POSTERS

RETROMOLAR SMALL CELL NEUROENDOCRINE CARCINOMA: CASE REPORT

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Small cell carcinoma (SmCC) is a poorly differentiated neuroendocrine carcinoma that has been reported in several sites throughout the head and neck region, including salivary glands where it is a rare primary tumor accounting for less than 1% of all salivary gland tumors. We report a case of a 55-year-old man with problems consisting of neck pain and difficult swallowing induced by a retromolar mass. Physical examination revealed an exophytic infiltrative process in the right retromolar trigonum, measuring 2 centimeters in diameter. On cut surface the tumor was white and grayish. Microscopically, it was composed of sheets, ribbons and nests of mitotically active tumor cells set within a variably fibrous stroma. There was a positive immunohistochemical reaction for broadspectrum keratin, EMA, synaptophysin and chromogranin. The combination of findings was in favor of small cell neuroendocrine carcinoma with the probable origin from a small salivary gland. In the 2005 WHO classification of head and neck tumors, SmCC of salivary glands is defined as a rare malignant epithelial tumor. Differential diagnosis includes metastatic pulmonary SmCC and cutaneous neuroendocrine carcinoma (Merkel cell carcinoma). Although salivary gland SmCC does not metastasize as frequently as pulmonary SmCC, locoregional metastases are present at diagnosis in as many as 50% of cases. SmCC arising in major or minor salivary glands has a better prognosis than pulmonary SmCC, but in our case the patient survived for just one month after the diagnosis. The autopsy confirmed oropharynx as the primary location of the tumor. Besides multiple liver metastases, there were no signs of tumor anywhere else in the body.

MELANOMA METASTASIS TO THYROID FOLLICULAR ADENOMA

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Clinically significant metastases to thyroid gland are very rare. The incidence of thyroid involvement by metastatic disease ranges from an average of 3.1% in surgical series to 5.3% in autopsy series. Metastases to pre-existing thyroid neoplasms are distinctly uncommon. Malignant melanoma is one of the tumors that may metastasize to thyroid gland. We describe a case of a woman with thyroid metastases from a nodular melanoma discovered by fine-needle aspiration biopsy of thyroid nodule. Six months before, a 67-year-old woman was diagnosed with malignant nodular melanoma on the right upper arm. Axillary lymph nodes were positive. Follow-up examination revealed nodular enlargement of the right thyroid lobe. Fine-needle aspiration (FNA) showed the presence of epitheloid cells with nuclear atypia and cytoplasmic pigmentation. Morphological features suggested thyroid metastasis from malignant melanoma and thyroidectomy was performed. Pathologic examination revealed a completely encapsulated nodule measuring up to 1 cm in diameter, showing histopathologic features of follicular adenoma with no evidence of capsular or vascular invasion. The adenoma was infiltrated by a nodule of immunohistochemically HMB45 positive malignant cells containing dark pigment. The incidental metastatic nodule was found in the opposite thyroid lobe. Thyroid nodule in patients with a history of malignancy can be a benign lesion, new primary carcinoma or distant metastasis. Our case supports the argument that any patient with a thyroid mass and a history of malignancy should be considered to have a metastasis until proven otherwise. FNA has an important role in differentiation of benign, malignant and probably

malignant cell cells in thyroid gland. However, due to the possible mimicking metastases that simulate primary thyroid neoplasm, histopathology examination and appropriate use of immunohistochemistry remain the gold standard in achieving an accurate diagnosis.

COEXPRESSION OF 4-HYDROXYNONENAL AND PROMININ-1 IN ASTROCYTOMAS

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Oxidative stress (OS) is a condition that occurs when antioxidative capacity of tissue and cells is overcome. The oxidative damage of cells is caused by free radicals which are products of OS. In equilibrium, free radicals are disintegrated by enzymatic and non-enzymatic proteins. Lipid peroxidation is an autocatalytic process caused by OS, which damages lipids and causes production of highly reactive species such as hydroxynonenal (HNE). HNE is thought to be the second toxic messenger that damages cells causing their death. Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are products of OS and they play an important role in both initiation and promotion of carcinogenesis. The brain is very vulnerable to damage mediated by ROS when cells in the central nervous system (CNS) have low levels of antioxidant defenses, high iron content and high level of poly-unsaturated fatty acids. The cancer stem cell hypothesis suggests that not all cells in the tumor have the same ability to proliferate and maintain the growth of the tumor. Only a relatively small fraction of cells in the tumor, termed cancer stem cells, possess the ability to proliferate and self-renew extensively. Prominin-1 (CD133) has been identified in both human and mice, and was originally classified as a marker of primitive hematopoietic and neural stem cells. Different tissue damages to CNS, such as trauma, viruses and ischemia, increase the amount of OS product which damages the endothelial cells, which consequently increase production from bone marrow-derived endothelial progenitor cells (EPCs). EPCs are immunoreactive for CD133 and CD34 and thus important in the process of angiogenesis. The aim of this study was to determine the coexpression of HNE-histidine conjugates and CD133 in astrocytomas. The expression of HNE in 30 diffuse astrocytomas (DA), 30 anaplastic astrocytomas (AA), and 30 glioblastomas (GBM) was analyzed using monoclonal antibody on HNE-histidine conjugates and polyclonal antibody on prominin-1 (CD133). HNE immunopositivity was found in all astrocytomas and the intensity was proportional to astrocytoma malignancy. The weakest presence of HNE was found in DA, followed by AA and GBM. The remarkable immunopositivity for HNE was found in tumor cells, stroma and blood vessels in malignant variants of astrocytomas (AA and GBM). CD133 was found in all astrocytomas and the intensity was also proportional to astrocytoma malignancy. The remarkable immunopositivity for CD133 was found in tumor cells and stroma in AA and GBM. The coexpression of HNE and CD133 was significant in tumor cells and stroma of AA and GBM compared to DA. The increase in HNE and CD133 immunoreactivity in tumor cells, blood vessels and stroma in astrocytomas with an increase in their malignancy indicates that both markers could be good prognostic indicators.

