhabdomyomas usually occur in middle-aged women and have rarely been reported in males in para-testicular region.
Methods: We present a case of a 39-year-old male, with right sided painless scrotal swelling, gradually increasing in size during the past 3 years. Serum markers were within normal limits. Ultrasonography and MRI revealed a well-defined oval mass, measured 25x20 mm, superior to the right testis inseparable from the epididymis. Conservative excision was done and intraoperative frozen section examination was performed.
Results: Grossly, the mass was well-circumscribed, measuring 3x2x2 cm with a homogenous white solid cut section. Frozen section diagnosis coincided with a benign neoplasm (adenomatoid tumour versus rhabdomyoma). Formalin-fixed paraffin-embedded H&E stained sections revealed a neoplastic growth made up of haphazardly arranged large rhabdoid cells and strap-like cells in a collagenous stroma with occasional lymphoplasmacytic aggregates. The tumour cells had abundant eosinophilic cytoplasm with uniform eccentric rounded vesicular nuclei and binucleate forms. There was no evidence of atypia or necrosis, and the mitotic activity was insignificant. Immunohistochemically, the tumour cells showed diffuse strong positive reaction for desmin, however calretinin, S100 and CK were negative. Ki-67 proliferation index was less than 1%.
Conclusion: Although, genital type rhabdomyomas are quite rare in males, yet they should be considered in the differential diagnosis of masses in paratesticular region. The accurate interpretation of intraoperative frozen sections helps to formulate the proper management decisions and prevents unnecessary radical orchiectomy. Wide local excision of rhabdomyoma remains the treatment of choice, owing to their benign biologic behaviour and low recurrence rate.

E-PS-22-008

Primary osteosarcoma of the urinary bladder metastatic to lung: a case report

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Background & objectives: Extra-skeletal osteosarcoma (ESOS) is a rare malignant neoplasm that represents less than 2% of all soft tissue sarcomas. ESOS arising primarily in parenchymatous organs is extremely uncommon, with the involvement of the urinary bladder is even rarer.
Methods: A 48-year-old male patient, who presented to oncology clinic, complained of haematuria. Ultrasonography and computed tomography (CT) revealed a urinary bladder large polypoid soft tissue mass with extravesical extension, had peripheral rod like macro-calcifications. A transurethral biopsy was performed and was sent to our pathology lab.
Results: Microscopically, the fragments were focally ulcerated, infiltrated by sheets of non-cohesive malignant epithelioid cells exhibited marked pleomorphic hyperchromatic nuclei with bizarre multinucleated forms. Mitotic activity was plentiful. The tumour cells were embedded in an eosinophilic osteoid matrix with focal calcification. Immunohistochemically, the tumour cells were diffusely positive for vimentin and SATB-2, while were negative for CK. The lack of urothelial carcinoma component had qualified the diagnosis of primary osteosarcoma. The patient received one cycle of Cisplatin 60 mg/m2 - Adriamycin 60 mg/m2 cycles. Follow up CT chest after one-month revealed bilateral pulmonary nodules some of them were calcified, likely metastatic. The patient then lost to follow up two-months after diagnosis.
Conclusion: Primary urinary bladder sarcomas are uncommon and represents less than 1 % of all urinary bladder malignancies, and osteosarcomas in particular are exceedingly rare. The main differential diagnosis is carcinosarcoma and urothelial carcinomas with osseous metaplasia. However, the distinction from carcinosarcoma does not have major therapeutic implications, as both require aggressive therapy, yet the distinction from low-grade urothelial carcinoma with osseous metaplasia is important.

E-PS-22-009

Epithelioid angiosarcoma of the urinary bladder - a case report

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Background & objectives: Primary angiosarcoma of the bladder is rare. The epithelioid variant of angiosarcoma is characterized by malignant endothelial cells with epithelioid appearance. We present a case of primary bladder epithelioid angiosarcoma in a patient with history of irradiation for rectal adenocarcinoma.
Methods: A 70-yr-old man presented with haematuria. Ten years earlier, he was diagnosed with colorectal adenocarcinoma and treated with surgery and radiation. Cystoscopy at an outside hospital revealed solid bladder mass. Transurethral resection was performed, and the case was diagnosed as muscle-invasive high-grade urothelial carcinoma. The patient decided to continue treatment at our institution, which included neoadjuvant chemotherapy and radical cystectomy.
Results: On gross examination, there was an ulcerated red-brown haemorrhagic mass in the anterior bladder wall measuring 3cm. Microscopic examination showed high-grade solid tumour with extensive haemorrhagic background composed of large atypical epithelioid cells with abundant eosinophilic cytoplasm, large hyperchromatic nuclei and prominent nucleoli. Occasional intracytoplasmic vacuoles were also seen. Immunohistochemically, the tumour cells were positive for CD31,

Factor-VIII-related-antigen and ERG. Cytokeratin was focally positive. GATA3, P63, CK7, S100, CD34 and LCA were all negative. These findings confirm the diagnosis of primary epithelioid angiosarcoma of the urinary bladder.
Conclusion: Primary angiosarcoma of the urinary bladder is rare. The epithelioid variant of angiosarcoma might be misdiagnosed as high-grade urothelial carcinoma, especially because of positive immunohistochemical staining for cytokeratin.

E-PS-22-010
Sarcomatoid carcinoma of the urinary bladder with heterologous element of rhabdomyosarcoma – a case report
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Background & objectives: Sarcomatoid urothelial carcinoma is a malignant tumour that exhibits morphologic or immunohistochemical evidence of both epithelial and mesenchymal differentiation. Heterologous elements may be present. We present a case of sarcomatoid carcinoma of the bladder with heterologous component of rhabdomyosarcoma.
Methods: A 74-yr-old woman presented with macrohematuria. Cystoscopy revealed a 5cm solid partially necrotic mass in the posterior bladder wall. Transurethral resection of the mass was performed.
Results: Microscopic examination showed malignant tumour with biphasic pattern consisting of sarcomatoid component admixed with carcinomatous areas. The sarcoma displayed atypical spindle cells and areas composed of round blue cells. Rhabdomyoblastic differentiation characterized by cells with eccentric nuclei and abundant eosinophilic cytoplasm was seen in these areas. The carcinomatous areas composed of epithelial atypical cells with large hyperchromatic nuclei and eosinophilic cytoplasm. Immunohistochemical stains for Pancytokeratin, CK7, P63, EMA and GATA3 were focally positive in these areas, consistent with invasive high-grade urothelial carcinoma. In the sarcomatous component, vimentin was positive, and GATA3 was focally positive. The heterologous component of rhabdomyosarcoma was confirmed by positive immunohistochemical staining for MyoD1, MYF4 and desmin.
Conclusion: Although rare, sarcomatoid carcinoma is more common than primary bladder sarcoma. Pathologists should be aware of this entity, and to the fact that heterologous elements in the form of rhabdomyosarcoma or other sarcomas may be present in these tumours.

