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Unraveling Adult Renal Cell Tumors: Exploring the Role of Lipocalin-2

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Objective: This study aims to scrutinize LCN2 expression in different types of adult kidney tumors and ascertain its potential significance as a diagnostic and prognostic marker.

Introduction: Renal cell carcinoma (RCC) poses a growing health concern with its escalating incidence and diagnostic complexities. Lipocalin-2 (LCN2) is a multifaceted protein expressed across various tissues, engaging in diverse biological functions. However, its involvement in modulating the proliferation, invasion, and metastasis of RCC remains inadequately explored.

Material and Methods: A cohort of 206 patients undergoing nephrectomy at the Urology Clinic, Clinical Center of Serbia, constituted the study population. Patient demographics, tumor dimensions, and survival data were extracted from medical records. Tissue microarrays were constructed following established protocols and immunohistochemically stained for LCN2. Subsequent staining evaluation and statistical analyses, encompassing descriptive statistics, chi-square tests, and Kaplan-Meier curves, were conducted. Results: Moderate cytoplasmic expression of LCN2 was discerned in healthy tubular cells. Notably, a statistically significant correlation between histological tumor type and LCN2 expression was identified, with elevated expression in renal oncocytoma (RO) and heterogeneous expression in clear cell RCC (ccRCC). While LCN2 did not exhibit prognostic utility in this study, its ubiquitous presence across RCC types intimates a plausible involvement in tumor progression.

Conclusion: Our findings underscore the substantial expression of LCN2 in diverse kidney tumors, particularly RO, with notable heterogeneity observed in ccRCC. Despite its non-identification as a prognostic marker, the pervasive

occurrence of LCN2 across RCC variants hints at its involvement in tumorigenesis. Further investigations are imperative to elucidate LCN2's precise role in kidney cancer pathogenesis and its potential as a diagnostic and prognostic biomarker.

Keywords: lipocalin-2; renal cell carcinoma; oncocytoma; ccRCC

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Spectrum of microscopic changes in testicular specimens during physical adaptation of male to female

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Objective: To provide a clinicopathological review of features identified in testicular tissue specimens after bilateral sex-affirming orchiectomies were performed.

Introduction: Hormonal therapy use of antiandrogens in combination with estrogen before sex reassignment surgery is the basis of preparation for people with gender dysphoria. The Endocrine Society guidelines recommend gender confirmation surgery after at least 1 year of continuous and coordinated hormonal preparation.

Material and Methods: We analyzed and statistically processed data on age, length of hormone therapy and testicular histopathological changes in patients who underwent bilateral orchiectomies from January 2019 to January 2023 for gender reassignment.

Results: A total of 117 persons were analysed aged from 18 to 66 years (average, 31.71 ± 11.74). The mean length of hormone therapy was $28,78 \pm 31.23$ months (range, 12 to 240 months). Mean testicular mass was $13,97 \pm 4,50$ g (right) and $13,79 \pm 5,32$ g (left). There were no germ cell

tumors, sex cord-stromal tumors, or germ cell neoplasia in situ. Thickening of the basement membranes of the seminiferous tubules and edema were found in all testicular samples. Sertoli cells occurred in 114 (97,4%), hypospermatogenesis in 44 (37,6%), normal spermatogenesis in 4 (3,4%), and 30 (25,6%) testes showed fibrosis/obliteration. All results were statistically significant ($p < 0,0001$). There was no statistical significance between the length of hormone therapy and the pathological changes in testicular tissue.

Conclusion: Our results represent a rare institutional experience of physical adaptation of male to female persons. The spectrum of pathohistological findings corresponds to changes in testicular tissue after the preoperative application of hormone therapy.

Keywords: Orchiectomy; Testes histopathology; Transgender

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Clinicopathological features of Renal Collecting Duct Carcinoma - Institutional experience

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Objective: We aim to analyze the frequency and clinicopathological features of Renal Collecting Duct Carcinoma (CDC) diagnosed at our Institute over twelve years.

Introduction: CDC represents a rare primary renal cell adenocarcinoma that arises from the principal cells of the distal nephron and accounts for less than 1% of primary renal malignancies. CDC is an aggressive tumor with 67% of patients dying within the first 2 years. Due to diverse morphology and unspecific immunophenotype pathohistological diagnosis of CDC is challenging.

Material and Methods: A surgical pathology archive from

2012 to 2024 has been searched for cases of CDC in the final diagnosis. Patients' age, gender, tumor size, stage group (SG), morphologic patterns, mucin presence, and tumor immunophenotype were analyzed.

Results: From a total of 1693 patients with performed nephrectomy for the surgical treatment of renal tumors, CDC was diagnosed in 11 cases (0.65%). Ten patients were males and one was female. The average age was 58.45 ± 12.59 . The mean tumor size was 103.73 ± 45.52 mm. Seven patients were in SG III and four patients were in SG IV. Papillary and tubulopapillary patterns predominate in seven cases. Tubular and microcystic patterns predominate in four cases. Stromal desmoplasia, mixed inflammatory infiltrate, and the focal presence of mucin were detected in all cases. Immunophenotype was unspecific with the most commonly positive reaction for HMWCK.

Conclusion: CDC is a rare high-grade adenocarcinoma in an advanced stage at the time of diagnosis with the most common papillary pattern and mucin presence. The final diagnosis implies the exclusion of other primary and secondary kidney malignancies.

Keywords: Collecting Duct Carcinoma; CDC; High-grade.

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Pathohistological characteristics of bone marrow in patients with multiple myeloma

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Objective: To find out proportion of pathologically verified MM in the total number of clinically suspected cases, as well as correlation with the patients gender and age and pathohistological characteristics of the bone marrow.

Introduction: Multiple myeloma (MM) is a hematological neoplasm characterized by clonal expansion of B-lymphocytes, specifically plasma cells in the bone marrow. The diagnosis of this malignancy requires bone marrow biopsy with pathohistological analysis.

Material and Methods: A-6-year retrospective study (2018-2023) involved 438 patients with a referral diagnosis of MM. Monitored variables were age, gender, bone marrow cellularity, atypical plasma cells infiltration percentage and clonality, the reticulin grade (G0-G3) and all were compared between the group with a pathohistological confirmed MM and the group that remained clinically suspected.

Results: Within the observed sample, the proportion of clinically suspected (30.6%) and confirmed diagnoses (69.4%) didn't significantly change over the years. The average patient's age was 65 with slightly male predominance (54%). The largest number of pathohistologically confirmed cases was in year 2023. Cellularity and reticulin fibers were increased in group of proved MM with average plasmacytic infiltration of 50%. Kappa monoclonality was registered in 58% of all cases and in all years separately except during 2019 when lambda was slightly more expressed.

Conclusion: MM is a disease of the older population with heterogeneity in general demographic characteristics as well as in the bone marrow pathohistological findings, therefore the key of care and survival of patients is early diagnosis, adequate therapy and timely treatment of complications.

Keywords: multiple myeloma; kappa; lambda; bone marrow

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MALT lymphoma and Helicobacter pylori infection, 10 years, single institution

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Objective: To find out the association between Helicobacter pylori infection and gastric MALT lymphomas in a 10 years material in our hospital.

Introduction: MALT lymphomas make about 9% of all lymphomas and about 50% of gastric lymphomas. There is a well-known association of Helicobacter pylori, Borellia Burgdorferi, Chlamydia, Campylobacter jejuni and Achromobacter xylosoxidans infection with gastric, cutaneous,

ocular, intestinal and pulmonary MALT lymphoma respectively.

Material and Methods: All biopsies of gastric MALT lymphomas diagnosed at the Oncology Institute of Vojvodina from January 2010 to March 2020. Demographic and medical data were taken from the hospital information system. HE and HP Giemsa staining and immunohistochemistry were performed according to standard procedures. Microsoft Excel and IBM SPSS Statistics were used for data analyses.

Results: There were 79 patients, which makes 6,5% of all lymphomas during this period. There were 32 men (29 to 81 years old) and 47 women (30 to 82 years old). Patients were on average about 60 years old and median 63 for both sexes. Helicobacter pylori infection was present in 52,63% of all cases, equally in both sexes.

Conclusion: Patients were mostly elderly, without any statistically significant differences between sexes. The incidence of disease is similar to neighboring countries and the USA but lower than in western Europe. The incidence of Helicobacter pylori infection in our patients is higher than in western Europe and similar to European data from a few decades ago, probably due to insufficient diagnosis of gastric problems and consequently insufficient eradication therapy for Helicobacter pylori.

Keywords: B-cell lymphoma, Helicobacter pylori, MALT lymphoma

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JAK2 mutations and endogenous erythroid colony formation in patients with polycythemia vera

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Objective: The aim of this study was to determine the frequency of JAK2V617F and JAK 2 exon 12 gene mutations and to compare the results with the presence of endogenous erythroid colony (EEC) formation.

Introduction: Polycythemia vera (PV) is a chronic myeloproliferative neoplasm characterized by increased red blood cells. The most frequent genetic abnormality is the somatic mutation of Janus kinase 2 gene (JAK2V617F) and it occurs in more than 95% of patients. In 2-5% V617F negative PV patients were detected JAK2 exon 12 mutations.

Material and Methods: Peripheral blood and bone marrow samples of 116 patients with PV were analyzed. The diagnosis of PV was established according to the bone marrow criteria of the World Health Organization (WHO). Mutation of JAK2V617F was determined by allele-specific PCR (AS-PCR) analysis. A group of exon 12 mutations (I540-E543Del, R541-E543Del, F537-K539Del, H538-K539Del, K539L, N542-E543Del) were determined by RQ-PCR mutations screening based methodology. Assay for human clonal hematopoietic progenitor cells with agar-leukocyte conditioned medium (Agar-LCM), without recombinant human erythropoietin (EPO), was used for detection of EEC.

Results: Mutation of JAK2V617F was found in the samples of the peripheral blood in 108/116 (93%) PV patients. EEC formations were obtained in the sample of bone marrow in 109/116 (94%) PV patients. In 106/116 (91%) patients we detected presence of EEC formation and mutation of JAK2V617F at the same time. One JAK2V617F unmutated patient, with EEC, has mutation in JAK2 exon 12 gene.

Conclusion: Presence of JAK2 mutation and EEC are essential characteristics of PV. Considering these results, it is clear that the EEC formation observed in PV, are the part of the JAK2-dependent activation signaling pathway.

Keywords: EEC, JAK 2

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Detection of JAK2 (V617F), CALR and MPL mutations in patients with thrombocytosis

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Objective: Detection of most frequent gene mutations, involved in pathogenesis of myeloproliferative disorders.

Introduction: Mutations in JAK2, CALR and MPL genes, were introduced as diagnostic parameters. The aim of detecting those mutations, in the patients with persistent thrombocytosis, is to establish differential diagnose of myeloproliferative neoplasia (MPN). JAK2 encodes for a non-receptor tyrosine kinase. CALR gene is coding multifunctional protein, named calreticulin, which is involved in control of gene activity, cell growth, proliferation, migration, adhesion and apoptosis. MPL is oncogene, which encodes for thrombopoietin receptor.

Material and Methods: We analysed 708 pts with persistent thrombocytosis, by the ARMS-PCR method for JAK2 V617F mutation detection. We selected 20 JAK2 negative pts, for further analysis of MPL W515K/L and CALR mutations, by the RQ-PCR mutation detection kit. DNA was extracted from peripheral blood, according to standard procedures.

Results: JAK2 V617F mutation was positive in 372 pts. (52.5 %). CALR mutations were detected in 10 out of 20 pts. (50%), predominantly Type I (6 pts, 60%) and Del I (6pts, 60%) , Type II (3pt, 30%), Del II (0%), Del III (3 pt, 30%) . Eight of ten (80%) had more than one mutation. The Del II mutations were not detected. MPL W515L/K mutations were not detected too, in this group of pts.

Conclusion: We provided a diagnostic parameters which differentiate a group of MPN pts. with thrombocytosis. Further investigations of new diagnostic mutations, in the genes involved in pathogenesis of MPNs, are important for defining new potential targets for molecularly targeted therapy, in treating malignant diseases.

Keywords: CALR, JAK2V617F, MPLW515K/L, MPN

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Immunosuppressive features in epithelial ovarian tumors

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Objective: We analyzed differences in PD-L1 expression in epithelial ovarian tumors.

Introduction: Ovarian tumors can suppress the host's immune responses by activating the PD-1/PD-L1 mechanism. PD-L1 immunosuppressive function can make tumor cells resistant to effector lymphocytes, which leads to aggressive clinical behavior.

Material and Methods: PD-L1 expression was analyzed in 328 subjects, 122 with epithelial ovarian carcinoma (OC), 42 with atypical proliferative tumor (APT), and 164 with benign epithelial ovarian tumor (BOT). Immunohistochemical analysis was performed using the tissue microarray and correlated with a set of histopathology parameters.

Results: The higher PD-L1 expression was found in OC than in APT/BOT. The intensity of PD-L1 expression was higher in serous (79.6%) than in mucinous or endometrioid OCs ($p < 0.001$). PD-L1 expression was higher in high-grade serous carcinoma (HGSC) than in low-grade serous carcinoma (LGSC) ($p = 0.007$). The high level of PD-L1 expression was more frequent in OCs with stage FIGO III/IV than in those with lower stages ($p < 0.001$). PD-L1 high expression level was significantly more frequent in OCs with tumor necrosis, lymphovascular invasion, and lymphocytic infiltration.

Conclusion: We showed a significantly higher level of PD-L1 expression in OCs than in APT/BOT, most frequently in the HGSC histology type. These findings underline the possibility of the usage of PD-L1 inhibitors in patients with more aggressive ovarian cancers, such as HGSC.

Keywords: immunosuppressive; epithelial ovarian tumor; PD-L1

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Prognostic value of separate extramural vascular invasion reporting in rectal cancer

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Objective: The aim of this study was to examine the prognostic significance of pathohistologically detected EMVI in untreated rectal cancer and its implications in separate reporting.