NEUROENDOCRINE CANCER OF THE BREAST: A REPORT OF 11 CASES

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Neuroendocrine cancer (NC) of the breast is rare, usually showing alveolar structures or solid sheets of cells with a tendency to produce peripheral palisading. The expression of neuroendocrine markers chromogranin and/or synaptophysin in more than 50% of the cell population confirms neuroendocrine differentiation. Depending upon the cell types, grade and degree of differentiation, NC has been categorized into the following subtypes: solid, small cell and large cell NC. All 11 patients were aged from 48 to 86 (median 57) years. The tumor size median was 17 mm (10-48 mm) in diameter. Eight tumors were classified as solid, two as small cell and one as large cell type. Immunohistochemical examination was carried out using the following antibodies: chromogranin A, synaptophysin, estrogen receptor (ER), progesterone receptor (PR), androgen receptor (AR), human epidermal

growth factor receptor-2 (HER-2) and Ki67. Positive reactivity for chromogranin A (8/11) and synaptophysin (11/11) confirmed neuroendocrine differentiation in 11 cases of breast cancer. Immunohistochemically, the tumors expressed ER (11/11), PR (8/11) and AR (10/11), while HER-2 was negative in all cases. Median value for Ki-67 was 18% (range 7%-55%) and for the number of mitoses 4 (range 3-31). In one-way analysis of variance, histologic grade was influenced by the number of mitoses (*P*=0.0096) and tumor size (*P*=0.0035). Axillary lymph nodes were positive in two patients (2/11). Disease recurrence with distant metastases occurred, after 20 months, only in the patient with large cell subtype. All other patients were free of disease at the time of writing. Median follow-up was 20.5 (range 11-45) months. NC of the breast frequently expresses ER, PR and AR, while HER-2 is negative. Histologic subtype, grade and size of tumor are very important prognostic factors. More cases and longer follow-up periods are required to determine the behavior of these tumors.

PROPOSAL OF CLAUDIN-LOW BREAST CARCINOMA MODEL TO UNDERSTAND ITS AGGRESSIVE BIOLOGICAL PROPERTIES

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The claudin-low subclass has emerged relatively recently as a further subtype of triple negative breast carcinomas. Although it has a very low incidence, understanding its behavior is crucial for its poor prognostic properties and therapeutic importance. Claudin-3, -4, -7 and E-cadherin are able to separate the claudin-low subtype of tumors with reasonable confidence both at RNA and protein level. An elevated expression of claudin-4 has been described in basal-like breast cancer, and further characterization of this subgroup has led to the identification of claudin-low carcinomas with low claudin-4 expression. Due to their rarity, claudin-low breast carcinomas pose a great challenge for the breast cancer research community. As human triple negative carcinomas bear myoepithelial properties and claudin-low tumors are considered to originate from their progenitors, the stem cells, we undertook a hypothesis driven approach to propose a claudin-4 low expression model of canine breast cancers for human claudin-low tumors as 1) mammary cancer is the most common type of cancer in female dogs and with a lifetime risk of over 24% when dogs are not spayed; 2) these carcinomas frequently show an aggressive phenotype with 3) their cells displaying myoepithelial features. We were able to confirm the raising based on the following: histologic appearance (in order to find the common and the divergent features) and claudin-4 expression in metastasizing carcinomas of dogs compared to human triple negative breast carcinomas; identification of the claudin-low group of cancers amongst dog's and human triple negative breast carcinomas; and comparison of the biological behavior of the claudin-low tumors in the two species.

VERMINOUS PNEUMONIA IN CALIFORNIA SEA LIONS: CORRELATION BETWEEN GROSS AND HISTOPATHOLOGIC LESIONS

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Respiratory tract nematodes, along with gastrointestinal (GI) tract nematodes, are common findings in marine mammals rescued along the California Coast. Most of the parasites commonly found are metazoans: small and large roundworms (*Otostrongylus circumlitus*, *Anisakis* sp., *Parafilaroides decorus*). The animals typically present with severe weight loss, weakness, anorexia, and respiratory distress, in addition to dark diarrhea associated with GI parasitism. Pinnipeds are either primary, intermediate or transport hosts for many parasites in the marine environment, and therefore are intimately involved in movement of parasites between aquatic birds, fish, and other aquatic mammals. In this research, we studied the morphology and histopathology of respiratory tract lesions associated

with verminous pneumonia in California Sea Lions (*Zalophus californianus*). Tissue specimens were obtained from 30 stranded pinnipeds necropsied at the local rehabilitation centers in the period of 3 years. The lesions were identified, evaluated, and correlated with the associated gross pathological findings. Adults and larvae of metazoans were found in the pulmonary parenchyma and airways, with a considerable variation in the response of the host tissue to the parasite. The goal of this project is to identify common histopathologic findings of verminous pneumonia in California Sea Lions, evaluate the extent of different parameters present, and correlate histopathologic lesions with gross pathological findings. These results are expected to provide a useful reference for gross morphological and histopathologic evaluation of lesions associated with respiratory parasites in pinnipeds at necropsy.