E-PS-22-011
Ipsilateral renal agenesis accompanying cystic dysplasia of the rete testis in a young adult: a case report
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Background & objectives: A 31-year-old man was referred from an outside (external) institution to the department of urology under the suspicion of a testicular tumour, with left-sided testicular pain lasting a couple of months in duration.
Methods: Physical examination showed a hard, thickened and small left testis on palpation. The left testicle showed a diffuse, inhomogeneous ultrasonographic appearance. After urologic examination a left-sided inguinal orchidectomy was performed. The testis and epididymis with funiculus were sent to pathology.
Results: On gross examination, a cystic cavity filled with brown fluid content and surrounding brownish parenchyma measuring up to 3.5 cm in diameter was found. Histologic examination showed cystically dilated rete testis lined with cuboidal epithelium with a positive immunohistochemical reaction to cytokeratins. The cystic cavity was microscopically a pseudocyst filled with extravasated erythrocytes and abundant clusters of siderophages. The siderophages extended into the testicular parenchyma, surrounding the seminiferous tubules and spreading out around ducts of the epididymis, which were also cystically dilated with siderophages inside their lumina.
Conclusion: On the basis of clinical data, histological and immunohistochemical analysis, a diagnosis of cystic dysplasia of the rete testis was established. According to the literature there is a very well-known association between cystic dysplasia of rete testis and ipsilateral genitourinary anomalies. The patient was referred to the department of radiology and a multi-slice computed tomography scan revealed ipsilateral renal agenesis, right seminal vesicle cyst reaching up to the iliac arteries and a multicystic formation cranial to the prostate.

E-PS-22-012
Concurrence of bladder lymphoma and urothelial carcinoma. A case report
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Background & objectives: Bladder cancer accounts for 3% of global cancer diagnosis. Bladder lymphomas are extremely rare, accounting for 0.2% of primary neoplasms. We present a case of concurrence of Non-Hogkin B-cell lymphoma and urothelial carcinoma in a bladder tumour.
Methods: A 75-year-old male was admitted for haematuria investigation. Cystoscopy revealed a large papillary mass and a transurethral resection of the bladder tumour was performed. The patient mentioned a history of non-Hodgkin lymphoma without providing further details about the histological type.
Results: Histopathologic examination of the specimens revealed a superficial high-grade urothelial carcinoma with papillary and solid architecture. In the subepithelial connective tissue, infiltration of a malignant lymphoma with follicular and diffuse growth pattern was found. The lymphoid population consisted of small, atypical cells with clear cytoplasm and mild mitotic activity. Immunohistochemical staining was positive for: CD20, PAX5, BCL2, CD5, CD38 and negative for: CD3, CD5, CD10, CD23, BCL6, SOX11, ZAP70, regarding the lymphoid malignant cells. The results set the diagnosis of a Marginal zone B-cell lymphoma (MZBCL). The urothelial cancer cells were positive for CKAE1AE3 and GATA3.
Conclusion: Most common bladder lymphomas are Marginal zone B-cell lymphomas, followed by Diffuse large B-cell lymphomas. This is the second case of concurrence of bladder lymphoma and urothelial carcinoma reviewed in the literature. In both cases the lymphoid malignant component was a MZBCL.

E-PS-22-013
Acquired cystic disease–associated renal cell carcinoma in acquired solitary kidney from unilateral nephrectomy
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Background & objectives: Acquired cystic disease–associated renal cell carcinoma (ACD-RCC) is the main type of malignancy in patients with end-stage renal disease (ESRD). We present a case of ACD-RCC in a patient with acquired solitary kidney and a long history of haemodialysis.
Methods: A 57-year-old male patient with ESRD and ACD due to long term haemodialysis (since 1996) as result of nephrectomy performed in 1991 for nephrolithiasis complicated with pyonephrosis, was diagnosed with a tumour mass developed in a large renal cyst. The patient presented to the Urology Department for surgery. The nephrectomy specimen was processed for standard histological and immunohistochemical analysis.
Results: Macroscopically, the parenchyma was atrophied, with numerous variably sized cysts. A circumscribed tumour measuring 4.6 cm in diameter was identified at the lower pole of the kidney, filling a large cystic

space. The histological examination revealed an intracystic tumour proliferation with cribriform, solid, papillary and tubulocystic architecture; the cells had abundant eosinophilic cytoplasm and pleomorphic nuclei (WHO/ISUP 3); polarizable calcium oxalate crystals were found within the tumour structure. The remaining parenchyma showed ESRD-specific lesions and multiple cysts commonly lined by normal epithelium, focally with stratified atypical epithelium and small papillae. The tumour was positive for AMACR and focally for CK7.
Conclusion: The final diagnosis was acquired cystic disease-associated renal cell carcinoma. The key element of this case consists in the development of a tumour mass within an acquired solitary kidney due to unilateral nephrectomy. Neoplasms are often incidental findings in patients with long-term haemodialysis and subsequently acquired cystic disease. These patients have an increased risk of developing renal carcinoma; therefore, an active monitoring is necessary.

E-PS-22-014
Undifferentiated carcinoma of the urinary bladder with osteoclast-like giant cells. A diagnostic challenge
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Background & objectives: Undifferentiated carcinoma of the urinary bladder with osteoclast-like giant cells (UCOGC) is a rare urothelial carcinoma variant with few reported cases in the literature. We herewith present a case of UCOGC.
Methods: A 77-year-old female was admitted to our hospital due to hypogastric pain. Cystoscopy with transurethral resection of bladder tumour was performed. After a diagnosis of poorly differentiated urothelial carcinoma with invasion of muscularis propria, a radical cystectomy was performed. On gross examination of the urinary bladder, a 2.5 cm large tumour in the right lateral bladder wall was found.
Results: On microscopic examination, the tumour consisted of mononuclear cells with several interspersed multinucleated giant cells. The mononuclear cells were characterized by round- to oval shaped highly pleomorphic nuclei with vesicular chromatin and prominent nucleoli. Up to 16 mitoses/10 HPF were found. The osteoclast-like giant cells had multiple, round to oval, bland appearing nuclei and eosinophilic cytoplasm. Numerous areas of necrosis and haemorrhage were also found. Mononuclear cells were stained for CKAE1/AE3, CK7(focally), CK5/6, P63 and P53. Multinucleated giant cells were stained for CD68, while epithelial markers were negative. Both components were negative for GATA3. Our diagnosis was UCOGC based on the above findings.
Conclusion: The differential diagnosis of UCOGC includes other high-grade tumours with giant cells [sarcomatoid urothelial carcinoma, pleomorphic giant cell carcinoma (PGCC) of the bladder and PGCC of the prostate]. UCOGC usually presents at an advanced stage and its prognosis is very poor.