Introduction: Vascular invasion, especially extramural vascular invasion (EMVI) has emerged as prognostic parameter for rectal cancer (RC) in recent years. Prediction of recurrence and metastases development poses a significant challenge for oncologists, needing markers for prediction of adverse outcome.

Material and Methods: We examined 100 untreated RC patients who underwent curative resection from January 2016 to June 2018 with follow up of 5 years. Patients were divided in equal EMVI- and EMVI+ groups based on histological examination of H&E stained postoperative surgical samples. Exclusion criteria were neoadjuvant treatment and distant metastases. Overall and disease-free survival distributions were estimated by the Kaplan-Meier method.

Results: Out of the total RC patients, 66% were still alive during the follow-up period (median 56, range 12-76 months), while 30% had verified recurrence of the disease. The median survival without recurrence of the disease was 52 (range 4-76) months. EMVI+ patients had significantly shorter average OS (56.230 ± 3.350 months) compared

to EMVI- patients (64.640 ± 2.845 months) ($p=0.040$). Among EMVI+ cases, significantly shorter DFS was recorded than within EMVI- cases (52.162 ± 4.319 vs. 61.338 ± 3.041 months, $p=0.028$). Concerning LVI, differences in OS between LVI+ and LVI- patients were not statistically significant ($p=0.068$), while LVI+ patients had significantly shorter DFS ($p=0.024$).

Conclusion: Obtained results strongly suggest significance of separate reporting of EMVI from lympho-vascular invasion, as it is potentially a surrogate marker for adverse prognosis and outcome.

Keywords: rectal cancer, extramural venous vascular invasion

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EGFR mutation analysis in cytological specimens: An institutional experience

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Objective: To evaluate EGFR mutation testing in cytological lung adenocarcinoma (LUAD) specimens.

Introduction: Epidermal growth factor receptor (EGFR) is a predictor for tyrosine kinase inhibitor (TKI), which is efficient in LUAD treatment. Activating EGFR mutations are usually found in never smokers, females, and Asian population. The most of LUAD patients are diagnosed at advanced stages of the disease when surgical resection is not possible, so cytological specimens is alternative for EGFR mutation detection.

Material and Methods: This prospective study included 101 cytology samples (bronchial brushing, fine needle aspiration, transbronchial needle aspiration or pleural effusion) who underwent EGFR mutation analysis during a 6-months period at the Institute for Pulmonary Diseases of Vojvodina. DNA was isolated using the Cobas®DNA Sample Preparation Kit. The target DNA was detected using real time PCR Cobas®EGFR Mutation Test v2.

Results: There was 69 (61.4%) men and 32 (38.6%)

women included in the study. Median age was 65.4 (62.8 women and 67.1 men). Majority of patients were active or former smokers (54.5% and 32.7%). EGFR mutation rate was 9.9%. The most common mutation type was deletion in exon 19 (5/10 specimens), L858R mutation in exon 21 (4/10 specimens). In one specimen G719 point mutation in exon 18 was detected. There was no significant correlation between the number of tumor cells and the DNA concentration. One mutation positive specimen had extremely low DNA yields (0.71ng/ μ l).

Conclusion: Our results confirmed the effectiveness of a sensitive real-time method in EGFR gene mutation detection in cytology specimens.

Keywords: Keywords: adenocarcinoma, cytology, EGFR, mutation test

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Cytological evaluation of breast lesions with histopathological correlation

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Objective: To find out cytological and histopathological correlation in patients with surgical resection of breast lesions. Introduction: Cytology is a fast and non-invasive diagnostic procedure and part of tumor board for evaluation of breast lumps.

Material and Methods: Retrospective study of 198 patients included 90.4% (179/198) women and 9.6% (19/198) men, age between 15 and 93, average 57.80 ± 18.78 .

Cytological material was sampled using ultrasound-guided fine-needle aspiration (FNA) in 39.9% (79/198) patients, FNA in 33.33% (66/198), core biopsy in 18.69% (37/198) and breast secretion smear in 8.08% (16/198) patients. Surgical treatment was indicated after cytological evaluation in 52.02% (103/198) patients.

Results: In 50.50% (100/198) of patients sample was

obtained from left breast, and in 28.4% (56/198) from upper lateral quadrant. Cytological samples were divided into 5 categories: 19.2% (38/198) non-diagnostic, 42.4% (84/198) benign, 8.6% (17/198) atypical, 9.6% (19/198) suspicious for malignancy and 20.2% (40/198) malignant. The most frequent cytological diagnosis in 27.78% (55/198) patients was adenocarcinoma, following fibrocystic breast changes in 18.18% (36/198).

There were statistically significant more women ($p < 0.001$), adenocarcinoma diagnosed by cytology ($p < 0.001$) and ductal carcinoma as histopathological diagnosis ($p < 0.001$). There was no statistically significant difference in lump localization ($p = 0.829$). Cytological and histopathological correlation was high ($r = 0.163$).

Conclusion: Cytology has important role in breast lump diagnosis. Even there are more core biopsies instead of FNA due to majority of possibilities of additional studies on samples, we can still use cytology for fast evaluation.

Keywords: cytology, breast, ductal carcinoma, FNA

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A Case of Unexpected Autopsy Diagnose

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Objective: Sarcoidosis is a chronic granulomatous disease of uncertain etiology involving various organs. Pathologically, it is characterized by the presence of noncaseating granulomas in affected tissues, usually lungs. The age of presentation is between 30 and 50, commonly women. Cardiac involvement is seen in 2-5% of patients with systemic sarcoidosis and is often clinically undetected.

We present a case of unexpected diagnosis of systemic sarcoidosis involving the heart, lungs, liver and spleen.

Case report: A 74-year-old female with atherosclerosis,

diabetes mellitus, ischemic cardiomyopathy and hypertension who died under respiratory insufficiency clinical picture was autopsied at the Center for Pathology and Histology at the University Clinical Center of Vojvodina, using standard autopsy procedures. Routine hematoxylin and eosin–stained slides were prepared, as well as special stains Grocott methenamine silver stain for fungi and Ziehl–Neelsen stain for acid–fast bacilli, in addition. Single and confluent non-necrotizing granulomas were found in the heart, lungs, liver and spleen, composed of epithelioid histiocytes with abundant eosinophilic cytoplasm and a variable number of Langhans and other giant cells and lymphocytes. We also found intracytoplasmic inclusion bodies, Schaumann bodies. Stains for fungi and acid-fast bacilli were negative. Additionally, we noticed a post–myocardial infarction scar of the anterior wall and massive cardiac lipomatosis.

Conclusion: Since there is no targeted therapy for sarcoidosis, early diagnosis and treatment of the disease remain an important priority, especially when it involves vital organs such as the heart.

Keywords: autopsy; granulomas; sarcoidosis.

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Polyarteritis nodosa manifested as hypovolemic shock: an autopsy case

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Objective: Vasculitis involves fibrinoid necrosis and inflammation of blood vessels.

Case report: A 63-year old male presented with nausea, progressive weight loss (15 kg for 6 months), night fever, myalgia, and arthralgia. Blood count showed hypochromic, microcytic anemia without known underlying cause. Polyneuropathy of lower extremities was noted. Colonoscopy,

esophagogastroduodenoscopy, and computed tomography (CT) of the abdomen and pelvis were unremarkable. PET CT showed a cystic lesion in the tail of the pancreas. Markers of inflammation were significantly elevated (CRP, SE, ferritin). Antinuclear antibodies (ANA) were present (1:160), whereas other markers, namely antimitochondrial, anti-MPO ANCA, anti-smooth muscle, anti-transglutaminase, and anti-LKM antibodies were negative. Testing for HBsAg, anti-HCV, anti-HIV, quantiferron and PPD test, tumor markers CEA, CA 19-9, CA 72-4, AFP, PSA, CYFRA 21-1, and NSE, was negative. Electrophoresis of urine showed protein in urine. The patient was still losing weight. After thorough workup, the patient deceased. At the autopsy, cachexia was prominent. Retroperitoneal hematoma along with hemato-peritoneum and hypovolemic shock was noted due to ruptured dilated blood vessels in the kidneys. Histopathological examination of the kidney and pancreas showed fibrinoid necrosis with transmural inflammation (neutrophils, mononuclear cells) in middle-sized blood vessels. Some walls of blood vessels were nodular and fibrotically changed with narrowing of the lumen. Diagnosis of polyarteritis nodosa was made.

Conclusion: Clinical presentation of polyarteritis nodosa can be a diagnostic challenge since there is no marker specific for this disease, and it should be considered in differential diagnosis, particularly in cases of progressive cachexia and loss of blood in the body.

Keywords: polyarteritis nodosa, vasculitis, cachexia, shock

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Triploid syndrome – A Case Report

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Objective: Triploidy is a numerical chromosomal aberration with the presence of an extrachromosomal haploid set that can be maternal or paternal in origin. In the first trimester of pregnancy, triploidy is one of the most common reasons of spontaneous abortions.

Case report: A 28-year-old patient, first time pregnant, without previous births and spontaneous or artificial abortions. In the first trimester, routine screening was performed, during which reduced values of pregnancy markers (Free beta hCG 0.047 MoM, PAPP-A 0.230 MoM, NT 1.0 mm). Because of slower growth and development, reduced quantity of amniotic fluid in the 18th week of pregnancy (on ultrasound gestational age was estimated as 16th week), an early amniocentesis was performed. Based on the results of the amniocentesis, it was established that the karyotype of the fetus is 69,XXX. Ultrasound examination revealed that the lateral cerebral ventricles were dilated, and that the transcerebral diameter was reduced with hypoplasia of the cerebellum and agenesis of the vermis.

Conclusion: Based on the results of the amniocentesis and ultrasound examination, triploidy of the fetus was confirmed with hypoplasia of the cerebellum and agenesis cerebellar vermis as well as reduced quantity of amniotic fluid with stagnation in growth and development. Keeping in mind the above data, abortus was indicated, and with the consent of the ethics committee of the Clinic for Gynecology and Obstetrics, the pregnancy was terminated.

In the autopsy report multiple syndactyly on both hands and feet, hypertelorism, micrognathia and agenesis of cerebellar vermis were observed.

Keywords: Triploid syndrome

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Goblet cell adenocarcinoma of appendix, presented with local peritonitis, diagnosed by autopsy

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Objective: Goblet cell adenocarcinomas (GCC) are rare, distinct tumors primarily arising in the appendix, characterized by their unique mix of neuroendocrine and mucinous features, presenting primarily as goblet or signet ring-like cells. Unlike typical neuroendocrine tumors, GCCs manifest a peculiar cellular composition which sets them apart.

Case report: A 72-year-old female presented with acute lower right abdominal pain, nausea, dyspnea, and atrial fibrillation and died on the day of admission. An autopsy revealed an appendix perforation leading to a periappendicular abscess adhering to the parietal peritoneum, with accumulation of pus in the peritoneal cavity, severe pulmonary edema, and bilateral hydrothorax. The histopathological examination showed diffuse alveolar damage indicative of respiratory distress syndrome. The appendix tissue showed large eosinophilic cells with intracellularly localized mucin and peripheral nuclear position. Tumor infiltration extended through the mucosa, submucosa, muscular layer, and subserosa, alongside neutrophilic infiltration across all layers and an abscess within the subserosa. Peritoneal surfaces exhibited extensive inflammation which extended to deeper structures of the abdominal wall, including skeletal muscle. Immunohistochemical staining for Mucicarmine, MUC2, SATB2, CDX2, and Ki67 was positive within the tumor cells, whereas neuroendocrine markers (Synaptophysin, Chromogranin A, and INSM1) were negative.

Conclusion: This case underscores the insidious nature of GCC, which remained asymptomatic until resulting in a fatal outcome through respiratory distress syndrome, propelled by appendicitis and peritonitis. The tumor can be clearly identified under light microscopy as GCC, confirmed by positive staining for MUC2 and Mucicarmine, with the absence of neuroendocrine immunopositivity as reported in

the literature.

Keywords: autopsy, goblet cell adenocarcinoma, appendix

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Mixed Epithelial and Stromal Tumor of the Kidney with Myopericytoma/Myofibroma as Stromal Component

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Objective: This case report emphasizes the differentiation of the stromal component of Mixed Epithelial and Stromal Tumor of the Kidney.

Case report: A 75-year-old male was admitted to the hospital for surgery due to incidental finding of a kidney tumor during an ultrasound examination of the abdominal cavity. Partial nephrectomy was performed, and the tumor was histopathologically examined. Gross examination revealed a partially cystic tumor with a solid appearance, measuring 26 mm in maximum diameter. Histomorphological analysis showed cysts lined with a layer of cuboidal cells, surrounded by ovarian-like stroma. The solid component of the tumor consisted of bundles of elongated cells with eosinophilic cytoplasm, oval nuclei without atypia, and exhibited angiocentric growth. Nuclear atypia and mitoses were not observed. Focally, a ribbon-like hyalinized matrix was present between the cells. Blood vessels were increased, small, with a split like lumina. Immunohistochemically, the epithelial component showed positivity for CK7, CK20, Pax-8, Pax-2, Gata-3, ER, and PR, while the stromal component was positive for SMA, HHF-35, h-Caldesmon, ER (focally), PR (diffuse), Glut, Reticulin, and Collagen IV. Immunohistochemical stain on CD34, CD31, and CD99 were negative. The diagnosis of mixed epithelial and stromal tumor of the kidney (MEST) with myopericytoma/myofibroma as the stromal component was made.

Conclusion: MEST is a benign kidney tumor, predominantly observed in perimenopausal women, with leiomyoma being the most frequently diagnosed stromal component. Rare cases of malignant transformation have been reported. The prognosis of this tumor is favorable in nearly all cases published so far.