PRIMARY THYROID LYMPHOMAS: MOST COMMON SUBTYPES OF NON HODGKIN'S LYMPHOMA

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Primary lymphoma in the thyroid gland (PTL) is a relatively rare disease. Elderly individuals and females are mostly affected. Definitive diagnosis of primary thyroid extranodal lymphoma can only be established by exclusion of extranodal progression of any subtype of primary nodal lymphoma. Diffuse large B-cell lymphoma (DLBCL) and extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) are the most common subtypes in thyroid gland. The aims of this review were to evaluate the spectrum of PTLs using the WHO classification schemes (2008) and immunohistochemical markers in our institution. The majority of cases (n=7) were received as consultations from 2003 to 2009 and clinical data were unavailable. There were seven women and one men, mean age at diagnosis 79.8 years. PTLs were classified as MALT lymphoma (n=1), DLBCL (n=6), and follicular lymphoma grade 3 (n=1). Immunohistochemical staining was performed using diagnostic panel of primary antibodies (CD20, CD79a, CD3, CD23, CD43, CD10, CD5, CD23, CD43, BCL6, BCL10, BCL2, thyroglobulin). The tumor most commonly presented as diffusely enlarged, rubbery firm thyroid gland. When forming mass, the tumor ranged in size from 1 to 19.5 cm. In our cases, morphology characteristics were those of DLBCL, MALT and follicular lymphoma, respectively. The cases of DLBCL showed immunohistochemically positive results for CD20, CD79a and negative for CD3, CD23, CD43, CD10. The case of MALT lymphoma was positive for CD20, while CD5, CD23, CD43 were negative. The case of follicular lymphoma was positive for CD20, CD10, BCL6, BCL2 and negative for CD3. In this small series and in the published literature, a striking female predominance for PTL was noted. Histologically, it can be very difficult to distinguish PTL from anaplastic thyroid carcinoma as well as Hashimoto's thyroiditis due to their similar appearance. The study by Smedby *et al*. showed an increased risk of non Hodgkin's lymphoma (NHL) in patients with autoimmune disorders such as Sjögren's syndrome, systemic lupus erythematosus, autoimmune hemolytic anemia, and celiac disease. These results may be based on the common mechanisms of lymphomagenesis for NHL and autoimmune disorders. Future efforts should involve chronic antigenic stimulation (especially in thyroid gland) and lymphoid malignancy including molecular studies of the population in our country. It may help define the underlying biological mechanisms and give important clues to lymphomagenesis.

EXPRESSION OF TUMOR NECROSIS FACTOR-ALPHA (TNF-A) AND VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) IN GASTROENTEROPANCREATIC NEUROENDOCRINE TUMORS (GEP-NETS) AND THEIR CORRELATION WITH TUMOR AGGRESSIVENESS

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Angiogenesis is a crucial step for tumor growth. Vascular endothelial growth factor (VEGF) is a potent endothelial cell mitogen, known to induce vascu-

lar permeability. Its expression is under the influence of proinflammatory cytokines, mainly tumor necrosis factor-alpha (TNF-α). Recent clinical data have proved the correlation between microvessel density and tumor progression with VEGF expression in tumor tissue. As gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are highly vascularized neoplasms with still unknown etiopathogenesis, we investigated the expression of proinflammatory cytokine TNF-α and VEGF in 48 GEP-NET tissues, and correlated it with the expression of Ki67. Surgical and biopsy specimens from 46 gastrointestinal neuroendocrine tumors (GI-NETs) and 2 pancreatic neuroendocrine tumors (PETs) were examined for TNF-α and VEGF expression by immunohistochemistry. Of GI-NETs 15 were of foregut (14 gastric and 1 duodenal) and 31 of midgut origin (12 small intestine, 12 appendix and 7 colon). Among tumors, overall 21 had high proliferative index (>2% Ki67 positive tumor cells) and 27 (including 2 PETs) had low proliferative activity. Immunostaining was graded as follows: 0 no positive cells; 1 ≤25% positive GEP-NET cells; 2 >25%-50% positive GEP-NET cells; and 3 ≥50% positive GEP-NET cells. Spearman test was used on correlation of TNF-α and VEGF with Ki67. Results were considered significant at $P<0.05$. Weakly positive TNF-α staining was detected in one PET, 4 foregut and 12 midgut tumors, while stronger TNF-α expression (2 and 3) existed in 1 foregut and 17 midgut tumors. Overall 13 tumors were negative for TNF-α. Strong cytoplasmic VEGF immunostaining was detected in 30 midgut and 5 foregut GI-NETs and both PETs, while 5 GI-NETs of foregut origin completely lacked VEGF expression. When TNF-α and VEGF expression was correlated with Ki67, there was a statistically significant correlation between TNF-α and Ki67 ($P=0.03$), and a tendency to statistically significant correlation between VEGF and Ki67 ($P=0.09$). Our study has demonstrated that neuroendocrine cells are a major source of TNF-α and VEGF, particularly in midgut GI-NETs. This finding suggests that the mentioned cytokines/growth factor are needed to maintain the differentiated state of capillary vessels in these highly vascularized tumors but also, as there was a correlation between the TNF-α and VEGF expression and tumor proliferative activity, that they are important for tumor progression.

LARGE CELL NEUROENDOCRINE CARCINOMA OF THE COLON AND RECTUM: A REPORT OF 7 CASES

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Neuroendocrine tumors encompass a wide range of pathologic entities that display distinct biologic behaviors. Large cell neuroendocrine carcinoma (LCNEC) is a highly aggressive neoplasm with a very low frequency in the gastrointestinal tract, usually resulting in unfavorable outcome. We present a series of seven patients diagnosed with LCNEC of the colon and rectum in the time period between 2005 and 2010 at Ljudevit Jurak University Department of Pathology, Sestre milosrdnice University Hospital. The average patient age was 64 (range, 34-94) years. There were five female and two male patients. The mean tumor size was 7.8 (range, 2-15) cm. Five tumors were located in the colon (1 ascending, 1 transverse, 2 descending and 1 sigmoid), 1 in cecum and 1 in rectum. Grossly, tumors were of endophytic/ulcerative, annular and polypoid appearance. Histologically, the tumors were composed of large cells of organoid, nesting, trabecular, rosette-like and palisading pattern and had a high mitotic rate. All seven tumors stained positive for immunohistochemical neuroendocrine markers, including chromogranin (4/7), synaptophysin (5/7), and/or neuron specific enolase (6/7). Tumors were advanced at the time of diagnosis: stage II (n=1), stage III (n=4) and stage IV (n=2). We present cases for being rare and to emphasize the need of increased awareness of the condition as one of the poorest prognostic subgroups among primary colorectal tumors.