E-PS-22-015
SDH-deficient renal cell carcinoma: a case report associated with a novel germline mutation
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Background & objectives: Succinate dehydrogenase (SDH)-deficient renal cell carcinomas (RCCs), account only for 0.05 to 0.2% of all renal carcinomas, with limited studies due to their rarity. Here we report a new case of SDH-deficient RCC.
Methods: Routine examination of an asymptomatic 40-year-old female patient revealed a right unilateral and unifocal renal mass. The patient underwent a partial nephrectomy, and the renal specimen was sent for histopathologic examination.
Results: The tumour was characterized by a solid growth pattern and consisted of eosinophilic cells with cytoplasmic vacuoles and flocculent quality. Immunohistochemically the tumour was negative for SDHB determining the diagnosis of SDH-deficient RCC. Molecular testing revealed a heterozygous variant NM_003000.3:c.412G>T, p.(Asp138Tyr), in SDHB gene, that has not, so far, been associated with another SDH deficient renal cell carcinoma. 12 months following tumour resection, the patient did not show any signs of regression or metastasis.
Conclusion: We report this case to draw attention to this entity and notice that eosinophilic RCCs should be examined thoroughly for SDH- deficiency because of its highly syndromic nature.

E-PS-22-016
Mast cells of the bladder with intestinal cystitis
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Background & objectives: Interstitial cystitis is common in older men with prostate adenoma. With interstitial cystitis, an increase in the number of functionally active mast cells, is observed. It is possible that mast cells may serve as cell markers of this disease.
Methods: The study was carried out on 30 male rats. Experimental animals were injected into the bladder cavity with protamine sulfate (1st group); into the wall of the bladder with 0.9% NaCl solution (group 2). The 3rd group of animals was intact.
Results: On histological sections after 21 days, an increase in the number of leukocytes in the tissues of the urinary bladder wall of animals of the 1st group compared with the groups 2 and 3 ($p < 0.05$) was revealed. In animals of the 1st group, inflammatory infiltration of the bladder wall with lymphocytes and neutrophils was noted. In the sections of the bladder wall of the animals of the 2nd group, oedema, single lymphocytes and neutrophils were revealed. Mast cells were detected in sections of the bladder wall of groups 1 and 2, but in group 2 their number was 14 times higher than in group 1 ($p < 0.05$).
Conclusion: Mast cells are local regulators of homeostasis, secreting inflammatory mediators and neurotransmitters. Perhaps their participation in the mechanisms of inflammatory processes in interstitial cystitis.

E-PS-22-017
Extensive intestinal metaplasia of renal pelvis: a rare case report
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Background & objectives: Intestinal metaplasia of the urothelium in the pelvis is a rare finding. Only a few cases have been reported in the literature worldwide.
Methods: We report a case of a 89 year-old woman, who came to the ER department, complaining for pain in the right side of the back. X-rays revealed nephrolithiasis. Right nephrectomy was performed.
Results: Macroscopically, the kidney weighed 321gr. and measured 15X8X6,6cm. The pelvis was dilated, filled with pus. Two large calculi 2,5 and 1,2 cm were also found in the kidney's calyxes.
The histological examination revealed features of acute pyelonephritis and necrosis, atrophy and thyroidisation of the renal tubules, lymphoplasmacytic cell infiltration, fibrosis and extensive intestinal metaplasia of the transitional epithelium of the pelvis. Immunohistochemistry study showed CK20 expression in the goblet cells, CK7 positivity in the residual transitional epithelium and low ki67 index.
Conclusion: Despite the fact that the specific histological findings were benign, intestinal metaplasia is usually a high-risk factor for cancer in similar cases.

E-PS-22-018

Hydrocele in a young patient with an unexpected histopathological diagnosis: epithelioid mesothelioma of the tunica vaginalis testis

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Background & objectives: Malignant mesothelioma of the tunica vaginalis testis is an extremely rare tumour of the paratesticular region, representing <5% of all mesotheliomas.
Methods: We present a case of a 34 years old male, who was admitted to the Urologic Department with painless tumefaction of the left scrotum, without any history of scrotal trauma or asbestos exposure. The clinical signs were suggestive for hydrocele and a hydrocelectomy was performed. The intraoperatory findings revealed a diffuse thickening of the tunica vaginalis which was surgically removed.
Results: The tunica vaginalis was infiltrated by an epithelial neoplasm with tubular and papillary architecture, lined by unistratified cuboidal cells with eosinophilic cytoplasm, slightly pleomorphic nuclei and rare mitotic figures. The peritumoral stroma was desmoplastic. The tumour cells expressed Calretinin, WT-1 and EMA, the Ki-67 proliferative index was <2%. The diagnosis of malignant epithelioid mesothelioma was made. The patient underwent to a CT-scan and a diffuse thickening of the left paratesticular region was described, without any evidence for abdominal or thoracic spread of the disease. An inghinal left orchiectomy was performed and the tumour has infiltrated the tunica vaginalis and albugineea, without invasion of the testicular parenchyma, epididimis or spermatic cord.
Conclusion: The clinical diagnosis of mesothelioma can be very challenging due to its rarity. Majority of the cases are diagnosed incidentally. Testicular mesotheliomas tends to appear in older patients, with a mean age of 60 years. Hydrocele is the most common clinical sign that can be associated with painful scrotal masses. The aetiology remains still unclear: asbestos exposure, scrotal trauma and long lasting hydrocele has been reported as possible risk factors.

E-PS-22-019

Rare malacoplakia of the prostate: presentation with three cases

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Background & objectives: Malakoplakia is rare type of inflammatory reaction that usually results from Escherichia coli infection of the genitourinary tract. İt is emphasised that recognition of prostatic malakoplakia as an entity will prevent its confusion with prostatic carcinoma.
Methods: The 63-58-73 years old men presented with a history of increasing difficulty of urination, frequency, and nocturia for several years. E. coli was the causative microorganism in only one of the case urine culture. No microorganism growth was observed in urine culture in the other two cases. Them had firm and nodular prostates in his digital rectal examination.
Results: Case 1 - Prostatectomy was performed and a prostatic mass weighing 20 g was submitted for histological examination. Histologically collections of clear foamy histiocytes (Von Hansemann), lymphocytes, plasmocytse were seen nearby the acinar adenocarcinoma component.
Case 2 - TUR-P materials were evaluated with hematoxylin eosin stains and under light microscopy. Final pathological diagnosis was malakoplakia for prostate specimens.
Case 3 - Transrectal ultrasonography by prostate size was measured 42 cc and the prostate parenchyma was heterogeneous. Prostate tru-cut biopsy specimens were evaluated with hematoxylin eosin stains and under light microscopy. The staining reactions of these were similar to those of case 1and 2 with light microscopic findings, PAS reactions and positive Prussian blue reaction.
Conclusion: We defined malacoplakia as adjacent to a prostate tumour in one of our cases and as a solitary lesion in the other two cases. E. coli was detected in the urine culture of only one of every three cases. We wanted to share with the literature that malacoplakia can mimic carcinoma with its clinical findings and it is a rare entity that should be kept in mind in both TUR-P and prostate core biopsies.