Keywords: Kidney tumors, MEST, myopericytoma/myofibroma, immunohistochemistry

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Unusual site of metastatic clear cell renal cell carcinoma in pyriform sinus - Case report

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Objective: This is a case report of an unusual site for metastatic disease.

Case report: Here we present a 56-year-old female admitted to the hospital due to the presence of granulations in the left pyriform sinus, accompanied with pain in the left half of larynx and hoarseness. A biopsy was performed, and the specimen was sent for pathohistological examination. Histological examination revealed fragments of mucosa lined with squamous stratified epithelium, without atypia, infiltrated by tumor tissue. The tumor was composed of cells with clear cytoplasm and moderate nuclear pleomorphism, forming solid fields and alveolar structures. The stroma was scanty but rich in arborized blood vessels with thin walls. Immunohistochemical analysis revealed positivity for CKAE1/AE3, CAM5.2, Pax-8, Pax-2, Vimentin, and CD10, and negativity for RCC, TTF1, and Thyroglobulin. The morphological findings, in accordance with immunohistochemical analysis, corresponded to a metastasis of clear cell renal cell carcinoma (ccRCC). According the medical documentation, the patient had a left radical nephrectomy four

years ago with the diagnosis of ccRCC; therefore, our diagnosis correlates with the diagnosis of the primary tumor. **Conclusion:** ccRCC is the most common type of kidney cancer in adults, accounting for approximately 70-80% of all RCC cases. It is distinguished by the presence of clear cells due to the accumulation of lipids and glycogen within the cells. The most common sites for ccRCC metastasis include the lungs, lymph nodes, bones, liver, brain, and adrenal glands. The pyriform sinus is an extraordinary site for metastatic RCC. According to our knowledge, only one case has been reported so far, highlighting the rarity of this metastasis location.

Keywords: pyriform sinus, ccRCC, metastasis

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A Series of Two Cases and the Role of Immunohistochemistry in Differential Diagnosis

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Objective: The case report is on two distinct instances of urachal carcinoma, and emphasizes the clinical presentation, diagnostic process, and histopathological findings. The cases underline the importance of considering urachal carcinoma in the differential diagnosis of bladder tumors and highlight the distinguishing features from more common malignancies such as colorectal carcinoma infiltrating the urinary bladder.

Case report: Here we present two cases of urachal carcinoma in patients aged 47 and 69. Both individuals, identified as male, were admitted to the hospital presenting exten-

sive hematuria and a confirmed tumor mass in the urinary bladder as evidenced by magnetic resonance imaging. The 47-year-old patient underwent total, while the 69-year-old patient partial cystectomy. Pathohistological examination was conducted on the specimens. Histologically, both tumors were identified as adenocarcinomas, characterized by mucin-producing cells originating from urachal remnants. Immunohistochemical analysis demonstrated focal positivity for CK7, CK20, CDX-2, and diffuse membrane positivity for beta-catenin, establishing the diagnosis of urachal carcinoma of the urinary bladder and ruling out metastatic colorectal carcinoma.

Conclusion: Urachal carcinoma is an uncommon and aggressive malignancy originating from the urachus, a fetal remnant connecting the urinary bladder to the umbilicus. It is crucial to differentiate it from colorectal carcinoma infiltrating the urinary bladder, which is more commonly diagnosed. These cases contribute to the broader understanding of urachal carcinoma's clinical and pathological characteristics, aiding in timely and accurate diagnosis and management.

Keywords: pyriform sinus, ccRCC, metastasis

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Testicular epidermoid cyst of an adult patient: A case report

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Objective: We present a case of testicular epidermoid cyst—a type of prepubertal teratoma that arose in the testis of an adult (postpubertal) patient.

Case report: A 30-year-old man admitted to the University Clinical Center of Vojvodina, urology clinic for surgical treatment of a right testicle tumor, which is manifested by local pain. A scrotal ultrasound was performed, which

revealed a 12x12 mm, well-circumscribed, heterogeneous intratesticular mass in the upper pole of testis. Laboratory evaluation included elevated level of lactate dehydrogenase (LDH-290 IU/l), alpha-fetoprotein (AFP) and beta-human chorionic gonadotropin (beta-HCG) were normal. The patient underwent enucleation of the tumor through a right inguinal incision with intraoperative frozen section which was confirmed benign lesion. The surgical treatment went well and the testicle was preserved. Macroscopic examination revealed a well-circumscribed, whitish, oval mass. It contained yellow-white keratinous material with a hint of concentric lamellar arrangement. Microscopic analysis on standard HE staining, showed a cyst that is lined with flattened squamous epithelium and contained keratinized debris. The surrounding testis tissue appears normal and did not show any atypia or germ cell neoplasia in situ (GCNIS) which was confirmed by immunohistochemical analysis-PLAP + and SALL4 +.

Based on morphological and immunohistochemical findings, the diagnosis was made: Testicular epidermoid cyst/Teratoma testis-prepubertal type. The patient was examined two weeks after surgery and recovered well.

Conclusion: The importance of preoperative suspicion and intraoperative frozen section confirmation of benign testicular tumor, especially in postpubertal patient in reproductive age is crucial for prevention of radical orchiectomy.

Keywords: teratoma testis, epidermoid cyst, GCNIS

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Spleen metastasis as the first sign of urothelial carcinoma

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Objective: Urothelial carcinoma is carcinoma derived from the urothelial cells lining the urinary tract. The most com-

mon sites of bladder cancer metastasis are lymph nodes, bones, lung, liver and peritoneum.

Case report: A-70-year old male came to abdominal surgeon due to spleen haematoma that had been diagnosed in other hospital. The patient complained of abdominal pain. After routine preoperative preparation, splenectomy was performed and intraoperatively subcapsular haematoma was registered with capsular rupture and haematoperitoneum. The specimen was sent to pathology. Macroscopically, the spleen was with ruptured capsule and with haemorrhage areas, but serial cuts showed focal nodular change in the parenchyma measured 35x35x20 mm, solid, round shape and greyish-whitish colour. Standard hematoxylin-eosin stainings showed tumor tissue made up of atypical cells with an increased mitotic index and visible pathological mitoses arranged in nests and solid areas with focal necrosis. Immunohistochemically, expression of markers CK7, GATA3, p63 and Uroplakin was registered, CK20 was focally observed and PAX8 negative so the first differential was urothelial carcinoma. The surrounding splenic parenchyma has the usual histomorphological features with areas of hemorrhage.

Conclusion: Malignancies metastasizing to the spleen are very rare, isolated metastases especially. Spleen exhibit many immune functions, including the development of immunogenesis and tolerance, so it can be possibly the key in inhibiting the development of spleen metastases. In order to understand those inhibiting mechanisms that prevent metastatic deposits in the spleen, further research are required.

Keywords: urothelial carcinoma; metastasis; spleen;

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Neuroendocrine carcinoma of the cervix: a case report

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Objective: Neuroendocrine neoplasms of the gynecological tract comprise less than 2% of all gynecological cancers.

Case report: A 72-year-old woman presented with profuse postmenopausal vaginal bleeding. She reported dull pain in lower abdomen that started 2 years ago. More than a month ago, she presented with nausea and vomiting and pain in her lower back. She lost 10 kg in past 3 months. Multidetector computed tomography showed multiple deposits in the liver, presumably metastatic deposits. In the pelvis, a tumor mass of 98×74×71 mm infiltrated the cervix, the uterus along with adnexal structures, and parietal wall structures. Biopsy of the cervix showed tumor cells infiltrating the cervix in a diffuse arrangement with hyperchromatic nuclei, scarce cytoplasm, overlapping of the nuclei, and "crash artefact" with extensive areas of tumor necrosis. Tumor cells were positive for CKAE1/3 (scattered, dot-like in the cytoplasm), EMA, INSM1, synaptophysin, CD56, p16 (diffusely and strongly), and p53 (weakly), and negative for CK5/6, CD45 (LCA), p63, p40, CK7, CK20, CDX-2, chromogranin, TTF-1, PAX8, mCEA, ER, and PR. Ki-67 was positive in more than 90% of tumor cells. Mitotic activity was 21/10 hpf. Diagnosis of high-grade neuroendocrine carcinoma of the cervix was made. The patient passed away a day after diagnosis.

Conclusion: Neuroendocrine carcinomas of the cervix are very aggressive tumors with poor prognosis. Due to their rarity, those neoplasms can present a diagnostic challenge, especially in the context of limited pathologist's experience.

Keywords: cervix, neuroendocrine carcinoma, immunohistochemistry

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Echinococcal cyst of the uterus: a rare site of presentation

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Objective: Echinococcus granulosus is an anthroponosis most commonly involving the liver and lungs. The female genital tract is an extremely rare site of development. We aimed to report a case of an echinococcal cyst (EC) discovered in the uterus.

Case report: A 64-year-old postmenopausal woman presented with a three-month history of persistent lower abdominal discomfort and previous liver EC in 2022. Transvaginal ultrasound showed a thickened endometrium measuring 12mm and an unilocular cystic formation arising from the anterior wall of the lower uterine segment, approximately 50x40mm in greatest dimension. Magnetic resonance imaging (MRI) of the pelvis strongly indicated EC of the uterus. Serum tumor markers were unremarkable. The patient underwent explorative curettage due to endometrial thickening and microscopy revealed an endometrial polyp. Serological results with the enzyme-linked immunosorbent assay (ELISA) and confirmatory testing by Western blot were positive for Echinococcus granulosus. The surgical approach was a classical abdominal hysterectomy with bilateral adnexectomy after three cycles of albendazole therapy. The pathological assessment showed scoleces with a row of hooklets, and periodic acid-Schiff (PAS) staining accentuated the laminated layer. The patient is currently receiving a fourth cycle of albendazole therapy.

Conclusion: Awareness of extrahepatic manifestations of EC is very important since unusual sites of involvement are possible. The correct diagnosis demands a detailed clinical examination of pelvic masses, especially in endemic areas supported by serological tests and histopathological examination.

Keywords: uterus; Echinococcus granulosus; echinococcal cyst; diagnosis.

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Histomorphology pattern specific for certain molecular alterations in uterine leiomyoma

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Objective: Leiomyoma with (fumarate hydratase) FH deficiency manifests certain histological characteristics which should arouse suspicion for further immunohistochemical analysis and diagnosis confirmation. Patients with such leiomyomas have a five to six times increased risk for the development of aggressive forms of renal cell carcinomas. Detection of FH-deficient tumors is very important because of their hereditary association.

Case report: We represent two uterine leiomyomas with rare histomorphological characteristics, significant for prognosis and further treatment of such patients. Patients were 25 and 28 years old and both were treated at the gynecological clinic for an incidental finding of uterine leiomyoma. They have similar benign clinical and imaging presentations. Microscopic examination showed marked nuclear atypia, intracellular eosinophilic globules, and abnormal intratumoral vessels making a doubt for specific leiomyoma subtypes, which have predictive significance for additional hereditary cancer syndromes. Considering specific histomorphological characteristics we did FH and Succinat dehydrogenase, subunit B (SDHB) immunohistochemical analysis which confirmed metabolic deficiency in their tumor cells. Based on the combined histomorphological and immunohistochemistry results we suggested a diagnosis of uterine leiomyoma with FH deficiency.

Conclusion: Uterine leiomyomas with such characteristics are rare and easily unrecognized. They have predictive significance because their specific mutation point to additional hereditary cancer syndromes and the need for further examinations.

Keywords: leiomyoma; fumarate/succinat deficiency

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Uterine adenomatoid tumor: a case report of an incidental finding

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Objective: Adenomatoid tumors are uncommon benign tumors most frequently seen in the genital tract of both sexes. There are usually incidental findings in the female genital tract, most often located in the fallopian tube and uterine serosa, but these are not so common in the myometrium.

Case report: A 50-year-old female attended the gynecology clinic with lower abdominal pain, malaise, anemia, and, for the past two years, menorrhagia. Since 2005, she has known about the existence of fibroids. Now, ultrasound confirms an enlarged uterus with multiple fibroids. The patient underwent a hysterectomy, and the specimen was sent for histopathological analysis. At the gross examination, the uterus measured 17x9x11 cm. In the myometrium, multiple circumscribed masses were found, with a gray to white cut surface and the largest diameter of 7 cm. Histological examination showed interspersed smooth muscle fascicles with inconspicuous nuclei (Dx: Leiomyomas). One histological specimen contained, between the muscle cells, a focus with tubular, pseudovascular and gland-like structures lined by flat to cuboidal cells. There is no nuclear atypia, mitotic activity, or necrosis. Lining cells expressed immunoreactivity for CK AE1/ AE3, Calretinin, and D2-40 and were negative for PAX8 and CD34. Based on the histopathological and immunohistochemical findings, the diagnosis of adenomatoid tumor of the uterus was established.

Conclusion: The true incidence of uterine adenomatoid tumors may be significantly higher. Pathologists should be aware of these tumors and advised to interpret morphologic

findings together with the results of a concise immunohistochemistry panel to avoid misdiagnosing.

Keywords: adenomatoid tumor, leiomyoma, uterine neoplasma, mesothelium

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Cervical Squamocellular Carcinoma with unusual presentation

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Objective: Tumor growth in cervical tissue was mostly locoregional in the stroma as a destructive, infiltrative pattern. In some cases, a growth pattern can be superficial with intraepithelial progression. A very uncommon and rare pattern is the proximal spreading of squamocellular carcinoma (SCC) with endometrial and adnexal colonization.

Case report: We represent microinvasive SCC with secondary endometrial and adnexal involvement, whereas the most invasive cancer behavior was in tubal segments. The patient had severe recidivate cervical epithelial dysplasia which after two years progressed to microinvasive cervical SCC. After radical hysterectomy micro-invasive cancer was confirmed with deep of invasion less than 1mm. Pre-operative imaging did not detect neoplastic features in the endometrium or adnexal structures. Histomorphology examination showed unexpected SCC in the proximal uterine and adnexal structure. The mostly whole upper endometrium was colonized. We noticed micro-invasive focuses in the myometrium very similar to those in cervical tissue. Ovaries were without malignant features. In the right tubal

epithelium, we found segments with remarkable neoplastic intraepithelial in situ lesions. In the extended sections, we noticed micro-invasive SCC focuses in the tubal wall. However, unlike SCC, in the cervix, here we additionally observed an invasion of lymphatic and vascular vessels.