STEREOLOGY OF THE RAT PLACENTA IN THE LAST TRIMESTER OF GESTATION

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Because of the numerous roles of the placenta in fetal period, it is important to understand its devel-

opment and structure, and due to similarities with human placenta, rat is an appropriate experimental model. Animals were sacrificed on 16th or 19th day of gestation. The uterus was removed, the placentas were isolated, fixed in 10% formalin and a complete series of histologic sections of 10-µm thickness was made. Thirty five rat placentas were collected, 21 in the experimental group of 16th and 14 in the experimental group of 19th day of gestation. Three randomly selected placentas from each group were stereologically analyzed. Absolute volumes of placentas and their compartments (labyrinth, basal portion and decidua) were estimated. Using volume density, we calculated the share of glycogen cells and trophoblast giant cells (TGC) in the basal part of the placenta. The average absolute volume of the placenta on 16th day of gestation was 0.064 cm^3, from which a labyrinth made 0.027 cm^3, basal part 0.027 cm^3, and decidua 0.009 cm^3. The average absolute volume of the placenta on 19th day of gestation was 0.163 cm^3, of which the labyrinth made 0.0923 cm^3, basal part 0.059 cm^3 and decidua 0.011 cm^3. In the 16th day of gestation, volume density of TGC in the basal layer was higher (0.174) in comparisson with 19th day of gestation (0.107). The volume density of glycogenic cells was 0.379 on the 16th day and 0.236 on the 19th day of gestation. In conclusion, the absolute volume of the whole placenta on 19th day of gestation significantly increased, as well as the share of the labyrinth as the most important part. The volume densities of glycogenic and giant trophoblast cells were higher on the 16th day of gestation compared to the 19th day, because the 19th day marks the time when the trophoblast invasion is finished and the definitive placenta is formed.

CHOLESTASIS AS THE INITIAL PRESENTATION OF ILLNESS IN A FEMALE PATIENT – DIFFERENTIAL DIAGNOSIS IN LIVER BIOPSY

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The aim is to underline the importance of bilirubin laboratory findings in the interpretation of liver biopsy performed for the evaluation of cholestatic jaundice. We report on retrospective study of repeat liver and colon biopsies in a 24-year-old female patient with cholestasis. Twelve years before, the patient was diagnosed with autoimmune hepatitis and hyperbilirubinemia associated with ulcerative colitis that presented as a dysplasia associated lesion or mass (DALM). Genetic analysis showed heterozygous TATA genotype for bilirubin uridine diphosphate-glucuronosyltransferase (UGT-1A1) detecting Gilbert's syndrome (GS). Since then, the patient has been under continuous therapy with immunosuppressive drugs and corticosteroids. During the last hospitalization, the course of autoimmune hepatitis and ulcerative colitis was reevaluated. Both liver biopsy specimens, one performed in 2004 and the other at the time of present hospitalization were cut in three step sections and stained with hematoxylin and eosin. Seven additional sections were stained; one with a trichrome method, the next four with pigment detection methods, and the last two were immunohistochemically analyzed for CK7 and 19. All specimens were scored using the histological activity index (HAI) of Ishak *et al*. In addition, all colon biopsy slides were reevaluated to confirm the initial diagnosis of DALM. Revisited colon biopsy specimens confirmed the initial diagnosis of DALM. Additional colon biopsy was preformed one month before the present liver biopsy. It showed only mild lymphocytic infiltrate and no evidence of DALM. Liver biopsy performed in 2004 was scored according to the histological activity index of Knodell *et al*. and reevaluated together with the new liver biopsy according to Ishak *et al*. There was no significant difference in liver biopsy scoring by the two methods mentioned. Histology revealed only mild portal chronic inflammation with few piecemeal necroses, occasional lymphocytic spillover and only 4 spotty acinar necroses along the whole cylinder, which measured up to 2.3 cm. Portal tracts were slightly enlarged due to mild fibrosis. Periportal and intralobar bile ducts showed mild periductal fibrosis and in one lobar bile duct lymphocytic cholangitis was detected by immunohistochemistry. Predominant histological and immunohistochemical findings were periportal proliferation of slightly dilated bile ductules with no bile concretions. Reported HAI grade was 3, and fibrosis staging score 1. In conclusion, histological features were consistent with chronic hepatitis of minimal necroinflammatory activity. Mild histological findings in liver biopsy

resembling almost normal liver that do not correlate with cholestatic jaundice require additional attention of the pathologist. Potential pitfalls could be bypassed with good clinician-pathologist cooperation. First, if the hyperbilirubinemia is of the unconjugated type, clinicians should think about GS. Failure to consider GS as the cause of jaundice may lead to diagnostic misinterpretation and, consequentially, inappropriate therapy. It is estimated that GS is found in about 5% in Caucasians. Although some other conditions can present with cholestasis, no additional symptoms in a patient with unconjugated hyperbilirubinemia present the clue in differential diagnosis. Liver biopsy is not a helpful tool in the diagnosis of GS.