E-PS-22-020

Poorly differentiated prostatic adenocarcinoma of basal cell/adenoid cystic type

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Background & objectives: Basal cell/adenoid cystic adenocarcinoma is an exceptionally rare prostatic malignancy with distinctive histopathological and biological features and behaviour varying from indolent to extremely aggressive. We present a case of poorly differentiated, aggressive, basal cell/adenoid cystic prostatic adenocarcinoma with fulminant progression.
Methods: A 65-year-old male was admitted to our hospital with elevated serum PSA (29ng/ml). Imaging tests showed a prostatic tumour infiltrating the urinary bladder and rectum, a left kidney solid mass, involvement of abdominal lymph nodes, liver and bone secondary lesions. Biopsy of the prostatic tumour was performed. The patient deteriorated rapidly and succumbed 20 days after his arrival.
Results: Histopathologic examination revealed a malignant neoplasm composed of small to medium sized cells with distinctive eosinophilic nucleoli and high mitotic count, arranged in solid nests with focal adenoid formations. Immunohistochemically the neoplastic cells were positive for CK903, AR and bcl-2, focally positive for PSAP and p63 (few cells), and weakly positive (few cells) for Chromogranin-A and CDX-2. PSA, AMACR, Synaptophysin and CD56 were negative. Ki-67 was 80%, c-kit was expressed in 80% of tumour cells and HER-2 was negative (CISH method). The morphological and immunohistochemical findings were compatible with a poorly differentiated prostatic adenocarcinoma of basal cell/adenoid cystic type.
Conclusion: Basal cell/adenoid cystic prostatic adenocarcinoma is an extremely rare neoplasm with poor prognosis for advanced and metastatic cases. The management strategy for those cases isn't well defined yet. Although current literature considers this as an indolent neoplasm with relatively low metastatic potential our case not only stands against it but also poses plausible diagnostic dilemmas. It's a malignancy that shouldn't be disregarded at the differential diagnosis considering its unique clinical and biological features, treatment implications and potentially lethal prognosis.

E-PS-22-021

Feasibility of using 34betaE 12, D2-40, and AE1/AE3 cytokeratins in P504S-positive ASAP and prostate adenocarcinomas

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Background & objectives: It is necessary to clarify which markers are more effective for identification of the basal epithelium in the diagnosis of precancerous processes and prostate carcinoma. Pancytokeratin AE1/AE3 is a promising marker for stratification of patients by risk groups.
Methods: We used prostate biopsy samples obtained from 90 patients, which were divided into 6 groups according to the morphological diagnosis: ASAP and the carcinomas of Grade Groups 1-5. Normal prostate tissue samples served as controls. We performed an immunohistochemical staining method using 34betaE12, D2-40, AE1/AE3, and P504S antibodies. We applied non-parametric statistical methods.

Results: In the control group, the 34betaE12 expression [Me = 13% (3-36)] was noted in 100% of cases. In ASAP and Grade Group 1-5 adenocarcinomas, there was a complete absence of 34betaE12 in all cases. The level of D2-40 expression in the basal epithelial cells was found only in the control samples (Me = 37.5% [14-47]). In ASAP (P504S+ phenotype) and Grade Group 1-5 adenocarcinomas, D2-40 was not expressed. The highest and most intense expression of AE1/AE3 was observed in Grade Group 2 adenocarcinoma (3 points) [Me = 67% (61-69)]. The lowest level of pancytokeratin AE1/AE3 expression was in Grade Group 5 adenocarcinoma ($p < 0.0001$).
Conclusion: D2-40 and 34betaE12 markers can be interchangeable in the diagnosis of adenocarcinoma. Taking into account the "dose-dependent" effect of the AE1 / AE3 marker may help to stratify patients by risk groups.

E-PS-22-022
Cystic trophoblastic tumour: a rare case presenting as post-chemotherapy mediastinal tumour
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Background & objectives: Cystic trophoblastic tumour (CTT) is an uncommon germ cell tumour that is usually seen as residual disease in post-chemotherapy retroperitoneal lymph node dissection (RPLND) in patients with testicular germ cell tumour; however, they may also occur in the untreated testis.
Methods: Our case is a 21-year-old male patient diagnosed with mixed germ cell tumour (embryonal carcinoma 80%, teratoma 20%) after left orchiectomy. In the follow-up of the patient who received chemotherapy after orchiectomy, there was a mild serum ß-hCG elevation (11 mIU/mL) and multiple masses in the mediastinum were detected on thorax CT imaging. Three of these masses were resected.
Results: Macroscopically, the largest of the tumours was 11 cm in diameter and all had a similar appearance. The cut surfaces are heterogeneous with solid and cystic areas. Solid areas were predominantly composed of cartilage. Histopathology of resection specimens demonstrated pure teratoma. However, in the examination of the largest tumour, a cystic space lined with non-epithelial cells and filled with eosinophilic fibrinoid material was noted. The cyst was lined by varying thickness of mostly mononucleated degenerative-looking trophoblastic cells with abundant eosinophilic cytoplasm and smudged nuclei. Some of the cells had intracytoplasmic lacunae. Immunohistochemically, these cells were nuclear positive with p63 and GATA3 and negative with SALL4, human placental lactogen and hCG.
Conclusion: CTT is a relatively new and uncommon entity. After chemotherapy, CTT does not show the high frequency of progressive disease and it does not warrant additional chemotherapy, although it is important to continue to carefully monitor these patients on follow-up. The distinction between CTT and choriocarcinoma is very important as it has important implications for patient management and prognosis. Unlike CTT, patients with residual choriocarcinoma after chemotherapy have a poor prognosis and aggressive treatment is warranted.