Conclusion: Such unusual presentation of cervical SCC should be highlighted because it could be easily mistaken with primary adnexal tumors. This pattern of tumor growth should be especially considered for patients who are proposed for sparing surgical procedures. A detailed and multidisciplinary approach for every patient is very important because unpredictable cases are present.

Keywords: cervical cancer; superfital spreading

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Adenosarcoma cervicis uteri- case report

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Objective: Adenosarcoma is a relatively rare tumor (about 10% of all gynecological tumors), composed of a malignant mesenchymal and a benign glandular component. During the routine histopathological examination, cervical curettage with endocervical polyps occurs very often, but is every polypoid structure always really only a polyp? In this case, we emphasize the significance of adequate histopathology analysis of material obtained by exploratory curettage considering sarcoma features in differential diagnosis.

Case report: We present a 38-year-old female with metrorrhagia and a clinically determined usual endocervical polyp. Histomorphological analysis showed tubular, slightly elongated endocervical glands, lined with uniform endocervical epithelium without signs of atypia. In some parts glands were discreetly compressed lumens. Endocervical stroma was mostly uniform and focal with remarkable fibrovascular spaces. Detailed analysis of stromal parts

around the glands showed a discreet increase of cellularity, without remarkable cytonuclear pleomorphism and without conspicuous increased number of mitotic figures. Such stromal features and slightly distorted glands indicate suspicious malignant lesions. Immunohistochemical analysis confirmed our doubts. The patient underwent a radical hysterectomy with bilateral adnexectomy and bilateral pelvic lymphadenectomy. Examination of the operative material confirms the definitive diagnosis of adenosarcoma of the cervix.

Conclusion: Adenosarcomas arising from the cervix can be clinically and pathologically very often confused with a benign cervical polyp. The described endocervical stromal pattern should raise doubt for neoplastic stromal features, which is crucial for further treatment.

Keywords: adenosarcoma; polypus; cervix

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Cotyledonoid dissecting leiomyoma of the uterus with intravascular growth: a case report

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Objective: Uterine leiomyomas have numerous morphologies, among which cotyledonoid dissecting leiomyoma, also known as Sternberg tumor, is a very unusual benign form of leiomyoma with an uncommon macroscopic appearance, often confused with malignant or non-uterine lesions.

Case report: A 50-year old woman presented with abdominal pain and irregular menstrual cycles. Physical examination detected an abdominal mass. A CT scan was performed, and revealed inhomogeneous, well-vascularized formation in the pelvis, 14 cm in diameter, in contact with both sides of the uterine body without clear demarcation. The patient underwent radical hysterectomy with

bilateral adnexectomy. Grossly, uterus was enlarged due to presence of intramural solid-cystic nodule measuring 6cm which dissects the myometrium to the serosal surface and descends in a form of paracervical multicystic formation downward towards the vagina. Histologically, tumor presented as a bundles of oval and spindle-shaped smooth muscle cells without elements of cytologic atypia. Atypical mitotic figures and fields of necrosis were not observed. Tumor tissue dissected myometrial fibers, with elements of stromal edema, hydrops changes, cystic degeneration and hyalinization. The described cells in a circular arrangement surround blood vessels with thickened walls with foci of intravascular propagation. Tumor cells showed SMA, Desmin, Caldesmon, Estrogen receptor positivity and CD10, AE1/AE3, HMB45, Melan-A negativity. Ki-67 proliferative index was less than 5%.

Conclusion: It is important to be aware of this entity to prevent overly aggressive treatment of this benign smooth-muscle neoplasm.

Keywords: cotyledonoid dissecting leiomyoma; leiomyoma; leiomyoma variant; sternberg tumor.

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Aggressive angiomyxoma of uterus – A Case Report

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Objective: Objective was to show case of a rare uterine tumor, aggressive angiomyxoma.

Case report: A 42 year-old female with the symptoms of lower abdominal and back pain was admitted to CGO. She

stated that the symptoms had started two weeks before admission. Preoperative ultrasound showed a tumor in the lower part of uterine body, initially described as leiomyoma. From personal history we found out that the patient was nulliparous, with regular menstrual cycles and without any known family history of gynaecologic diseases. Surgery was indicated and tumor mass was partially excised. On frozen sections it was decided that it is necessary to postpone final diagnosis until standard HE staining would be done. Grossly tumor was described as multiple, soft, yellowish fragments, measuring 13,5cm in total diameter. On standard HE staining tumor was described as myxoid, with oval cells that had elongated eosinophilic cytoplasm and with middle to large blood vessels with thick muscular, partly hyalinized walls. Immunohistochemically tumor cells were: Desmin+; SMA+; CD34-; Caldesmon-; ER+; PR-/+; S100-. Following these findings a final diagnosis of deep aggressive angiomixoma was made. Two month after the initial surgery hysterectomy with bilateral salpingectomy, partial omentectomy and peritoneal biopsy was performed and tumor tissue was identified in the cervix.

Conclusion: Aggressive angiomixoma is a rare type of mesenchymal tumor with uncertain behavior, usually located in vulva and/or pelvic cavity and occurring mostly in reproductive age women. Tumor has a high tendency for recurrence but usually very small metastatic potential.

Keywords: Aggressive angiomixoma, uterus

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Disseminated peritoneal leiomyomatosis: A case report

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Objective: To show a case of disseminated peritoneal leiomyomatosis (DPL).

Case report: 38-year-old female, gravida 5 para 2 (two cesarean deliveries), with a history of primary hypertension, was admitted for cesarean delivery due to oligohydramnios and intrauterine growth restriction at 34 5/7 weeks. Following relaparotomy multiple small nodules up to 5 mm in diameter were noted upon anterior uterine wall and adjacent peritoneum. Biopsy of the nodules on standard HE staining showed well-circumscribed masses consisting of intersecting fascicles of monotonous spindle cells with eosinophilic cytoplasm, cigar-shaped nuclei, and fibrous stroma with foci of hyalinization. Spindle cells were immunohistochemically positive for SMA, Vimentin, WT1, Desmin, and Estrogen, while the Ki67 proliferative index was extremely low. Microscopic and immunohistochemical analyses together with clinical presentation confirmed diagnosis of disseminated peritoneal leiomyomatosis.

Conclusion: Disseminated peritoneal leiomyomatosis is a rare benign disease characterized by the presence of multiple smooth muscle nodules scattered throughout the peritoneal cavity thus mimicking malignancy. It predominantly affects women during their reproductive age. The development of DPL is affected by genetic factors, steroid hormones, metaplasia of mesenchymal stem cells, and iatrogenic factors. Latter one, such as the frequent use of laparoscopic power morcellation nowadays has increased the incidence of DPL. It is usually asymptomatic or presented with non-specific symptoms such as abdominal pain and distension, therefore in most cases is being discovered incidentally. The risk of malignant transformation is low, but as no spontaneous regression has been reported treatment is required with surgical resection being the main choice.

Keywords: Estrogen, disseminated peritoneal leiomyomatosis, DPL, morcellation

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Malignant Brenner tumor – Two cases of rare ovarian neoplasm

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Objective: Objective was to show two cases of rare malignant Brenner tumor (MBT).

Case report: A 62 year-old with symptoms of lower back and abdominal pain was admitted to CGO. On MRI and ultrasound complex left adnexal mass was seen. Left adnexectomy with partial omentectomy was performed and on frozen sections Brenner tumor was suspected. Tumor was mostly solid white-yellowish with smaller cystic formations and calcifications, measuring 13cm. Pathohistologically tumor was composed of highly atypical cells resembling transitional epithelium arranged in solid sheets, nests, cystic and papillary formations with atypical mitoses. Tumor cells were GATA3+, p63+, ER-, PR-, p53- with extremely low Ki67. Pathohistological and immunohistochemical analysis confirmed MBT (FIGO stage IA). Two months after initial surgery, hysterectomy with right adnexectomy, omentectomy and left inguinal lymph node extraction was performed with no evidence of disease dissemination.

A 78 year-old with symptoms of uterine prolapse and recurrent bleeding was admitted to CGO. Following complex right adnexal mass on ultrasound, adnexectomy was performed and malignant tumour was confirmed on frozen sections. Additional hysterectomy, left adnexectomy and omentectomy were performed. Tumor was described as multilocular cystic formation measuring 6cm with papillary proliferations. Pathohistologically tumor was composed of highly atypical cells resembling transitional epithelium, arranged in cystic formations, solid nests and papillary proliferations with atypical mitoses and foci of mucinous and squamous differentiation. These findings confirmed diagnosis of MBT with no evidence of disease dissemination (FIGO stage IA).

Conclusion: Malignant Brenner tumor is a rare ovarian neoplasm with unclear origin cell and favourable prognosis in early stages.

Keywords: Malignant Brenner tumor

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Tubular adenoma of the breast: a case report

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Objective: Tubular adenoma of the breast is a rare fibroepithelial tumor accounting for 0.13-2.8% of all benign breast lesions, most commonly discovered in young women. It typically presents as a solitary, palpable, well-circumscribed mass, but clinical and radiological features are often nonspecific. Microscopically, it is characterized by densely arranged round to oval glandular structures lined by inner epithelial cells and an outer myoepithelial layer surrounded by a thick stroma. These lesions are not associated with increased malignancy risk and surgical excision is the treatment of choice.

Case report: A 43-year-old woman presented with a firm, mobile, palpable mass in the lower outer quadrant of the left breast which was surgically excised. Gross examination of the specimen showed a grayish, well-circumscribed, lobulated tumor measuring 10 x 9 x 5 mm. Histopathologically, it consisted of a well-defined proliferation of round and uniform tubular structures with a basal myoepithelial layer, lined by an inner layer of regular epithelial cells, with a surrounding scant fibrovascular stroma. The luminal cells exhibited immunoreactivity for AE1/AE3, while the myoepithelial layer demonstrated positive expression for p63, Calponin, CD10, and SMA, confirming the diagnosis of tubular adenoma.

Conclusion: Tubular adenomas of the breast are rare, benign lesions that might be challenging to distinguish from other benign or malignant breast masses without histopathological confirmation. Acquiring a comprehensive understanding of the pathological and immunohistochemical features of this uncommon neoplasm is essential for accurately determining the appropriate diagnosis.

Keywords: breast, myoepithelial cells, tubular adenoma

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Myofibroblastoma of the breast in a male patient – a case report and literature review

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Objective: Myofibroblastoma, a rare benign stromal breast tumor, is primarily diagnosed in elderly men and postmenopausal women. Clinically, it presents as a palpable, firm, mobile mass, but may also be discovered incidentally. Mammography shows myofibroblastomas as oval or lobulated, well-defined masses, while sonography shows variable echogenicity. Myofibroblastomas have various histopathological variants: collagenous, cellular, infiltrative, myxoid, lipomatous, epithelioid, and decidual types. The classic histopathological appearance involves bundles of spindle cells separated by broad bands of hyalinized collagen stroma. Immunohistochemically, most myofibroblastomas are positive for vimentin, desmin, actin, CD34, CD10, estrogen, progesterone, and androgen, and negative for cytokeratins, EMA, S100, HMB-45, and CD117. The treatment of choice is wide surgical excision, and the prognosis is excellent, with no malignant potential nor risk of recurrence.

Case report: A 62-year-old male presented for a clinical examination due to a palpable, mobile tumor mass measuring approximately 4 cm at the junction of the upper quadrants of the left breast. Mammography revealed a lobulated tumor shadow measuring 42 x 29 mm at the indicated location. The lesion was surgically excised. The histopathological examination revealed a stromal tumor that was positive for CD34, caldesmon, Bcl-2, desmin, actin, estrogen, progesterone, and androgen, but negative for CKAE1/AE3, S100, and p63, leading to the diagnosis of cellular myofibroblastoma.

Conclusion: Since the clinical and radiological features of myofibroblastoma are nonspecific and differential diagnoses encompass a wide spectrum of breast conditions, histopathological and immunohistochemical verification after

core biopsy and/or excision is crucial for establishing the diagnosis of this rare entity.

Keywords: male breast tumors, mesenchymal tumors, myofibroblastoma

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Ductal carcinoma in situ within fibroadenoma - case report

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Objective: Fibroadenoma (FA) is a common, benign, biphasic tumour composed of stromal and epithelial elements. This report aims to present a rare case of ductal carcinoma in situ (DCIS) within a fibroadenoma.

Case report: A 37-year-old woman presented with a tumour in both breasts that was classified as BI-RADS 4A on mammography. A core needle biopsy of the tumour in the right breast revealed that it is a cellular complex fibroadenoma. A tumorectomy was performed, and a gross examination showed a well-encapsulated tumour measuring 18 mm in diameter with a grey-white, slightly firm, and lobulated cut surface. The histological diagnosis was low-grade DCIS within a FA. The stromal component was benign, however the epithelium consisted of ductal cell proliferation with cribriform and solid growth patterns. Immunohistochemical examination revealed that myoepithelial cells were positive for p63 and calponin. Tumour cells had an immunoprofile of estrogen receptor (ER) 8 and progesterone receptor (PR) 7. Because of the positive surgical margin, a subcutaneous mastectomy was performed, followed by ex tempore examination of two sentinel lymph nodes, both of which were without metastases.

Conclusion: Although FAs are a common subtype of benign tumours, they can be associated with DCIS. This case report, along with others like it, should increase awareness and encourage physicians and pathologists to consider this entity.