APOPTOSIS IN TESTICULAR TERATOCARCINOMA

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Apoptosis is an active process which occurs in both physiological and pathological conditions. It serves to eliminate cells that are no longer needed or are potentially harmful. Testicular teratocarcinoma is a very interesting tumor because of its two completely different components: mature, differentiated tissue and carcinomatous, undifferentiated part. The aim of this study was to compare the number of apoptotic cells in these two components of testicular teratocarcinoma. Fifteen paraffin blocks with the diagnosis of mixed germ cell tumor (containing both components of mature teratoma and embryonal carcinoma) from the Ljudevit Jurak University Department of Pathology archive were used in the study. Apoptotic cells were counted *per* 10 high power fields (HPF) under light microscope. The number of apoptotic cells in teratoma ranged from 18 to 31 in 10 HPF (mean 24.9/10 HPF) and in carcinoma from 30 to 38 in 10 HPF (mean 35.3/10 HPF). In teratoma, columnar epithelium had a mean of 52.6 apoptotic cells/10 HPF, stratified epithelium 8.7 apoptotic cells/10 HPF and cartilage 2.6 apoptotic cells/10 HPF. This was a pilot study in which we detected an increased number of apoptotic cells in the component of embryonal carcinoma compared to teratoma. In columnar epithelium of teratoma, the number of apoptotic cells was higher than in carcinoma, which can be explained by its physiological function. Further studies on more samples and comparison between p53 expression and apoptotic index in different parts of tumor are needed.

PAPILLARY RENAL CELL CARCINOMA WITH SMOOTH MUSCLE RICH STROMA: CASE REPORT

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Papillary renal cell carcinoma (PRCC) is the second most common malignant epithelial renal neoplasm. PRCCs exhibit a broad morphological spectrum; areas containing classic papillary, papillary-trabecular, and/or papillary-solid patterns of growth are seen in virtually all cases. True papillae with a fibrovascular core lined by neoplastic epithelial cells are the hallmark of the tumor. Merino *et al*. have recently reported a series of 6 unusual renal cell tumors with prominent proliferation of smooth muscle and tubular, cystic and papillary elements. We report a case of PRCC composed of smooth muscle rich stroma in a 44-year-old man with no prior history of disease. Grossly, the tumor measured up to 6 cm in greatest diameter, had a moderate consistency, with a gray-white color and necrosis presenting in up to 30% of tumor tissue. It penetrated the capsule and invaded the perirenal fat. No lymph nodes were encountered. Histologically, the tumor was composed of papillary and micropapillary fronds with prominent proliferation of fibrous tissue and smooth muscle in the tumor stroma. Immunohistochemistry revealed positive reaction of tumor cells for cytokeratin, CK7, vimentin, CD10 and RCC, while CK20 was negative. Tumor stroma stained strongly positive for SMA. There was no VHL mutation. The smooth muscle rich stroma in a PRCC is a new finding; further research is necessary to clarify the path ogenesis of this tumor.

APOPTOSIS IN EXPERIMENTAL MOUSE TERATOCARCINOMA

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The aim of this study was to determine the intensity of apoptosis in experimental teratocarcinoma during its development, especially during the period of its intensive growth (6th-8th week). The 7.5-day-old C3H embryos were transplanted under the kidney capsule of syngeneic adults. Tumors were isolated and weighted after 2, 4, 5, 6 and 8 weeks. The other group of animals were treated twice a week for 4 weeks with the demethylating agent 5-azacytidine (5azaC) immediately, at one week, two weeks or four weeks after transplantation. Apoptosis was analyzed by counting apoptotic cells *per* 10 microscopic fields on hematoxylin-eosin slides under X400 magnification. On statistical analyses, Student's *t*-test was used. Results showed the apoptotic activity to rise during 8 weeks of teratocarcinoma development in untreated animals. No difference was observed in the number of apoptotic cells between differentiated and undifferentiated tissue compartments. In 6th week of development, apoptosis was significantly higher in differentiated compartment, whereas in 8th week it was higher in undifferentiated compartment. Apoptosis in 5azaC treated tumors seems to have occurred with no difference during development except for a more pronounced apoptosis in differentiated compartment in 5th week. Apoptosis was significantly lower in tumors treated with 5azaC in 6th and 8th weeks of development compared to controls. It is concluded that apoptotic activity rises during teratocarcinoma development in untreated animals, with a specific shift of apoptotic activity in the period of the most intense teratocarcinoma growth. The demethylating agent 5azaC slightly suppressed apoptotic activity during the most intense teratocarcinoma growth period as compared to untreated tumors.

CAROTID BODY PARAGANGLIOMA: TWO CASE REPORTS

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Paragangliomas of the carotid body are rare tumors (incidence 0.012%) originating from sympathetic fibers at the carotid bifurcation. Their growth is slow, becoming symptomatic through local mechanical compression of neighboring vascular and neural structures. The aim of the current report is to present the evaluation, management and final outcome in two patients with carotid body tumor. The first case was a 27-year-old woman who presented a cervical tumor detected by self-examination. Hormonal status was: high serum serotonin (362 ng/mL), normal catecholamines and chromogranin A. MRI revealed a 2-cm mass near the left external carotid artery. Immunohistochemical examination showed chromogranin A and synaptophysin positivity, and a 2%-5% Ki67 proliferative index. Octreoscan did not identify any other localization. After surgery, serum serotonin descended to normal levels in three months. The second case was a 40-year-old woman who presented with a neglected 7-year-old latero-cervical tumor, with progressive enlargement. Preoperative serum serotonin level was two times above normal; cathecolamines and chromogranin A were normal. The histopathological and immunohistochemical examinations revealed a paraganglioma of the carotid body with positivity for neuron specific enolase, chromogranin A in tumoral cells, and S100 protein (in numerous dendritic cells); Ki67 proliferative index was 5%-10%. Postoperatively, serum serotonin persisted at high levels. Under treatment with octreotide LAR 20 mg/month, serotonin decreased to normal in 6 months. Surgical excision of carotid body tumors is curative. Due to a potentially infiltrating and disseminating growth, carotid body tumors should be regarded as semi-malignant and should therefore be indicated for surgery at the time of diagnosis.