E-PS-22-023
Perirenal metastasis of melanoma: a rare case report
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Background & objectives: Melanoma metastases cause the vast majority of morbidity and mortality associated with this disease. Melanomas are capable of metastasizing to both regional and distant sites. The most common clinically apparent sites of distant metastases are lung, skin, liver and bone.
Methods: A 45-year-old Tunisian woman, with a history of melanoma of the thigh treated surgically, consulted for lumbago. Imaging revealed a mass of the left renal compartment measuring 20 cm taking the kidney and the adrenal gland and suggesting a primary tumour or a metastasis.
Results: During the surgery, six biopsies were taken and sent to our Pathology Department for frozen section examination, which concluded to a malignant proliferation. The surgeon found that the mass was too close to vascular structures and judged that the mass was inextirpable. Other biopsies were realized. After formalin fixation and paraffin embedding, the histopathological examination confirmed the malignant proliferation. The tumour cells were highly atypical. They had large oval or pleomorphic hyperchromatic nuclei, eosinophilic cytoplasm and some distinct nucleoli. Many mitotic figures and melanin pigments were present. On immunohistochemistry, the tumour cells were HMB-45 and Melan-A positive. The mass was diagnosed as a metastasis of melanoma to the renal compartment.
Conclusion: Although malignant melanoma is known to metastasize to all organs, it is almost impossible to predict which localization will be invaded from a given primary site. Clinical diagnosis of metastatic melanoma in the kidney, ureter, prostate, and other parts of the genitourinary tract is still difficult. Consequently, the diagnosis of metastatic melanoma remains based on microscopy and immunohistochemistry findings.

E-PS-22-024
Sarcomatoid carcinoma of the prostate with chondrosarcomatous differentiation: a rare case presenting as lower urinary tract symptoms
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Background & objectives: Sarcomatoid carcinoma of the prostate is an uncommon diagnosis. They portend aggressive behaviour and a dismal prognosis.
Methods: We report a rare case of sarcomatoid carcinoma of the prostate with chondrosarcomatous differentiation which presented with a history of lower urinary tract symptoms and unusual radiological findings
Results: A 65-year-old man presented with dysuria and hesitancy. Serum PSA level was 8.77 ng/mL. MRI revealed a large heterogeneous mass involving the entire prostate seen extending up to the right lateral pelvic wall. On PET-CECT, foci of uptake were seen in the prostate and multiple enlarged right external iliac lymph nodes. Histomorphology confirmed a biphasic epithelial and mesenchymal malignancy with prostatic adenocarcinoma component of Gleason pattern 4 and the sarcomatous component composed of chondrosarcomatous and undifferentiated spindle cell sarcoma. The adenocarcinoma component was positive for AE1/AE3, PSA, NKX3.1, AR and HMWCK (focal), while are negative for GATA3, p63, p40 immunostains The sarcomatous component was negative for PSA, NKX3.1, GATA3.
Conclusion: Sarcomatoid carcinoma of the prostate is an aggressive variant of prostate cancer. It may present as locally advanced prostate cancer. Chondrosarcomatous dedifferentiation is extremely rare in prostate carcinoma.

E-PS-22-025
A rare case of paratesticular mesothelioma successfully treated by surgery and adjuvant chemotherapy
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Background & objectives: Mesothelioma is a malignant neoplasm that arises most commonly from body cavities such as pleura, peritoneum and pericardium. Its occurrence in the paratesticular region is an extremely rare event.

Methods: We describe a case of a 31-year-old male patient, smoker, who presented with left hydrocele that gradually increased in size for 8 months duration. Imaging studies revealed a paratesticular mass. Surgical resection of the mass and histopathologic examination along with appropriate panel of immunohistochemical stains were performed.
Results: Magnetic resonance imaging (MRI) revealed a well-defined tunica-based soft tissue mass measuring 4 cm with another smaller nodule on left scrotal sac measuring 0.9 cm. Radial orchiectomy was performed. Histopathologic examination revealed two foci of tumour, both are composed of solid sheets of epithelioid tumour cells that are diffusely immunoreactive for WT1, calretinin, D2-40, but negative for Ber-Ep4, CEA and CD15. The diagnosis of multifocal epithelioid mesothelioma was rendered. There was no previous history of asbestos exposure. The patient received 6 cycles of cisplatin and pemetrexed. He was followed up by imaging studies for 1 year, which revealed no evidence of local recurrence or distant metastasis.
Conclusion: Paratesticular mesotheliomas are rare. Only 30-40% of cases have previous history of asbestos exposure. Although unusual, mesothelioma should be considered in patients presenting with hydrocele of unknown aetiology, so they can get utmost benefit of early diagnosis and treatment.

E-PS-22-026

Primary neuroendocrine carcinoma of the testis with a Merkel cell carcinoma-like immunophenotype: does primary testicular Merkel cell carcinoma exist?

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Background & objectives: Testicular neuroendocrine neoplasms (NENs), which account for less than 1% of testicular tumours, can be divided into three categories: pure well-differentiated neuroendocrine tumours (NETs), well-differentiated NETs associated with teratoma elements, and secondary NENs, including rare Merkel cell carcinoma (MCC) metastases.
Methods: An 80-year-old man, without a NEN history, underwent radical orchifunicolectomy for a painless left testicular mass. On gross examination, the testis was partially replaced by a nodular, yellow-tan, unevenly capsulated mass, measuring 2.5x2x1 cm. Both testis and tumour mass were entirely submitted. No clinical or imaging evidence of synchronous neoplastic lesions was found.
Results: The neoplasm was confined to the testicular parenchyma and was composed of small, highly atypical cells with a high nuclear/cytoplasmic ratio and hyperchromatic nuclei, arranged in irregular solid islands and sheets. Stromal desmoplasia, necrosis and mitotic figures (>50/10HPF) were present; no teratomatous or non-neuroendocrine neoplastic (either seminomatous or non-seminomatous) components were identified. Neoplastic cells showed diffuse positivity for pan-cytokeratin, synaptophysin, CD56, Special AT-rich sequence-binding protein 2 (SATB2), and dot-like reactivity for cytokeratin 20, while stains for CD45, TTF1, and chromogranin-A were negative. Ki-67 proliferative index was 70%. The diagnosis of poorly differentiated neuroendocrine carcinoma (NEC) was made, with an immunophenotype resembling that of an MCC.
Conclusion: We here reported a unique case of a patient with a primary NEC of the testis with MCC-like immunophenotype, who is still alive 15 months after surgery. Although most of testicular NENs are primary well-differentiated NETs or secondary NECs, the exceptionally rare possibility of a primary NEC of the testis should also be considered.