Keywords: DCIS, fibroadenoma, breast tumour

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Breast lumps during pregnancy – differential diagnosis: a case report

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Objective: Pregnancy is a special condition in which an organism undergoes various changes. Breast lumps occurring during pregnancy are usually small in size about 3cm, painless, solid, well-circumscribed, and mobile nodule masses that tend to grow slowly. Generally, they represent a diagnostic challenge given the reduced sensitivity of both clinical examination and radiological findings, due to the high density of the breast tissue. Elevated hormone levels during pregnancy stimulate the proliferation of blood vessels and glandular tissue while reducing stromal tissue. This case aimed to report a lactating adenoma and distinguish this entity from other lesions during pregnancy.

Case report: We present a case report of a 34-year-old female with lactating adenoma. Her clinical presentation included a change in the breast in the third trimester of pregnancy. A circumscribed, painless, and mobile mass was discovered with no additional findings. Pathohistological examination of specimens revealed hyperplastic lobules with glandular formations showing more or less abundant hobnailing phenomena with intraluminal eosinophilic secretions and inconspicuous myoepithelial cell layer separated by delicate fibrovascular stroma. The immune profile of the preparations showed a positive reaction of CK14 and p40 markers, which proved the presence of myoepithelial cells and distinguished this case from other breast lesions.

Conclusion: Although, only 3% of solid breast masses are represented as breast carcinomas, surgical extirpation along with the following pathohistological and immunohistochemical analysis must be conducted to avoid overdiagnosing and distinguishing the benign lesions, such as lac-

tating adenomas or fibroadenomas, from malignant origin of the tumor.

Keywords: lactating adenoma; breast; pregnancy; case report

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Idiopathic granulomatous mastitis: a case report

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Objective: Idiopathic granulomatous mastitis (IGM) is a rare chronic inflammatory disease of the breast of unknown etiology and it is a diagnose of an exclusion so the other granulomatous inflammation's causative agents must be excluded.

Case report: A 37-years-old patient complained of redness, warmth and swelling of the left breast. On examination there was a palpable lesion of 3.5cm in diameter and the physician recommended MRI of the breast. Twenty days later, she came back with worsening symptoms, the lesion was punctated and sent for microbiology examination and it was sterile. In MRI, the inferior outer quadrant lesion was described as non-mass post-contrast signal intensity enhancement (PCSIE) measured 7 cm in diameter, which contained multiple ring-like zones of PCSIE and non-homogenic areas of edema. The retroareolar ducts were accented, the nipple was withdrawn with local skin edema. Core needle biopsy was performed and showed that breast lobular architecture was destroyed by presence of multiple granulomas. The centers of described granulomas contained focal microabscesses with neutrophils and eosinophils admixed with necrosis or there were granulomas without central necrosis. All of described granulomas were made of Langhans giant cells, epitheloid cells and foamy macrophages with mononuclear collarettes, all separated with fibrous tissue. PAS and Ziehl Neelsen stain showed no microorganisms present, so diagnose was made by excluding all granulomatous inflammation causes.

Conclusion: IGM can mimic breast cancer clinical signs so

CNB of lesion can be useful tool for distinction between benign and malignant lesions but also rare diseases.

Keywords: Breast Diseases, Granulomatous Mastitis, Inflammation

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Myocardial infiltration and acute abdominal pain as a result of unrecognized diffuse large B –cell

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Objective: Diffuse large B-cell lymphoma (DLBCL) represents aggressive lymphoproliferative disease with frequent extranodal presentation. This disease represents almost 30% of all globally diagnosed lymphomas. Most commonly infiltrated extranodal organs are stomach, then structures of waldeyer ring, then bones, testicles, ovaries, spleen, salivatory glands, liver, kidney, and rarely other organs. In rare cases comes to infiltration of heart muscle by DLBCL. Choice of treatment is systemic immunochemotherapy based on Rituximab.

Case report: Female patient aged 54 years becomes hospitalized at gastrointestinal clinic of UCC of Nis due to acute abdominal pain, and shortly after all clinical protocols dies. After revision of medical documentation, we have discovered that she was psychiatric patient, under which circumstances, her presentation of symptoms is questionable. Autopsy has discovered presence of large quantities of free thoracic and abdominal liquid, and macroscopic detectable organ changes. Pathohistologic microscopic examination discovered tissue infiltration of almost all organs, and even heart muscle, giving the diagnose of non-Hodgkin large B-cell lymphoma, not otherwise specified (NOS), confirmed by immunohistochemistry cell markers: Vimentine -, CD20 +, antiCD45 +, CD163 +, CD38 -/+, CD56 -/+, Lambda +, Kappa +, CD3 +/-, CD68-, CD117-, S100-, CKAE1/AE3 -.

Conclusion: From this case report we can concur that DLBCL can remain undetected because of polymorphic un-

specific clinical presentation and in rare cases even heart muscle can be affected.

Keywords: DLBCL, heart infiltration

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Sporadic Burkitt's lymphoma of the large intestine in elderly patient, case report

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Objective: Burkitt's lymphoma is highly aggressive non-Hodgkin's lymphoma. Three forms are distinguished: endemic, sporadic and the immunodeficiency associated. The sporadic form is the most common lymphoma in USA and Western Europe and accounts for less than 1% of all adult non-Hodgkin lymphomas. It is most often diagnosed in children and young adults. It is the most common form of lymphoma in the pediatric population.

Case report: A 77-year-old female patient was operated for ileus. The distal part of the ileum, the cecum with the appendix and the ascending colon were removed. A 9.5 cm circumferential ulcero-infiltrative tumor was found in the area of the cecum with complete infiltration of the appendix and the adjacent part of the small intestine. Ileocecal valve is preserved. In the surrounding adipose tissue 17 lymph nodes were found, without tumors. Immunohistochemical stainings were positive for: CD 20 and BCL 6. Immunohistochemical stainings were negative for: CD3, cyclin-D1 and BCL2. The proliferative index (Ki-67) was 100%. After 40 days, the patient was operated again for ileus. A 110 cm long small intestine was surgically removed with fibrinous deposits on the serosa and diffuse and nodular infiltration by lymphoma cells. The patient died during postoperative

recovery.

Conclusion: Our case indicates that sporadic Burkitt's lymphoma of the large intestine can occur at an atypical age. Ileus was an absolute indication for operative treatment of the patient without a previous pathohistological diagnosis. Rapid and extensive postoperative disease progression indicate that operative treatment in these patients is a poor choice of treatment.

Keywords: Burkitt's lymphoma, large intestine, sporadic, ileus, elderly patient

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Unusual EMA and pan-keratin negative epithelioid sarcoma

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Objective: Epithelioid sarcoma is a rare malignant tumor that is positive for EMA and pan-keratin, with frequent loss of SMARCB1 expression.

Case report: We present the case of a 65-year-old patient with lower back pain and an ultrasound scan that showed an expansive formation in the abdomen with a diameter of 5.2 cm. Cytopuncture and core biopsy were performed under CT control. Cytologically, the smear showed a monomorphic population of poorly differentiated malignant cells. The cells formed clusters within which a homogeneous substance could be seen. Immunocytochemistry showed weak S100 positivity, while CK7 and CK20 were negative. It was

concluded most likely to be a tumor of mesenchymal origin. Histology showed clusters of uniform cells with scant cytoplasm, which were immunohistochemically negative for S100, melan A, CD45LCA, CKAE1/AE3, EMA, CD 138, factor VIII, desmin, SMA, MSA, chromogranin and synaptophysin, while CD99 was positive. For additional processing, prof. Abbas Agaimy, MD, PhD, (University Hospital Erlangen, Germany) was consulted, who was of the opinion that „this is a SMARCB1-deficient malignant neoplasm with rhabdoid features and an unusual complete absence of EMA and pan-keratin expression.“ He was also of the opinion that „primary tumor site in other organs should be excluded, after which the diagnosis of keratin-poor epithelioid sarcoma can be accepted.“ The patient underwent surgery and adjuvant chemoradiotherapy, which led to remission.

Conclusion: Further research is needed to better understand the role of SMARCB1 loss of expression in tumor immunogenicity, aiming to develop optimal immunotherapeutics and new treatment strategies for these aggressive tumors.

Keywords: core biopsy, cytopuncture, epithelioid sarcoma, SMARCB1

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Inflammatory myofibroblastic laryngeal tumor-case report

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Objective: Inflammatory myofibroblastic laryngeal tumor (IMT) is rare benign process which appears in lungs, but it is can also be diagnosed in other localizations such as ocular orbit, spleen, larynx. Although these tumors are histologically benign, they have tendencies to become locally aggressive, growing rapidly and and can be manifested by progressive symptoms. Main treatment is surgical excision. IMT is most often found on the vocal cords, even though it can be seen in the entire larynx.

Case report: Patient is 61 – year old female, admitted to the emergency center because of severe stridor breath-

ing. Patient reported that symptoms persisted for several days with worsening. The patient is a heavy smoker for 30 years, 30-40 cigarettes per day. Laryngeal imaging showed vocal cord swelling, myxomatotic tissue change, with sufficient breathing space, but due to inflammatory process, breathing is obstructed. Laryngomicroscopy with left and right vocal cord biopsy revealed presence of proliferation of spindle cells, localized in partially myxoid and collagenized stroma, and inflammatory plasmacytes and lymphocytes. Immunohistochemical analysis showed expression of vimentin and SMA, and Ki67 showed proliferate activity in about 10% of nuclei of tumor cells which confirmed pathohistological diagnosis of IMT.

Conclusion: Inflammatory myofibroblastic laryngeal tumor is a very rare neoplasm which can mimic malignant process. Immunohistochemistry plays main role in IMT diagnosis. Main choice of treatment is surgical excision with distance of surgical margins of at least 5mm each. Clinical follow-up is necessary with the aim of early detection of recurrence of the tumor.

Keywords: Inflammatory myofibroblastic tumor, IMT, larynx.

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Unique presentation of primary retroperitoneal PEComa with lymphoma-like symptoms: A case report

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Objective: Perivascular epithelioid cell tumor (PEComa) belongs to a family of rare mesenchymal neoplasms that can arise in various organs and are composed of cells that have myomelanocytic differentiation. We present histology and immunofenotype of PEComa of uncertain malignant potential.

Case report: A 73-year-old female patient presented with

elevated body temperature, night sweats and loss of 20kg of body weight during a couple of months. CT scan found 162x89mm retroperitoneal mass compressing left kidney and spleen. Surgical biopsy was performed and diagnosed as granular cell tumor. Six months later MRI showed mass size increase to 200x120mm. Surgical excision was performed.

Tumor weighted 2011g, with dimensions of 240x190x80mm. Capsule was intact, focally thickened with solid and cystic parenchyma, containing extensive areas of hemorrhage and necrosis.

Histological examination showed moderately to prominently atypical, polygonal cells with hyperchromatic nuclei and abundant, eosinophilic cytoplasm that focally contains dark pigment, in trabecular and solid arrangement. Mitotic count is low. Stroma is scant with thin walled blood vessels, without lymphovascular invasion. The immunohistochemical staining showed positivity to Vimentin, CD68, NSE, HMB45, Melan-A, CD117, CDK4 and Desmin, with no immunoreactivity to PAX8, ER, SMA, CD163, SOX-10, CD34, Calretinin, Inhibin, myoD1, MDM-2, CK20, CK7, PanCK, S-100, Synaptophysin, Chromogranin. Ki-67 proliferation index was expressed in 5% of tumor cells.

Conclusion: PEComas are rare tumors with variable malignant potential. Though surgical resection is the treatment of choice for PEComas, some studies showed potential benefits to using mTOR inhibitors as target treatment or radiation courses for patient at higher risk to prevent metastases or recurrence.

Keywords: PEComa, retroperitoneum, immunohistochemistry

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An incidental finding of a desmoid tumor in an inguinal hernia

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Objective: Desmoid tumors are benign neoplasms originating from connective tissue. The etiology of desmoid tumors remains unclear, although they are frequently associated with genetic predispositions, hormonal factors, trauma, and previous surgical interventions. They present diagnostic challenge due to their rarity, diverse clinical manifestations, locally aggressive behavior, and high recurrence rates

Case report: A 46-year-old male presented with a noticeable bulge in the right groin for the past two months. Clinical examination revealed a soft abdomen with a palpable, painless right inguinal hernia, which was reducible. The patient underwent hernioplasty. Pathologist received a tissue specimen measuring 6.8x6.0x0.2 cm. Gross examination revealed a whitish, spherical formation measuring 3.0x0.8x0.6 cm within the hernia sac. Histological examination revealed unremarkable mesothelium, beneath which was unremarkable connective tissue with blood vessels lined by normal endothelium. The above-described spherical lesion revealed spindle cell proliferation without atypia or mitosis, embedded in collagenous stroma with a partially keloid appearance. Immunohistochemical staining was positive for Smooth Muscle Actin, Beta-Catenin (nuclear and cytoplasmic), and, focally, Desmin. Other markers including CD34, ALK, S100, Calretinin, Cytokeratin AE1/AE3, and Cytokeratin 5/6 were negative. Fluorescence in-situ hybridization analysis for MDM2 gene did not show amplification. The lesion was diagnosed as a desmoid tumor.

Conclusion: Desmoid tumors can be challenging to manage due to their unpredictable behavior, and variable response to treatment modalities including observation, surgery, radiotherapy, and systemic therapy. Management should involve a multidisciplinary approach due to many treatment options and a crucial clinical follow up after treatment.

Keywords: Desmoid tumor, Fibromatosis, Hernia, Immunohistochemistry

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Kaposi sarcoma: a case report

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Objective: Kaposi sarcoma (KS) is an uncommon angioproliferative endothelial neoplasm with distinctive clinicopathological, epidemiological and immunophenotypic characteristics. KS is the most common neoplasm in people with human immunodeficiency virus (HIV) infection. Its pathophysiology has been associated with the presence of a member of herpes virus type 8 family.