NASAL MITES AND ASSOCIATED LESIONS IN THE UPPER RESPIRATORY TRACT OF CALIFORNIA SEA LIONS (*ZALOPHUS CALIFORNIANUS*)

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Upper respiratory parasites are uncommon finding in marine mammals. Although it is not a common practice to open and thoroughly examine nasal turbinates at the time of routine necropsy, we found nasal passages of several California sea lions (*Zalophus californianus*), to contain nasal mites (order *Halarachnidae)* of the genera *Orthohalarachne*, as reported in otarrid seals. Of these, most commonly reported in California sea lions are adults and larvae of *Orthohalarachne attenuata* and *O. diminuata*. Although accompanied by a mild nasal discharge, clinical observations have indicated that this infestation does not represent a serious clinical condition for the sea lions. However, histopathologic findings associated with a heavy parasitic load suggested different. Most common pathological findings include erosions of the respiratory mucosa surrounding attachment sites of the mites and accumulations of cellular debris, edema fluid and inflammatory cells (predominantly neutrophils and eosinophils) in nasal passages, nasopharynx, and larynx. In non-eroded areas, the epithelium varies from normal to atrophic, disorganized to hyperplastic. The histopathologic lesions observed suggest that sea lions could present with dyspnea due to blockage of upper respiratory passages and spread of adult mites and larvae deeper into the airways and lungs. We calculated the density of mites in nasal mucosa and suggest that large scale infestations of *Orthohalarachne* sp. in nasopharyngeal mucosa and spread into the pharynx could significantly affect the clinical condition of the affected animal. Also, the nasal mites could lead to lower respiratory diseases, pulmonary emphysema, and transmit other pathogens, so they should be considered of significance to the health and rehabilitation efforts of diseased California sea lions. Examination of nasal turbinates should therefore be recommended on routine necropsy of marine mammals.

LEYDIG CELLS, TESTIS VOLUME AND SPERMATOGENESIS IN PATIENTS WITH NON-OBSTRUCTIVE AZOOSPERMIA

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In males, Leydig cells are responsible for more than 95% of androgen production. The aim of our study was: (a) to assess morphological features and testosterone production *in situ* of Leydig cells in infertile patients; and (b) to correlate the above-mentioned Leydig cell parameters with testis volume and spermatogenesis. In total, 120 testicular biopsies were used (12 controls and 108 specimens from patients with non-obstructive azoospermia). The morphology of Leydig cells was assessed by semi-thin and ultrathin sections (transmission electron microscopy). Testosterone production *in situ* was visualized by immunohistochemistry, followed by morphometric (stereological) analysis. Testicular volume was determined by ultrasound and/or orchidometer, and the status of spermatogenesis by applying Johnsen's scoring system. Patients with non-obstructive azoospermia exhibited statistically significantly lower values of testicular volume and score. Morphological analysis indicated that some Leydig cells displayed an extensive change of the nucleus and cytoplasm, whereas the number of testosterone-producing cells was significantly lower in azoospermia cases. Based on our results, patients with azoospermia have significant changes in the morphology of Leydig cells and their capacity to produce testosterone. Some of these patients could be candidates for premature andropause.

WARTHIN-LIKE TUMOR VARIANT OF PAPILLARY THYROID CARCINOMA: CASE REPORT

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Papillary carcinoma is the most common form of thyroid carcinoma and generally has a more favorable prognosis than other carcinoma types. Within the

group of papillary carcinomas, several morphological variants have been described. We present a case of a rare variant of thyroid papillary carcinoma similar to Warthin's tumor of salivary gland. In a 67-year-old woman with euthyroid goiter and tumor nodule in the isthmus, fine needle aspiration was suspect of papillary carcinoma. Thyroidectomy was performed. An irregularly bordered grayish tumor nodule measuring 2 cm in diameter was found in the isthmus. The surrounding thyroid tissue was normal. Histologically, the tumor was composed of solid areas and papillary structures. The cells covering the papillae often had oncocytic appearance. Nuclei were monomorphous, clear and ground glass-like with grooves. The fibrovascular core of the papillae contained an intense lymphoplasmacytic inflammatory infiltrate. All these features resembled Warthin's tumor of salivary gland. Within the surrounding thyroid parenchyma there was nodular lymphocytic infiltration with germinal center formation. The lymph nodes were free from metastases. Two years after surgical therapy the patient is disease-free. This is a rare variant of thyroid papillary carcinoma showing histologic similarities to Warthin's tumor of salivary gland and therefore may present a differential diagnostic problem. Its clinical behavior does not differ from conventional papillary carcinoma.