E-PS-22-028

Rare presentation of a common childhood tumour: Wilms' tumour in an adult patient

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Background & objectives: Wilms' tumour (WT) is one of the most common malignant tumours of childhood. However, WT in adults is rare, about 3% of all described WT cases. There are diagnostic and therapeutic difficulties because there are no specific radiographic findings.
Methods: We report a 38-year-old female presenting with flank pain. CT examination revealed a solid mass measuring 9 cms, originates from the right kidney with several thoracal metastatic lesions. A clinical diagnosis of renal cell carcinoma was made, and radical nephrectomy was performed.
Results: Tumour was majorly composed of small to medium sized undifferentiated cells with relatively small regular nuclei and small nucleoli with frequent mitotic figures. Also, there were focal areas consisting of spindle shaped cells and poorly differentiated epithelial-like areas. Immunohistochemical studies showed diffuse nuclear staining with WT-1, and focal positivity with PANCK. CD99, CK7, Synaptophysin was negative. FISH examination for the EWSR1 gene showed no signs of fusion. Based on the presence of focal epithelial and stromal components together with undifferentiated component and compatible ancillary studies, this tumour was classified as a WT with dominant blastemal component. The tumour was staged as stage II according to Children's Oncology Group (COG) Staging System.
Conclusion: WT in adults is extremely rare and has a poorer prognosis than paediatric WT. Histopathologically, there is no difference between adult and childhood WT. Due to the scarcity of cases in the literature, there are no standard protocols for the management of adult WT, and therefore, it is managed as paediatric WTs.

E-PS-22-029

A 30-year-old man with testicular embryonal carcinoma presenting as a neck mass: a case report

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Background & objectives: Testicular germ cell tumours often show overlapping morphologic features and can mimic one another and mimic non-germ cell tumours. Embryonal carcinoma is the second most common histological type of testicular tumour. We presented an unusual case of testicular embryonal carcinoma.
Methods: We reported a case of a 30-year-old male who presented with a 2-months history of a progressively enlarging neck mass. Clinical details, pathologic features, immunohistochemical profile were analysed.
Results: CT scan of the neck showed a left supraclavicular neck mass (8.9 x 7.4 cm). The first tissue core biopsy showed solid tumour that was consisted of large, epithelioid cells with indistinct cell borders, pale cytoplasm and pleomorphic nuclei. Tumour cells were positive with TTF1 and negative with thyroglobulin. CT scan of chest was normal. The second core biopsy showed two histological tumour patterns: solid and pseudoglandular with fibrous stroma. Tumour cells were positive with CK, SALL4, OCT3/4, CD30 (focally) and Glypican 3 (focally). The α-fetoprotein (1000 ng/ml) and human chorionic gonadotropin (274 U/l) were increased. Ultrasound of left testicle demonstrated a solitary calcified mass (8.0 x 9.0 mm).
Conclusion: A high index of suspicion allows diagnosing testicular embryonal carcinoma. The first clinical manifestation of embryonal carcinoma can be as a large neck mass without local symptoms in testis.

Testicular cancer should be strongly considered in the differential diagnosis of neck lymph node metastases, especially in case, when tumour cell of testicular n embryonal carcinoma are positive with TTF1.

E-PS-22-030

Prostatic adenocarcinoma with Paneth cell-like neuroendocrine differentiation

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Background & objectives: Variants of conventional prostatic acinar adenocarcinomas are uncommon, accounting for 5% to 10% of the cases. Prostatic adenocarcinoma with Paneth cell-like differentiation is a rare subtype of prostate adenocarcinoma that usually presents with patchy cells having prominent eosinophilic neuroendocrine granules.
Methods: We present a case of a 65-year-old man that on a follow-up urologic consultation was submitted to a MRI that showed a right apex PI-RADS 5 lesion and a left apex PI-RADS 4 lesion. Subsequently, a guided prostate needle biopsy was performed, and the histologic examination showed an acinar adenocarcinoma Gleason grade 7 (3+4).
Results: The patient was submitted to a radical prostatectomy, and we received a prostatectomy specimen weighing 90g and measuring 6x5x5 cm. The cut surface was heterogeneous with microcystic and compact areas. The seminal vesicles and ductus deferentes were unremarkable. The histologic examination showed a bilateral acinar adenocarcinoma Gleason grade 7 (4+3) with some of the acini composed of cells resembling Paneth cells that immunohistochemically expressed neuroendocrine markers such as synaptophysin and chromogranin. The neoplasia infiltrated the peri-prostatic soft tissues and perineural invasion was observed. The seminal vesicles and ductus deferentes were not involved by the adenocarcinoma.
Conclusion: Paneth-Cell-like differentiation in prostate cancer is characterized by tumour cells with eosinophilic cytoplasmic granules that are positive for neuroendocrine markers by immunohistochemistry. Unlike Paneth cells of the small intestine, these cells are negative for lysozyme and IgA and positive for neuroendocrine markers. It is advocated that the Paneth cell component of these tumours should not be graded because they have a favourable prognosis even if they have an architecture that would be assigned a Gleason pattern 5.

E-PS-22-031

Renal pelvis urothelial carcinoma and concomitant incidental chromophobe renal cell carcinoma, a case report from an Egyptian cancer centre

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Background & objectives: Simultaneous ipsilateral renal pelvis urothelial carcinoma (UC) and renal cell carcinoma (RCC) is extremely rare, with less than 100 reported cases in the English literature. Herein, we report a case of renal pelvis UC with an incidentally found chromophobe RCC.
Methods: A 64-year-old man presented to our hospital with right flank pain and haematuria. Patient is a heavy smoker. Computed tomography (CT) revealed enlarged right kidney with dilated pelvicalyceal system with markedly thinned-out renal parenchyma. The lower calyx showed an irregular soft tissue mass lesion 5x4.5x8 cm, infiltrating perirenal fat. Multiple enlarged perihilar and aorto-caval lymph nodes were also seen.
Results: Right radical nephrectomy was performed. The specimen showed dilated pelvi-calyceal system with papillary tumour, invading renal capsule and peri-nephric fat. Also, incidentally found, a fairly defined renal cortex mass 2x1 cm, golden yellow in cut section. Microscopic findings of the pelvic mass showed a high-grade papillary UC, positive for GATA3 and negative for PAX8. invading the muscularis propria, renal parenchyma, renal capsule and perirenal fat. The cortical mass revealed chromophobe RCC, positive for PAX8, negative for GATA3. All L.nodes were negative for metastases. Postoperatively, the patient received adjuvant chemotherapy (Gemcitabine-Carboplatin protocol) for 6 cycles. MDT decided a follow-up cystoscopy every three months. No complication, or disease progression over the follow-up period.
Conclusion: Concomitant UC and RCC in the same kidney is extremely rare, with no readily identifiable risk factors for this simultaneous occurrence, yet 24% of the reported cases were smokers. In our case, RCC was pathologic stage pT1a and the UC was pT3. Pathologists should be aware of the possibility of synchronous renal tumours, as they do rarely occur. Proper extensive sampling and the use of proper immunostaining panels are both required and helpful to identify the rare concomitant renal tumours.