Case report: A 47-year-old male resorted to an outpatient clinic complaining of disseminated dermatosis. The patient referred multiple skin lesions that appeared two months earlier. Lesions were presented as erythematous livid plaques on the fourth finger of the left foot with rapid progression in a month to the trunk, right arm, right thigh, left lower leg, pubic region and right groin. HIV serology was positive. The method used for detection was chemiluminescence on Abbott's Alinity and the results were 1117.34 S/CO (reference value >1.00 S/CO). The patient also had positive anti-VZV IgG, anti-CMV IgG, anti-Toxoplasmosis IgG, anti-HBc, anti-HBs and TP antibodies.

A skin biopsy was performed as an excision biopsy from the right thigh. Histological examination demonstrated discrete nodules composed of intersecting fascicles of uniform spindle cells, intervening blood-filled spaces between spindle cells (slit-like and sieve-like). Endothelial cells formed a disorganized monolayer with dissolution of colla-

gen fibers. Immunohistochemistry was positive for CD34, CD31, D2-40, HHV8 with Ki-67 above 20%. These findings are compatible with pathological nodular stage KS.

Conclusion: In the Balkan countries the prevalence rate of HIV-1 infection is low, under 0.1%. Diagnosis of KS by histopathological examination is the gold standard and we hereby demonstrate the importance of the right diagnosis.

Keywords: AIDS-related Kaposi sarcoma, HIV, Human Herpesvirus 8, Kaposi sarcoma

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Giant cell tumor of bone during pregnancy resembling primary bone sarcoma: A case report

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Objective: Giant cell tumor of bone (GCTB) is a rare, locally aggressive bone tumor with only 32 cases reported during pregnancy or postpartum. We report this case to emphasize the importance of a multidisciplinary approach in the diagnostics and management of GCTB during pregnancy.

Case report: We present a case of an 18-year-old female at 32 weeks of gestation misdiagnosed with a knee contusion and conservatively treated for 1 month in a non-referral center. An X-ray revealed an osteolytic lesion 52x43mm, with cortex invasion and periosteal reaction causing a pathological fracture of the left distal femur, highly suspicious of bone sarcoma, considering the patient's age, radiologic, and clinical features.

The biopsy revealed a highly cellular tumor composed of a myriad of multinucleated osteoclast-like giant cells amidst oval and spindled mononuclear tumor cells with dispersed nuclear chromatin and small nucleoli with focal hemorrhage. Tumor cells showed p63 and CD68 immunoreac-

tivity. A diagnosis of giant cell tumor of bone was made. To preserve the patient's pregnancy, distal femur resection was performed with reconstruction of the defect according to the Campanacci technique. Grossly the distal femur resection measured 7x6x5cm containing an intramedullary soft, grayish tumor with a hemorrhagic appearance measuring approximately 6,5x6x4cm. Microscopically, the morphology was similar to that of the biopsy specimen, with recent hemorrhages, hemosiderin deposits, and necrosis present. Vascular invasion was identified.

Conclusion: A multidisciplinary approach is imperative for a correct diagnosis in cases of bone tumors during pregnancy offering the best treatment for preserving the mother and child's health.

Keywords: Giant cell tumor of bone, pregnancy, primary bone tumors, GCTB.

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Intramuscular granulomatous reaction after HPV vaccine injection

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Objective: This article describes a granulomatous reaction in a young woman as an adverse effect of a human papillomavirus (HPV) vaccine. The vaccine against HPV infection is recommended according to the Serbian National Immunization Program, for children and adolescents aged 9–19 years. The common side effects of HPV shots include pain, redness or swelling on the arm where the vaccine was administered, fever, dizziness or fainting, nausea, headache or fatigue and muscle or joint pain. A granulomatous reaction at the site of injection has rarely been described.

Case report: A 19-year-old female presented for clinical examination because of a palpable intramuscular tumor mass about 2cm in size on the upper arm. The lesion was

surgically excised. Histopathologic examination revealed an inflammatory granulomatous reaction with a necrotic/necrobiotic center surrounded by epithelioid histiocytes and lymphocytes. Immunohistochemical staining (CD68, LCA, S100, Cyclin D1, CD35, CD21, CK AE1/AE3 and Fascin) was performed. After a further clinical examination, we found that the patient had received an HPV vaccination.

Conclusion: We report a case characterized by the presence of a persistent nodule at the injection site of HPV vaccination, showing a granulomatous reaction with central necrosis, which should be considered an adverse effect of HPV vaccination due to the high vaccination rate in young women. Differential diagnoses should also be considered.

Keywords: granulomatous reaction, HPV vaccine, side effect

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Alveolar rhabdomyosarcoma in a patient with adenocarcinoma of the colon

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Objective: Rhabdomyosarcoma is a malignant tumor of striated muscle tissue. Alveolar rhabdomyosarcoma is a histological subtype that mostly occurs in children and adolescents, rarely in the adult population, with a high malignant potential and a frequent fatal outcome.

Case report: A 46-year-old man, undergoing chemotherapy due to a previously diagnosed mucinous adenocarcinoma of the colon, complains of pain in the left pectoral region of the chest. Computed tomography (MSCT) of the abdomen and chest was made with initial suspicion of metastatic lung deposits. MSCT showed soft tissue mass in left hemithorax at the level of VII, VIII and IX rib with pleural infiltration. A biopsy was performed and sent to pathology. Pathohistological analysis revealed the presence of scanty muscle and fat tissue with a neoplastic infiltration of strikingly pleomorphic, atypical cells, arranged in alveolar-like

spaces with fields of weakly cohesive cells. Numerous anaplastic giant multinuclear tumor cells, as well as cells of rhabdomyoid morphology, with the presence of patchy necrosis, were also seen. Immunohistochemical analysis demonstrated diffuse positive expression of Vimentin, Desmin, CD99, focal expression of CKAE1/AE3, while the rest of the analyzed markers were negative (Actin, SMA, CD10, CD34, CD68, S100, TTF1, LCA, p63, WT1, CDX2, CD56). Based on micromorphological and immunohistochemical analysis, the diagnosis of alveolar rhabdomyosarcoma (ARMS) was established. The patient was referred to multidisciplinary tumor board for further oncological treatment.

Conclusion: Although rare, alveolar rhabdomyosarcoma can also occur in adulthood, as evidenced by our case. Therefore, a multidisciplinary approach is very important in diagnosis of these soft tissue neoplasms with a special focus on improving both diagnostics and adequate therapeutic treatment.

Keywords: Alveolar rhabdomyosarcoma, pleura, mucinous adenocarcinoma, pathohistology, immunohistochemistry

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Case report: Rare polypoid lesion of sigmoid colon

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Objective: Gastrointestinal leiomyomas are benign smooth muscle tumors that occur most frequently in the esophagus, while the colorectum is a rare site, accounting for about 3% of all gastrointestinal leiomyomas. Mostly they have sessile growth pattern, and are often not detected by colonoscopy.

Case report: We present the case of a 66-year-old patient who was initially admitted to the Institute of Gastroenterology due to severe microcytic anemia. Colonoscopy, gastroscopy, and abdominal ultrasound were performed, along with extensive gastroenterological treatment. A sigmoid polyp measuring less than 10 mm was verified by colonoscopy (NICE I), and it was removed. The resected material was sent for further pathohistological analysis. Histologically, the received biopsy sample showed the mucosa of the large intestine on the surface, that was polypoidally raised, under which in muscularis mucosae there were clusters and bundles of bland looking spindle cells without atypia and mitoses. Necrosis was also absent. Immunohistochemically, the tumor cells were positive for SMA and Desmin, and negative for CK AE1/AE3 and CD 117. The histological and immunohistochemical profile corresponded to a gastrointestinal leiomyoma.

Conclusion: Although gastrointestinal leiomyomas are very rare, especially in the colon and rectum, they should be taken into account when making the correct diagnosis of stromal polypoid lesion, and it is necessary to exclude other mesenchymal tumors especially gastrointestinal stromal tumors (GIST).

Keywords: Leiomyoma, Polyp, Sigmoid Colon

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Human alveolar echinococcosis mimicking hepatic malignancy

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Objective: To present the second recognized case report of human alveolar echinococcosis in Serbia caused by Echinococcus multilocularis.

Case report: A 57-year-old man was admitted to our hospital due to 10-day lasting symptoms of jaundice, nausea and stomach pain. He had no family history of gastrointestinal malignancy or liver disease. Laboratory tests showed very

elevated liver enzymes, total bilirubin, and CRP. MRI showed an enlarged liver with heterogeneous, predominantly T2 hyperintense change, with zones of necrosis, enlarged hilar lymph nodes, and perilesional dilatation of intrahepatic bile ducts, primarily of infiltrative features, suspected to be a cholangiocarcinoma. The lesion of the liver underwent radical resection and was confirmed as alveolar echinococcosis by pathological examination. Histological criteria for diagnosis included the identification of multiple multilocular cysts covered with chitinous membranes, accompanied by numerous foreign body granulomas and broad areas of necrosis. Perineural propagation of echinococci and one hilar lymph node with wide necrotizing granulomas with chitinous membranes were also present. The patient had no surgical complications after the operation and was discharged with a 800 mg daily dosage of Albendazole.

Conclusion: Human alveolar echinococcosis is one of the most dangerous and potentially lethal parasitic zoonoses, with a mortality rate exceeding 90% in untreated patients. This case highlights the need for clinicians to include alveolar echinococcosis in the differential diagnosis of liver lesions, even in patients who have never lived in or traveled to known endemic areas, because of the high lethality of this disease and its infiltrating, metastatic, tumor-like behavior.

Keywords: echinococcosis, multilocular, liver

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Primary sclerosing cholangitis – A case report

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Objective: To show a case of primary sclerosing cholangitis (PSC).

Case report: A 72-year-old female patient was admitted to UC being disoriented and bradypsychic with symptoms of diarrhea, nausea, and vomiting that lasted five days while having a dry cough with pain in the upper abdomen for the last two weeks (heteroanamnesis). After CT of the endocranium and exclusion of acute neurological disorder, CT of the abdomen showed multiple hypodense abscess-like lesions in the right liver lobe. Laboratory showed increased values of bilirubin, ALT, AST, and APs. The following day, the patient had surgery, which showed multiple lesions in the S3, S4, and S8 segments of the liver. Cholecystectomy with S3 lesion biopsy (for ex tempore analysis which confirmed benign process) and subsequent resection were performed. Grossly, an off-white liver fragment, with a diameter of 15 mm, on a standard HE staining showed a classic “onion-skin” fibrosis around atrophic bile ducts, with fibrous scars in places of obliterated ducts, as well as large ducts rupture with prominent neutrophilic response (abscesses). Following surgery, the patient was in the intensive care unit for 5 days until stable and discharged on the 18th postoperative day.

Conclusion: PSC is a rare chronic and progressive cholestatic liver disorder. It is more common in men, and in half

of the cases shows no symptoms at the time of diagnosis. 10-20 % of patients develop cholangiocarcinoma. Increased liver panel and bile-duct strictures detected using either MR or ER cholangiography, while excluding secondary SC, confirms diagnosis with no need for biopsy.

Keywords: Primary sclerosing cholangitis, “onion-skin” fibrosis, cholangiocarcinoma.

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Exogenous lipid pneumonia associated with gastroesophageal reflux disease

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Objective: Exogenous lipid pneumonia (ELP) is caused by inhalation or aspiration fatty substance and can include numerous of differential diagnoses. Clinical manifestations can vary.

We report the case of 68 year old women with ELP.

Case report: A 68-year-old woman non-smoker presented with fever, cough and shortness of breath. Her past medical history was significant for gastroesophageal reflux disease and diabetes mellitus. Pulmonary auscultation revealed crackles. A chest CT scan showed ground-glass opacities in the right lung. These opacities were predominating in the lower lobe where a foreign body was seen during the sec-

ond bronchoscopy but not removed. After that, an antero-lateral thoracotomy with right lobectomy was performed. Macroscopically gross appearance of an ill-defined, pale yellow area of the lobe suggested lipoid pneumonia. The oil red staining demonstrate that the bronchiole and alveolar like structure filled with foamy histiocytes.

Conclusion: Medical history is often crucial in the diagnosis of ELP.

Keywords: Gastroesophageal reflux, exogenous lipoid pneumonia, oil red.

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Radiological-pathological correlation of pulmonary cavitory lesions: report of three cases

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Objective: Diverse etiologies cause pulmonary cavitory lesions, but the most common causes in adults include malignancy and infection.

Case report: This study presents three cases hospitalized at the Institute for Pulmonary Diseases of Vojvodina to explain the etiology of pulmonary cavitory lesions detected on computed tomography scans. In the first case, a 66-year-old male patient was operated on due to an irregular hyperdense lesion of 3 cm in diameter with a smaller central zone of excavation localized in the right upper lobe. Histopathological analysis showed circumscribed areas of fine-grained acidophilic necrosis surrounded by palisade-arranged epithelioid cells with positive acid-fast bacilli on Ziehl–Neelsen staining. The second case is a 58-year-old female patient who had a lobectomy to clarify the etiology of an irregular hyperdense lesion with a centrally excavated zone localized in the right lower lobe with an approximate diameter of 2.2 cm. Histopathological findings corresponded to a partially necrotic squamous cell carcinoma. The third case represents a 67-year-old female patient with a

radiologically suspected infiltrative lesion within complete atelectasis of the left lower lobe. The described lesion was poorly delineated and had a few smaller zones of hypodensity that could correspond to cavitations, followed by some calcifications. Actinomycosis was diagnosed after bronchoscopy and lobectomy, with the help of special stainings and characteristic histologic appearance.

Conclusion: Differential diagnosis of pulmonary cavitory lesions can be challenging, especially from radiological and pathological aspects. Therefore, these lesions should be cautiously evaluated by correlating pathological, radiological, and clinical findings.