EPIDEMIOLOGIC AND HISTOPATHOLOGIC FEATURES OF THYROID CANCER IN CROATIA

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Thyroid cancer is the most common malignant endocrine tumor. In a great number of countries, this neoplasm is among the ten most common malignancies. In recent decades, the incidence of thyroid cancer (mostly papillary cancer) in the world as well as in Croatia has increased dramatically, probably due to more efficient diagnostic tools. Between 1968 and 2004, the age standardized incidence rate of thyroid cancer in Croatia has increased 8.6 times in women and 3.6 times in men. Croatia is a country with a high incidence but a very low mortality rate of thyroid cancer. The most recent WHO histopathologic classification of thyroid tumors (updated and revised in 2004) distinguishes three major categories of thyroid tumors: 1) thyroid cancer (differentiated thyroid cancer – papillary and follicular; poorly differentiated thyroid cancer, medullary and anaplastic); 2) adenomas and related tumors; and 3) other tumors (thyroid lymphomas, metastatic tumors, etc.). Approximately 90% of thyroid cancers are differentiated thyroid cancers (mostly papillary) that are fortunately less malignant and have excellent prognosis. Detailed and exact histologic classification is of utmost importance not only to the pathologists but also to the clinicians because it can lead to better diagnosis and more rational therapy. The aim of this poster is to indicate thyroid cancer incidence and mortality rates in recent decades and to show changes in the histopathologic features of these cancers during this period in Croatia. The aim is also to discuss the probable influences of the modifications in histopathologic classification systems, iodine intake, ionizing radiation and other factors on thyroid cancer histopathology in Croatia. The data shown here have been assembled from the database of thyroid cancer patients treated at University Department of Oncology and Nuclear Medicine, Sestre milosrdnice University Hospital, in close cooperation with Ljudevit Jurak University Department of Pathology and University Hospital for Tumors.

APOPTOSIS IN CHROMOPHOBE RENAL CELL CARCINOMA AND RENAL ONCOCYTOMA

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Renal oncocytoma is a benign epithelial tumor composed of oncocytes, large eosinophilic cells. It accounts for 3%-9% of renal tumors. Chromophobe renal cell carcinoma (ChRCC) is a distinct subtype of renal cell carcinoma and comprises approximately 5% of all renal tumors. Two main variants are classic and eosinophilic ChRCC. Although considered less aggressive than other renal cell carcinomas, ChRCC has a metastatic potential. Due to overlapping morphological characteristics of renal oncocytoma and ChRCC, particularly its eosinophilic variant with the abundant

granular eosinophilic cytoplasm, making a correct diagnosis can be challenging. The aim of this study was to assess and compare the apoptotic index, defined as the absolute number of apoptotic cells *per* 10 high power fields (HPFs), in the two tumor groups. The files from Ljudevit Jurak University Department of Pathology, Sestre milosrdnice University Hospital were searched for cases of histologically confirmed ChRCCs and renal oncocytomas. Slides of 10 ChRCCs and 10 renal oncocytomas, stained by hematoxylin and eosin, were analyzed under the light microscope. Apoptotic cell was defined as a cell with dense, eosinophilic cytoplasm and picnotic or defragmented nucleus. The absolute number of apoptotic cells *per* 10 HPFs in the two tumor groups was counted. In the group of renal oncocytomas there were a mean of 7.8% apoptotic cells *per* 10 HPFs (range 4-12). In the group of ChRCCs there were 2.5% apoptotic cells *per* 10 HPFs (range 1-6). Apoptosis is the process of programmed cell death. Dysregulation of apoptosis is a key process in cancer development and progression. The aim of this study was to assess and compare the apoptotic index in the two tumor groups. Although there was visible difference in the mean number of apoptotic cells between the two tumor groups, this study was partially limited by the modest number of cases and further studies are needed to explore the possible use of apoptotic index assessment in the differential diagnosis between renal oncocytoma and ChRCC.

SCROTAL DIROFILARIASIS IN A 3-YEAR-OLD CHILD

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Dirofilariasis is an uncommon zoonosis caused by parasites of the genus Dirofilaria, most notably *D. repens* and *D. immitis* in Europe. Canines represent the reservoir of infection,

while human infections are sporadic. The infection is transmitted by the bite of a mosquito carrying parasitic larvae. We report a case of a 3-year-old boy with a scrotal nodule measuring up to 1 cm in diameter. Upon excision of the nodule, the surgeon noticed a thread-like parasite exiting the incision site, which he submitted separately from the nodule. Microscopic examination of the excision specimen revealed a canal of granulation tissue located in deep dermis, which did not extend to the excision margin. Microscopic examination of the thread-like material disclosed a parasite whose morphology was well-preserved in some of the sections. It was composed of a thick cuticle with longitudinal ridges (micro-ruffling of the surface), large lateral chords, tall, slender coelomian muscle layer, a single gut tube and spermatocytes in the genital tubule. The morphology of the parasite was consistent with a helminth from the genus Dirofilaria. In humans, dirofilariasis most often manifests as a subcutaneous nodule or less frequently as the so-called "coin lesion" in the lung comprising of microfilarial emboli in a branch of pulmonary artery. In Croatia, there have been approximately a dozen case reports of dirofilarial infection in humans. Most of the cases reported were from the Mediterranean part of Croatia, which may represent an endemic area of dirofilariasis. The diagnosis of subcutaneous dirofilariasis should be considered in the differential diagnosis of a subcutaneous helminthic infection. Physicians should be aware of this disease and its features for several reasons, primarily in order not to mistake coin lesions in the lung for malignancy and not to mistake dirofilarias in subcutaneous nodules for other, more harmful tropical parasites such as *Wuchereria bancrofti* or *Onchocerca volvulus*. In subcutaneous nodules, PCR analysis is an elegant way to overcome diagnostic obstacles caused by altered morphology and/or lack of familiarity with the specific morphology of filarial species. Surgical treatment of subcutaneous dirofilariasis in humans is considered curative and there is no need for further interventions besides clinical monitoring.