E-PS-22-032

A rare case of aggressive basal cell carcinoma of the prostate with infiltration of the urinary bladder

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Background & objectives: Basal cell carcinoma of the prostate (BCCP) is extremely rare and accounts for 0.01% of all prostate cancers with only 99 reported cases in the literature. We report a rare case of a BCCP with infiltration of the urinary bladder.
Methods: We present the case of a 53-year-old man who complained of lower urinary tract symptoms for 2 years. His serum prostate-specific antigen (PSA) was within normal range. Due to the persistent symptoms and suspected palpation findings, cystoscopy with subsequent transurethral prostate resection was performed. Histopathology of the resected specimens suggested BCCP. Radical cystectomy with lymph node dissection was performed.
Results: Pathological examination revealed a small nest-like basaloid cell carcinoma. Both urinary bladder sidewalls were infiltrated with basaloid cells with large pleomorphic nuclei and scant cytoplasm, with peripheral palisading. Tumour cells were forming large solid nests with central necrosis and were infiltrating the muscular layer. Immunohistochemical examination revealed that tumour cells were positive for p63, bcl2, 34betaE12, Ki-67 (15-30%) whereas for cytokeratins 7, 20, uroplakin, p504s and TTF-1 negative. PSA and androgen receptor (AR) were, however, partially positive. The resection margins were negative and there were no metastases in 34 examined lymph nodes. The patient was free from recurrence 6 months after operation.
Conclusion: BCCP is a very uncommon disease, and the most common symptoms include nocturia, urgency and acute urinary retention. Serum PSA levels are usually within normal range and according to the guidelines a Gleason score should not be assigned. Treatment strategies are limited and include hormone therapy, radiotherapy, radical surgical resection, or a combination but with poor prognosis.

E-PS-22-034

Mucinous tubular and spindle cell carcinoma: case report

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Background & objectives: Mucinous tubular and spindle cell carcinoma (MTSCC) is a relatively rare renal cell carcinoma (RCC) that was defined in the 2004 WHO Classification and initially presents as low-grade RCC. To report the pathologic features of case of MTSCC of kidney.

Methods: Morphology study and immunohistochemistry of MTSCC of kidney was performed. Immunohistochemistry profile: RCC negative with focal expression in the tubular structures, CK7, EMA and AMACR high and moderate positive with prevalence in the tubular component without mucin, totally positive Vimentin and focally NSE, CD10 and CK20 negative, Ki-67 proliferative index 0,9-2,8%.
Results: A 62yo man consulted following tumour of the upper pole of the left kidney. Nephradrenalectomy with lymphadenectomy was subsequently performed. Histologically, the tumour was well circumscribed with rim of compressed fibrous tissue but had focal invasion in the renal sinus and no metastases. MTSCC showed prevalence tubular and cord-like growth component with solidification and focal myxoid stroma with abundant extracellular mucin. Tumour cells had uniform, bland, low grade morphology with eosinophilic, focally vacuolated cytoplasm. Numerous haemorrhages and focal foamy macrophages was observed, with no necrosis and no inflammation. Although adjuvant chemotherapy was no performed, the patient is still alive 6 years after nephrectomy without metastasis and recurrence of the tumour.
Conclusion: We report case of MTSCC of kidney pT3aN0 Grade 2 shares histologic and immunohistochemical overlap with papillary renal cell carcinoma (RCC negative with focal expression, CK7, EMA and AMACR high and moderate positive with prevalence in the tubular component without mucin, Vimentin totally positive and focally of NSE, CD10 and CK20 negative, Ki-67 proliferative index 0,9-2,8%) with a favourable 5-year progression free survival prognosis.

E-PS-MD-01 | Molecular Pathology Diagnostics Symposium E-Posters

E-PS-MD-01-001
Evaluation of the Idylla NRAS/BRAF mutation test feasibility and performance for thyroid liquid-based fine-needle aspiration (LB-FNA)
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Background & objectives: Molecular exploration of thyroid nodules with indeterminate cytology of Bethesda classification has been recommended to improve the management. Here, we evaluated the feasibility and performance of a rapid and fully automated-PCR test (Idylla) for NRAS/BRAF mutation detection on LB-FNA.
Methods: 36 thyroid LB-FNAs were included. Residual PreservCyt materials were split in two aliquots; one to assess the BRAF/NRAS mutational status using the standard High-Resolution Melting (HRM) approach and the other to compare with the Idylla essay. For five samples, dilutions were made on a third split to assess the Idylla limit of detection.
Results: 36 samples presented either BRAFV600E mutation (n=25), BRAFK601E mutation (1), NRASQ61R mutation (5), or no mutation (5) on HRM. Idylla essay showed a sensitivity of 97% and a specificity of 83%, with only two discordant results (one was a BRAFK601E mutant, which is not covered by the Idylla test; the second, a BRAFV600E mutated FNA, showed a NRASQ61R false-positive result associated with a weak BRAFV600E amplification). Dilution of BRAFV600E (n=3) and NRASQ61R (n=2) mutated samples up to a DNA level of 50 ng showed concordant results on the Idylla essay.
Conclusion: This study demonstrates that the Idylla approach can be directly performed on residual PreservCyt material from thyroid LB-FNA. Idylla essay is sensitive with a limit of detection inferior to DNA amounts obtained in routine. A thorough verification of the amplification curves is necessary to avoid artefact curves. Idylla NRAS/BRAF mutation essay could be used in practice to quickly orientate the final diagnosis of indeterminate thyroid nodules.

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E-PS-MD-01-002
Evaluation of a rapid and sensitive molecular screening strategy for mutation detection in lung cancer (suitable for use in a pathology laboratory)
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Background & objectives: We propose that initial rapid pre-screening for KRAS mutations in NSCLC at initial histological diagnosis can identify patients not eligible for current tyrosine kinase inhibitor (TKI) therapies, thereby reducing unnecessary testing; provide cost savings and more timely, definitive treatment planning.
Methods: 57 NSCLC cases previously routinely screened for EGFR, ALK and ROS1 by real time PCR and immunohistochemistry (IHC) respectively were tested using the Real Time PCR Biocartis Idylla KRAS Mutation Test.
Results: KRAS mutations were found in 29.8% (17/57) of NSCLC cases. KRAS (G12C) was most commonly detected, accounting for 12 of the 17 KRAS mutated cases (70.5%). KRAS mutations were mutually exclusive of EGFR, ALK and ROS1. EGFR mutations were identified in 17% (10/57) of cases. Current NICE guidance recommends testing for EGFR, ALK and ROS1 with an approximate cost of £250 per patient. The proposed KRAS pre-screening method followed by single gene testing would cost an average of £252 per patient. Large panel next generation sequencing (NGS) costs approximately £350 per patient compared to rapid KRAS pre-screening prior to NGS testing which costs on average £308 per patient.
Conclusion: Our study shows rapid pre-screening for KRAS mutations in NSCLC can be achieved in a matter of hours from initial histological diagnosis along with PD-L1 status. It can eliminate the need for further single gene or panel testing in almost 30% of cases. These patients can begin a definitive treatment plan within days of diagnosis with no additional costs for testing and a potential reduction in clinical appointments.