Keywords: Actinomycosis, Pathology, Radiology, Squamous cell carcinoma, Tuberculosis

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Multilocular thymic cyst: a case report

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Objective: Benign thymic cysts are uncommon lesions, accounting for approximately 3% of all anterior mediastinal masses. They are typically multilocular and should be distinguished from congenital cysts for several reasons: they may recur after excision, they may be associated with thymic neoplasms such as thymoma or thymic carcinoma, and they may adhere to adjacent structures, mimicking invasive neoplasms during thoracotomy.

Case report: We present the case of a 70-year-old woman who underwent surgery on the aortic and mitral valves at our institution. During the chest opening in the anterior mediastinum, a tumor nodule was discovered, which was surgically excised entirely. The tumor nodule measured 8 x

6 x 4.5 cm, exhibiting a grayish-yellow color and a smooth surface. Upon sectioning, it appeared multicystic with cystic spaces filled with brownish paste-like material. Histologically, multilocular cystic formations were surrounded by connective tissue capsules with focal calcifications. The cystic spaces were lined by flattened and focally cylindrical epithelium with goblet cells and filled with abundant finely granular material, numerous foamy macrophages, and blood. Additionally, a marked giant cell reaction with numerous giant multinucleated cells resembling foreign body types with cholesterol crystals was observed within the cyst wall. Smaller foci of thymic tissue were also noted.

Conclusion: Multilocular thymic cysts are rare acquired lesions of the thymus, likely resulting from inflammation but may also be associated with neoplasia. Complete surgical resection and meticulous histopathologic examination are recommended for all patients suspected of having multilocular thymic cysts.

Keywords: cardiac surgery; mediastinum; thymic cyst.

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Pleural synovial sarcoma in a one-and-a-half year-old child: a case report

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Objective: Synovial sarcoma of the pleura is a very rare entity, particularly in pediatric population.

Case report: A one-and-a-half year-old female child presented with two weeks long cough, dyspnea and high fever. She was treated with antibiotics for presumed pneumonia. Chest X-ray showed shadowing of the right hemithorax. Multislice computed tomography (MSCT) showed expan-

sive tumor mass 10 x 10cm in this region, pushing liver caudally and trachea and heart to the left. Biopsy showed a lesion composed of spindle cells arranged in a fascicular growth pattern, with nuclear atypia and areas of necrosis. Immunohistochemistry demonstrated positivity with CKAE1/3 (focally), vimentin, TLE-1, CD99, bcl-2, CD56, and negativity for alfaSMA, H-caldesmon, CD117, desmin, myoD1, myogenin, S-100, SOX10, CD34, CD31, CK7, CK20, napsinA, and TTF-1. Fluorescent in situ hybridization for SS18:SSX rearrangement showed positive result and diagnosis of pleural synovial sarcoma was made. Neoadjuvant chemotherapy was given, followed by surgical resection of tumor. Histopathological examination of the resected specimen showed therapy response with necrosis in 93% of the tumor. After a 5-month follow up, there were no signs of recurrence or metastases.

Conclusion: Our case represents a rare presentation of synovial sarcoma of the pleura in a one-and-a-half-year-old child. This tumor is highly aggressive, especially due to localization, but in our case had an excellent treatment response. Synovial sarcoma of the pleura should be considered in differential diagnosis of mesenchymal pleural tumors, especially in children and adolescents.

Keywords: mesenchymal neoplasm, pleura, synovial sarcoma

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Harmonization of PD-L1 testing in non-small cell lung cancer (NS-CLC): challenges in daily practice

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Objective: Tumor expression of Programmed death-ligand 1 (PD-L1) is an important but imperfect predictive biomarker for treatment with immune checkpoint inhibitors. High tumor PD-L1 expression, detected by immunohistochemistry (IHC) typically on formalin-fixed paraffin-embedded (FFPE) histological specimens, is linked to better response. Multiple PD-L1 IHC assays have been approved by the FDA. However, different antibodies show different limitations in terms of sensitivity.

Case report: We present a 63-year-old male whose chest CT revealed a spiculated nodule on apicoposterior segment of the upper lobe of the left lung. First atypical resection, then sublobar anatomical resection with dissection of hilar and mediastinal lymphatics due to high operative risk was performed and histological examination revealed mixed-type adenocarcinoma (solid and acinar type). IHH showed positive napsin A and TTF1 stains. PD-L1 testing on Ventana BenchMark GX with SP263 antibodies showed a negative result (0%).

Four years later control CT showed an infiltrating mass on the edges of the earlier performed resection. Histological examination demonstrated relapsus of previously diagnosed adenocarcinoma. PD-L1 testing was performed again on Dako Autostainer Link 48 with Kit 22C3 pharmDx. Examination showed positivity in 80% of tumor cells.

Due to a discrepancy with previous results, we repeated PD-L1 testing on first tested FFPE with negative results now with Dako Autostainer Link 48 with Kit 22C3 pharmDx, tumor cells showed 60% positivity and on relapsing adenocarcinoma we used Ventana BenchMark GX with SP263 antibodies. Tumor cells showed 80% positivity.

Conclusion: We showed a consistent discrepancy in PD-L1 results when different antibodies were used.

Keywords: Adenocarcinoma of Lung, CD274 protein, human, Immune Checkpoint Inhibitors, Immunohistochemistry

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Liquid biopsy for the detection of EGFR mutations in lung cancer: A case report

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Objective: Activating gene mutations of the epidermal growth factor receptor (EGFR) are a predictive biomarker for therapy with tyrosine kinase inhibitors (TKIs). Liquid bi-

opsies are minimally invasive procedures based primarily on the molecular examination of circulating cell-free tumor DNA (ctDNA) isolated from body fluids.

Case report: An 82-year-old woman, a non-smoker with neuropsychiatric comorbidity, came to the Institute for Pulmonary Diseases of Vojvodina in September 2021 due to severe weakness and dyspnea. Computed tomography (CT) of the chest showed a massive bilateral pleural effusion, an irregular hyperdense lesion apically in the left lung, and mediastinal lymphadenomegaly. Cytology of the pleural fluid (cell block) confirmed lung adenocarcinoma. This sample was limited for EGFR, but insufficient for PD-L1 and ALK testing. DNA was isolated from the cell block using the Cobas® DNA Sample Preparation Kit. Due to the low DNA concentration, the Cobas® EGFR Mutation Test V2-based real time PCR analysis was not successful. A liquid biopsy was performed. ctDNA was isolated from 2 mL EDTA blood plasma using the Cobas® cfDNA Sample Preparation Kit. The EGFR test revealed the presence of deletion in exon 19. In November 2021, treatment was started with erlotinib, a first-generation TKI, at a dose of 150 mg/day. Due to the deterioration of the patient's performance status, the multidisciplinary tumor board decided to discontinue erlotinib in February 2022.

Conclusion: Tissue biopsy remains the gold standard for all molecular tumor tests. However, liquid biopsy may be an alternative approach for EGFR testing when an adequate histological or cytological sample is not available.

Keywords: Cell-Free Nucleic Acids, EGFR, Lung Neoplasms

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Lung cryptococcosis as a sign of an underlying immunocompromised condition – case report

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Objective: Fungal infections are emerging as a significant challenge to public health, especially with the rise in immunocompromised individuals worldwide. The radiological presentations of this condition encompass a diverse array of potential diagnoses, extending to include malignant diseases among them.

Case report: We present the case of an asymptomatic fifty-six-years-old male patient who underwent for surgical treatment as a diagnostic and therapeutic procedure for radiologically verified lung mass. Computed tomography revealed the presence of a 19 mm soft tissue excavated lesion in the upper lobe of the right lung. Additionally, discrete changes in density resembling ground glass opacities were observed in the remaining lung parenchyma. Imprint smear stained with MGG, GMS and PAS, as well as in histological samples stained H&E, GMS, and PAS showed necrotizing granulomatous inflammation with presence of rounded/oval shaped, fungi ranging from 2-15 μm which were GMS and PAS positive. Based on cytological, histological and molecular (PCR) analysis, fungi belongs to the *Cryptococcus neoformans* species. Due to the patient's poor general condition and the detected infection, further tests were conducted, confirming the presence of HIV infection.

Conclusion: Fungal lung infections are among the potential alternative diagnoses for suspicious lung lesions indicative of malignancy. Histological verification stands as the pre-

ferred diagnostic method for such lesions. Imprint cytology smears prove beneficial in revealing granulomatous inflammation and yeast organisms. Confirming the morphological diagnosis requires microbiological culture and molecular identification of the causative organism.

Keywords: cryptococcosis; mycoses; immunocompromised host; pulmonary fungal infections

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Pathological rib fracture as a presentation of Langerhans cell histiocytosis

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Objective: Langerhans cell histiocytosis (LCH) is a rare clonal proliferative disease caused by the aggregation of Langerhans cells in various organs. LCH most commonly affects the skeletal system, with the mandible being the most frequent site (30%), and the ribs being the least affected (6%).

Case report: A thirty-seven-year-old patient presented with left-sided chest pain persisting over the past 6 months. Computed tomography examination revealed an osteolytic lesion measuring 15 mm in diameter with a soft tissue component and a pathological rib fracture, located in the middle axillary line of the left fourth rib. Skeletal scintigraphy demonstrated a solitary focus of pathological hypercalcification in the fourth rib. A bone marrow biopsy ruled out hematological diseases, prompting the recommendation for partial rib resection to clarify the lesion's etiology. For histopathological analysis, a 4 cm segment of the rib was excised, focusing on a central thickening disrupting the bone structure upon cross-section. Microscopic examination revealed infiltration of tumor tissue within residual bone tissue. The tumor tissue consisted of histiocytoid large cells with oval to slightly elongated nuclei, irregular nuclear membranes, nuclear grooves, and abundant pale-eosinophilic cytoplasm. Immunohistochemical staining showed

positivity for CD1a and S-100, consistent with Langerhans cells. Additionally, dense infiltrates of eosinophilic granulocytes were observed between clusters of Langerhans cells and bundles of connective tissue.

Conclusion: LCH is a rare disease with variable manifestations. A solitary rib lesion with a pathological fracture is an uncommon presentation and can be easily misdiagnosed.

Keywords: chest wall; Langerhans cell histiocytosis; pathological fracture

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Mediastinal mixed germ cell tumor with a rare component – case report

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Objective: The range of microscopic entities found in germ cell tumors is highly diverse. The presence of a polyembryoma component is uncommon in gonadal locations and even more so in extragonadal sites, with only a handful of cases reported worldwide.

Case report: A twenty-five-year-old patient was admitted to the hospital for the treatment of an undiagnosed mediastinal mass. Among his symptoms, he reported chest pain over the past 10 days. The computed tomography scan revealed a soft tissue mass measuring 10x7.3x10.5 cm in the anterior mediastinum. Following appropriate preoperative preparations, the patient underwent surgical treatment with video-assisted thoracoscopy, followed by medial sternotomy in order to perform tumor excision. Macroscopically, the tumor appeared partially encapsulated with a nodular surface. Upon cross-section, it displayed a distinctly heterogeneous appearance with multiple cystic formations. Microscopic examination revealed that the tumor comprised several components: immature teratoma (50%), mature ter-

atoma (25%), polyembryoma (20%), and seminoma (5%). The polyembryoma component consisted of embryoid bodies composed of embryonal carcinoma cells (positive for CD30 and OCT3/4), situated within “amion-like” cavities surrounded by a yolk sac tumor component (positive for Glypican 3 and AFP). Tumor infiltrates were identified within samples of mediastinal pleura. Considering the histopathological findings, adjuvant chemotherapy and radiotherapy of the mediastinum are considered necessary.

Conclusion: We have reported the clinical presentation, histological and immunohistochemical finding of a mixed germ cell tumor with a polyembryonic component. The treatment of patients with germinal tumors depends entirely on a detailed histological examination of the tumor tissue.

Keywords: germ cell tumor; mediastinal neoplasms; immunohistochemistry

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Epithelioid hemangioendothelioma of the lung – case report

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Objective: Epithelioid hemangioendothelioma is a rare tumor with a wide range of differential diagnostic pathological entities, encompassing granulomatous pathology to primary lung cancers. Despite significant advancements in molecular diagnostics in recent years, which have facilitated more precise diagnosis and classification of soft tissue tumors, these tumors continue to pose a diagnostic challenge for both pathologists and clinicians.

Case report: The sixty-seven-year-old female patient was hospitalized to clarify the etiology and potential surgical treatment of the lesion in the lungs. The mass was discovered incidentally on a chest X-ray. Chest computed tomography showed a peripheral nodule in the VI segment

of the left lung. An atypical resection was performed with video-assisted thoracoscopy. Histopathological findings on frozen sections indicated that the lesion was benign. During the definitive histopathological examination, tumor tissue consisted of weakly to moderately cellular solid sheet-like arrangements of tumor cells, with uniform, round to slightly oval nuclei and a small amount of cytoplasm. The immunohistochemical profile of the tumor cells favoured tumors of vascular origin, as evidenced by positivity for CD31, CD34, D2-40, CD10, and vimentin, while showing negativity for KRT AE1/AE3, KRT7, EMA, TTF-1, Napsin A, ER, PR, and S-100. Based on the histomorphological features and the results of the immunohistochemical analysis, final diagnosis was consistent with epithelioid hemangioendothelioma. At the latest follow-up, conducted three months after surgery, the patient showed no signs of disease.

Conclusion: We present a case of a rare primary low-grade lung sarcoma, which will contribute to the limited literature available on this pulmonary entity.

Keywords: epithelioid hemangioendothelioma; primary pulmonary sarcoma; vascular tumors

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Pericardial cyst: case report

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Objective: A pericardial cyst (PC) is an uncommon benign dilatation of the pericardial sac surrounding the heart. PC is typically considered a congenital anomaly with most patients diagnosed via incidental findings on routine chest imaging and have been diagnosed in all ages. The incidence is 1 in 100,000 persons. Rarely PC can become symptomatic and require treatment or intervention.