E-PS-CP-01 | Computational Pathology Symposium E-Posters

E-PS-CP-01-001
Digital imaging of fluorescent in-situ hybridization in pathology: application procedure, experience and challenges
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Background & objectives: FISH is a time-consuming procedure on fluorescent microscope with interpretation errors, caused by fading or orientation problems etc. Digital scanning seems a good solution for these problems. Herein, we share our experience and challenges during digitalization procedure of FISH slides.
Methods: Slides of tissue microarrays and sections of individual cases immune-stained for dual HER-2 amplification probe and ALK, EWSR and SYT break-apart probes were evaluated by fluorescent microscope in 1000x magnification with immersion oil. After removing the immersion oil, slides were scanned via Olympus VS120 slide scanning system, and reviewed by OlyVIA Ver.2.9.1, reaching up to 1200x magnification.

Results: In the tissue microarray scanning procedure, we observed that auto-focusing was more difficult than manual-focusing. Besides, immersion oil residue caused both auto and manual focusing errors. In order to remove immersion oil, we used dripping alcohol by a pipette, and wiped it with tissue paper. The orientation of the tissue was better when a pathologist chose the proper area to focus. Scanning magnification was 400x, which provided an optimal resolution with optic + digital zoom (up to 1200x). However, in this magnification, scanning time increased up to 36 hours for whole TMA. For individual cases, we chose a representative limited area (max 3mm in diameter) to reduce scanning time.
Conclusion: Digital scanning of FISH slides seems a better option with better core orientation in scanned tissue microarrays, which is problematic in conventional fluorescent microscope. Additionally, it is a good solution to keep FISH slides without signal fading, ready to take picture any time. Another advantage, it provides higher magnification compared to conventional fluorescence microscope. The most prominent disadvantage is limited Z-axis compared to conventional microscope. Proper removal of the immersion oil is a key point for manual and auto focusing.

E-PS-CP-01-002
Upconversion nanoparticles as labels for histopathological tissue evaluation
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Background & objectives: H&E together with DAB labelling, the gold standard in pathology, suffer from narrow dynamic range, difficulties in quantification and limited possibilities regarding multiplexing. We present an upconversion-nanoparticle (UCNP)-based technique that allows to overcome problems associated with commonly used labelling techniques.
Methods: Formalin-fixed paraffin-embedded breast cancer cell line and human breast cancer tissue were sectioned and labelled. Upconversion imaging of the human tissue sections was conducted in our prototype device and compared with a standard DAB-based IHC. The combination of UCNP and haematoxylin counterstaining on the same slide was investigated.
Results: Images obtained with our novel device demonstrate that our UCNP bioconjugates are excellent labels for the detection of cancer markers in tissue sections. Brightfield images prove that UCNPs do not interfere with the standard tissue evaluation by a pathologist. Additionally, brightfield and luminescent images can be merged to provide a better understanding of tissue morphology.
Conclusion: The emerging field of UCNP-based labelling techniques provides new possibilities for more accurate diagnosis. Staining solutions and a novel device developed by us keep the advantage of H&E staining and combine it, in one image, with the UCNP luminescent data. The high-contrast images of the UCNP labelling–generated by our scanning device–set the foundation for generating ground truth for machine learning algorithms.

E-PS-CP-01-003
Annotation in digital pathology: how to get started? Our experience in classification tasks in pathology
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Background & objectives: Training machine learning models, for AI application in Pathology, often requires extensive annotation by human experts, but there is little guidance on this subject. We aim to describe our experience and fill in this gap.
Methods: The current study ran in parallel with the annotation of colorectal whole-slide images for the development of a classification algorithm. In this work, we followed a constructive design research method: 1. Choice of annotation level; 2. Choice of software (testing QuPath, Sedeen, Leica's Aperio ImageScope); 3. Choice of input device (mouse vs. pen/pad); 4. Addressing common problems in annotation.
Results: Phase 1. Performed in articulation with the IT team, defined the annotation level that was needed. The objective of our parallel study was to develop a classification algorithm, and we opted for a wide tissue segmentation approach (vs. gland-level segmentation). Cases with only slide-level labels were also added. Phase 2. Sedeen was the chosen annotation software (due to easy-to-use polygonal tool/erasing option and exportation format); Phase 3. Performance of the drawing pen/pad surpassed the mouse, but when considering cost-usefulness, the mouse was chosen; Phase 4. Some addressed problems were which fragments to annotate, how to deal with low image quality/colour discrepancies, needed detail when drawing/contouring, file transfer, etc.
Conclusion: Annotation methodology will vary significantly according to the study's objectives, but common issues will be present across different settings. It seems intimidating to initiate the annotation effort, since there is a lack of general guidelines. It is crucial that pathologists work closely together with the IT team to achieve the project objectives. Choosing adequate and comfortable tools is also relevant. Finally, we present solutions for common issues in the annotation procedure and provide guidance to beginners in this process.

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E-PS-CP-01-004
Machine learning in analysing of endometrial receptivity in assisted reproductive technology programs
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Background & objectives: Immunohistochemical analysis of endometrium with antibodies to oestrogen and progesterone receptors is a useful method for detection of the violation in their expression which helps to indicates the implantation window and implementation of implantation insufficiency of the eutopic endometrium.
Methods: The manual scoring of the slides is hard and thus prone to errors due to their size and the enormous amount of distinct objects, thus automated scoring methods are required. In the current work, we present a multistage machine-based approach, which can perform high efficiency and reproducible scoring of endometrial stained cells.
Results: The stages are the following: the segmentation of epithelium and stroma, nuclei detection and classification and the calculation of the score. The segmentation stage is based on the U-net model. Each stage is evaluated separately: for segmentation and detection stages two datasets were collected and labelled in manual and semi-manual manner. The segmentation model achieves 92% intersection over union (IoU). This framework provides not only a robust and reproducible scoring system but also has the advantage of the visualization and interpretation of the results obtained on different stages.
Conclusion: We believe that this approach can greatly increase the speed and the quality of immunohistochemical analysis.

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