Case report: A 60-year-old female presented with substernal pain radiating to the bilateral shoulders. A chest X-ray was suggested and performed which showed a round, rounded mass near the heart that was suggestive of a pericardial cyst. The dimensions of the cyst were 35x35x30cm. Surgical resection of the cyst was performed through a thoracotomy. The obtained material was sent for histopathological diagnosis. The delivered material corresponds to a

pericardial cyst with a diameter of 35x35x30 cm and a wall thickness of 0.5 mm, a smooth outer and inner surface, which is filled with clear liquid fluid. The wall of the cyst is made of fibrous tissue lined with simple cuboidal mesothelial cells.

Conclusion: The general prognosis is excellent for PC, not unexpected when one considers that the vast majority of patients are asymptomatic. Spontaneous resolution of lesions has even been reported.

Keywords: pericardial cyst, chest X-ray, histopathological diagnosis

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Solid pseudopapillary neoplasm- case report of the youngest patient

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Case report: Solid pseudopapillary pancreatic tumor, also called Frantz tumor after the author, represents 1-2% of pancreatic neoplasms. It is considered for tumor with low malignant potential, of unclear etiology. It occurs more often in women in the third and fourth life decade. In children, it usually affects the head of the pancreas, while the pancreatic body or tail in adults. The tumor is most often manifested as a palpable mass in the upper part of the abdomen, accompanied by pain, nausea and vomiting. However, it is most often discovered accidentally, by radiological examinations, where it presents as a clearly limited, encapsulated lesion, usually with areas of cystic softening.

A fourteen-year-old girl had a resection of the pancreas' head with a tumor formation, duodenum and part of the jejunum. Macroscopically, the tumor mass measuring 10x7x6 cm was partly solid, partly cystically altered, fulfilled with dark and bloody content. Pathohistologically, a solid pseudopapillary tumor was verified, consisting of uniform round epithelial cells without atypia that are distributed in pseudopapillary and partly solid areas, permeated with cholesterol crystals and dystrophic calcifications in a moderately abundant connective vascular stroma, without

necrotic areas. Pathohistological verification is necessary for confirmation of diagnosis. This case report is also a report of a rare neoplasm of the youngest patient who was diagnosed with a solid pseudopapillary tumor at the Center for Pathology and Histology of the University Clinical Center of Vojvodina.

After surgical resection, the prognosis of this disease is excellent.

Keywords: Frantz tumor; pancreatic neoplasm

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Progressive mucinous histiocytosis in a child – a report of a rare entity

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Objective: Non-Langerhans cell histiocytoses are heterogeneous disorders, some of which may predominantly affect the skin. The most common form in children is juvenile xanthogranuloma, while other forms are very rare and may be hereditary such as progressive mucinous histiocytosis.

Case report: We present a case of a nine-year-old girl with painless skin papules lasting for five years before the examination. Papules first appeared on the forearms and then on the face. Several papules were excised for histopathological examination. Papules were composed of a variable number of epithelioid or spindled cells with clear or light eosinophilic cytoplasm, without prominent nuclear pleomorphism. Cells showed loose or lobular arrangement in the superficial and mid-dermis and were embedded in a myxoid stroma. On immunohistochemical analysis, tumor cells showed positivity for CD68, Factor XIIIa, and Fascin, but were negative for CD163, S-100, CD1a, and Langerin. Diagnosis of progressive mucinous histiocytosis was made. Further clinical examination showed no other organ

was affected. Close clinical follow-up and examination of close relatives were suggested.

Conclusion: Progressive mucinous histiocytosis is a hereditary or sporadic disease, that predominantly affects skin without propagation to visceral sites. It often occurs in childhood, has a slowly progressive course, and may be treated surgically. Histopathological and immunohistochemical analyses are necessary for final diagnosis.

Keywords: non-Langerhans cell histiocytosis, pediatric skin tumors, myxoid histiocytosis

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Unusual presentation of pediatric carcinoma of unknown primary origin: a case report

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Objective: Pediatric carcinomas are often the first manifestation of various hereditary syndromes. In addition to being rare, these diseases have a different clinical presentation in children compared to adults, which often delays diagnosis. This report aims to indicate the importance of pathohistological diagnostics in such cases.

Case report: We present a case of a 14-year-old boy with clinical suspicion of lymphedema of unclear etiology due to unilateral elephantiasis and hydrocele. Deep vein thrombosis, hereditary angioedema and filariasis were excluded. Whole-body nuclear magnetic resonance imaging did not detect a tumor but only inguinal lymphadenopathy. Biopsy of the inguinal skin and subcutaneous tissue showed carcinomatous lymphangiosis of mucinous “signet-ring cell” carcinoma of unknown primary origin. Immunohistochemical evaluation pointed to a gastrointestinal origin of the primary tumor, including “goblet cell” carcinoma of the appendix (CK20+, CDX2+, Villin+, Synapthophysin+/-) but subsequent gastroscopy and colonoscopy with serial biopsies did not reveal the tumor. Additional immunohistochemical analysis showed loss of nuclear expression in

more than 30% of tumor cells for MSH6/MSH2 and MLH1/PMS2 suggesting microsatellite instability-high (MSI-H) cancer. There was no clinical improvement during chemotherapy and the patient died after one year of follow-up as a result of complications from pulmonary embolism and massive pleural effusions.

Conclusion: Although an incidental finding, the pathohistological analysis of the biopsy sample proved to be superior to other diagnostic methods in the detection of metastatic carcinoma in this case. Proven MSI-H in tumor tissue explains its early onset and in correlation with the assumed gastrointestinal origin are together a hallmarks of Lynch syndrome.

Keywords: pediatric carcinoma, microsatellite instability, Lynch syndrome

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Sacrococcygeal teratoma with Yolk sac tumor in newborn— case report

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Objective: To present a case report of a 7-day-old female newborn with a mature sacrococcygeal teratoma with a component of the yolk sac tumor.

Case report: A term newborn was delivered by cesarean section with a large mass in the sacrococcygeal area. After the seventh day of birth, a complete resection of the tumor was performed. Macroscopic examination revealed that it was a large tumor covered with skin, measuring 9.5 x 8.5 cm, partly solid and partly cystic, with a colorful appearance. Microscopically, the prominent component of the tumor was mature nervous tissue composed of neurons, nerves and ganglion cells. We found mucus producing cylindrical epithelium resembling gastrointestinal epithelium as well as cuboidal epithelium resembling ependyma. Other components in the tumor included skin, cartilage, smooth

and striated muscle tissue, mesenchymal tissue, gastrointestinal glands, retina, and numerous calcifications. In several foci, we observed necrotic tumor tissue composed of atypical cells with hyperchromatic to vesicular pleomorphic nuclei, acidophilic nucleoli in a glandular, alveolar, and microcystic arrangement. Schiller-Duval bodies were observed. After the performed immunohistochemical analysis (AE1/AE3 +, Glypican3 +, AFP+, GATA3 +, PLAP+ , Ki67 85%) the diagnosis of Yolk sac tumor was confirmed.

Conclusion: Yolk sac tumors are rare and highly malignant tumors that occur in children as well as in young adults. In conclusion, a sacrococcygeal mass, especially in children or neonates, requires rapid clinical evaluation and confirmation by histopathological examination.

Keywords: sacrococcygeal teratoma, Yolk sac, newborn

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Lymphangiomatosis of the small intestine

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Objective: Lymphangioma is nonencapsulated benign proliferation of lymphatic vessels. In most cases it is usually identified in infants and children around the head and neck, trunk or extremities. Lymphangioma cavernosum in the abdominal cavity is a rare benign tumor, account for 6% of gastrointestinal tumors in children. Variable clinical presentation, from asymptomatic to abdominal pain mass effect. May present as an incidental finding during surgical procedures performed for other conditions. Rarely complications include obstruction, infarct and perforation of small intestine. Complete surgical resection is considered the main method of treatment.

Case report: Our patient is a 14 year old girl, which appears to the pediatrican due to an increase in body temperature and pain in the lower abdomen. On the first ultrasound, a cystic change in the projection of the ovary was observed, and laboratory analyzes show inflammation (CRP 305, Le 12.2). After the given antibiotic therapy, the general condi-

tion improves. On the second ultrasound more clearly circumscribed hypoechoic areas were observed in abdomen, largest diameter up to 44mm. Surgical excision of the small intestine was performed and pathohistological examination, which showed dilated and anastomosed thin-walled blood and lymphatic vessels lined with endothelial cells of regular micromorphology.

Conclusion: Lymphangiomatosis of the small intestine is a rare benign neoplasma which can mimic a malignant process. The treatment of choice is surgical excision with clean margins. Postoperative follow-up is necessary to detect recurrence.

Keywords: lymphangioma, small intestine, abdominal pain

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Cytological diagnosis of metastatic pleomorphic sarcoma in the ascites fluid- case report

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Objective: Presentation of cytological diagnosis of metastasis of sarcomatoid malignancy in the ascites fluid and pathohistological confirmation.

Introduction: Sarcomas are unusual findings in cytological samples of body fluids and make up 3%-6% of malignant effusions. Morphological characteristics of sarcoma in cytological and pathohistological findings can be a great diagnostic challenge.

Case report: A 74-year-old woman, one month after a laparoscopic cholecystectomy, was hospitalized in a serious general condition, with advanced ascites. After drainage of the ascites fluid, the material was cytologically analyzed. In the cytological sample, in addition to inflammatory and mesothelial cells, numerous clusters of pleomorphic tumor cells with moderately abundant and partially basophilic and small vacuolated cytoplasm were found. Nuclei were eccentrically placed, focally with prominent nucleoli. Numerous multinucleated cells were observed. Diagnostics, according to the type of secondary deposit of non-small

cell carcinoma, was completed with cytochemical and immunocytochemistry staining. Only an intense reaction was found for vimentin, while reactions for CK7, CK20, estrogen, progesterone, EMA, CK5/6-, CDX2 were negative. In the differential diagnosis, cytologically, poorly differentiated sarcoma or sarcomatoid carcinoma was considered. After the MSCT examination, a biopsied change was observed in the liver. Pathohistologically, pleomorphic neoplastic cells were positive for vimentin, CD68, SMA, and focal S100. A primary undifferentiated pleomorphic sarcoma of the liver was diagnosed.

Conclusion: We analyzed rare localization of undifferentiated pleomorphic sarcoma in the liver with deposits in the ascites fluid. Its diagnosis can be difficult in exfoliated cytological samples, due to the epithelioid, mesothelial and sarcomatoid morphology of the tumor cells.

Keywords: Malignant effusions, Pleomorphic sarcoma, Cytology

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Neurological, cardiac and musculoskeletal anomalies in fetuses with aneuploidy

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Objective: Defining the frequency of neurological, cardiac and musculoskeletal anomalies during macroscopic analysis of fetuses with Down, Edwards, Patau, Turner, Klinefelter and 47 XXX syndrome.

Introduction: Aneuploidies represents disorders of the number of chromosomes within the human genome. The most common are: Down's, Edwards', Patau's, Turner's, Klinefelter's and 47 XXX syndrome. Neurological, cardiac and musculoskeletal anomalies are characteristic for all these syndromes.

Material and Methods: This research of retrospective character was conducted at the Center for Pathology and Histology of the University clinical center of Vojvodina. Autopsy reports were used as a source of data. The follow-

ing data were collected and statistically analyzed: maternal age, fetal sex and gestational age, the type of aneuploidy as well as neurological, cardiac and musculoskeletal findings. The study included 90 fetuses with autopsy performed in a three-year-period.

Results: Out of 90 fetuses, 32 were female, while 58 were male. The largest number of fetuses had Down syndrome - 56 (62.2%), followed by 15 fetuses with Edwards syndrome (16.7%), 7 with Klinefelter syndrome (7.8%), 5 with Turner syndrome (5.6%), 4 with 47 XXX syndrome (4.4%) and Patau syndrome, which was present in only 3 fetuses (3.3%). Of all anomalies analyzed, musculoskeletal were the most common, cardiac were found to a significantly lesser extent, while the least present were neurological.

Conclusion: The study confirmed the presence of anomalies in the analyzed syndromes, of which the following are represented: musculoskeletal, cardiac and finally neurological.

Keywords: aneuploidy; anomalies; syndrome; fetus

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Core needle biopsy of liver nodal lesion- from few cells to diagnosis

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Objective: The objective of this case report is to demonstrate difficulties that can arise in small biopsies and the importance of having an idea of a possible diagnosis.

Case report: Liver neoplasms whether primary or metastatic are quite common. About a quarter of all metastases are found in the liver, most commonly carcinoma metastasis, but other tumors such as sarcomas, melanoma, and lymphomas can metastasize to the liver as well. Minimally invasive small biopsies, e.g. FNA and CNB, are safe, quick, cost-effective procedures that facilitate the diagnosis of nu-

merous visceral changes.

We present a case of an FNA biopsy of solitary liver neoplasm in a 70-year-old man, found during a routine diagnostic for abdominal discomfort the patient had a couple of months before the procedure. On HE, pleomorphic tumor cells were embedded in the myxoid stroma with fragile blood vessels. Tumor cells had a sparse, eosinophilic cytoplasm and focally with granular brown pigment. Tumor cells showed positivity on Vimentin, S-100, SOX10, and PRAME, but a loss of staining for Melan A, HMB-45, and MiTF was observed. Pigment in tumor cells was stained with Masson Fontana.

Based on tumor morphology on HE, immuno- and histochemistry diagnosis of metastatic melanoma was made. The patient had no history of previously diagnosed melanoma.

Conclusion: Small biopsies are a powerful tool in providing material for pathohistological and molecular testing with minimal patient discomfort and few rare complications. However, considering that the small tissue fragment delivered through these procedures is just a minor part of a neoplasm can raise a question of adequacy and representativity of a sample, as well as the sufficiency of cytological and architectural characteristics to establish the right diagnosis.

Keywords: FNA biopsy, melanoma, liver metastasis