HISTOLOGIC SUBTYPES OF INVASIVE LOBULAR CARCINOMA IN CORRELATION WITH TUMOUR STATUS AND HORMONE RECEPTORS

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Invasive lobular carcinoma is a distinct biological entity with several histologic variants the prognostic

value of which has not yet been fully elucidated. The aim of this study was to determine the immunohistochemical expression of estrogen receptors (ER) and progesterone receptors (PR) in the subtypes of lobular breast carcinoma (classic and variant types) and to correlate them with clinical and tumor parameters. Fifty lobular carcinomas, 33 classic and 17 variant, were analyzed. The classic type was more frequent (66%) in older women (age 61) and smaller in size (1.5 cm), with N0 status and modestly positive ER and PR. Variant types were more frequent in younger women (age 55), larger in size (2.5 cm), with N1 status and maximal positive ER and PR. ER was expressed in 82% and PR in 78% of tumors, mostly with maximal expression without differences in the intensity among the subtypes. Only one tumor of classic type was HER/2neu 3+, ER and PR-. ER expression was significantly associated with a lower incidence of other proliferative lesions (P=0.043). The total sample and classic type were characterized by a significant positive correlation between ER and PR (P=0.004) and between tumor size and N status (P=0.005), and negative correlation between HER/2neu and N status (P=0.042). In variant types, larger tumors were related to higher N (P=0.021) and higher ER expression was associated with smaller tumors (P=0.044). The study indicated distinct biological features of lobular carcinoma subtypes and pointed to the need of a more selective therapeutic approach.

STRUMAL CARCINOID OF THE OVARY: A REPORT OF TWO CASES

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Strumal carcinoid is an unusual form of ovarian teratoma composed of an intimate admixture of thyroid and carcinoid tissues that vary in their relative proportions. We describe two patients with primary ovarian strumal carcinoid. Case 1: a 40-year-old woman was admitted to the hospital with a 4-year clinical history of myoma uteri and no symptoms, except for constipation persisting for several months. At laparotomy, a smooth, hard, solid tumor originating in the left ovary, measuring 9 cm in largest diameter, was found. Case 2: a 44-year-old asymptomatic woman was admitted to the hospital for a clinical finding of the left ovarian cyst. At laparoscopy, a multicystic left ovarian tumor with a smooth outer surface, measuring up to 9 cm in largest diameter, was found. Histopathologically, both tumors were composed of an admixture of carcinoid tumor and normal thyroid tissue. A trabecular variant of carcinoid was found in case 1 and insular variant of carcinoid in case 2. Immunohistochemically, the carcinoid cells were diffusely positive for synaptophysin and neuron specific enolase (NSE) and focally positive for chromogranin A. Thyroid tissue with typical thyroid follicles was immunohistochemically positive for thyroglobulin and TTF. Strumal carcinoid was definitive diagnosis in both cases. Primary ovarian carcinoid tumors are uncommon and account for less than 0.1% of ovarian malignancies. Secondary or metastatic carcinoids from the gastrointestinal tract in the ovary are four times less common than primary carcinoids. Patients with primary ovarian carcinoids show symptoms of an abdominal mass, or the tumor is an incidental finding. Some patients show signs of carcinoid syndrome (episodic cutaneous flushing, cyanosis, abdominal cramps, diarrhea, carcinoid heart disease, etc.), mediated by bioactive polypeptides produced by carcinoid tumor cells. Microscopically, there are four major variants of ovarian teratomas of carcinoid type: insular, trabecular, strumal and mucinous. Carcinoid syndrome is a very rare manifestation of strumal carcinoid. Even though carcinoids can typically cause the carcinoid syndrome, with diarrhea as one of the symptoms, several cases of strumal carcinoid were reported in patients exhibiting severe constipation, induced by the gut hormone, peptide YY that has a strong inhibitory effect on intestinal motility. The first patient we describe also suffered from constipation that was relieved after the surgery. Strumal carcinoid can also be responsible for carcinoid heart disease. The patients presented had ovarian tumors showing typical morphology of ovarian strumal carcinoids. Clinical follow up of the patients is only two years in case 1 and six months in case 2, and the patients have no signs of recurrence or distant spread of the tumor.

MULTIPLE METASTASES OF RENAL CELL CARCINOMA TO THE THYROID GLAND: CASE REPORT

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We present a rare case of multiple metastases of clear cell renal cell carcinoma (RCC) presenting as thyroid tumor 4 years after nephrectomy. The patient, a 75-year-old woman, was referred to Pula General Hospital for total thyroidectomy because of a giant, euthyroid, retrosternal struma, with the symptoms of tracheal compression. All laboratory findings including thyroid hormone status were within the normal limits. On gross examination, the thyroid gland was enlarged, with few well circumscribed, whitish nodes on the cut surface. On microscopic analysis, well confined solid and alveolar clusters of atypical epithelial cells were found in the thyroid gland. A distinct feature of tumor cells was their clear cytoplasm and a hyperchromatic nucleus. On immunohistochemical examination, tumor cells showed positive reaction for CD 10, EMA and vimentin. The reaction for TTF-1 was negative. According to history data, histologic examination and immunohistochemical analysis, the case was signed out as RCC metastases to the thyroid gland. One month after the operation, there were no signs of metastatic disease on postoperative computer tomography of the head and thorax and on abdominal ultrasound examination. All laboratory findings were within the normal limits.

ADRENAL MYELOLIPOMA

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Adrenal gland myelolipoma (ML) is a rare disease. Most lesions are discovered incidentally at autopsy or imaging studies performed for other reasons. Differential diagnosis of the suprarenal mass depends on preoperative imaging and biopsy. We performed a ten-year retrospective cross sectional study of 11 MLs. Diagnosis was established by the set of typical histologic findings on standard hematoxylin-eosin staining. In all 11 cases, ML was incidentally found by computer tomography (CT) scan. Seven MLs were found in six men (one man had bilateral adrenal ML) and four in women. The diameter of adrenal tumor mass ranged from 0.5 to up to 13.9 cm. Macroscopic examination revealed an oval encapsulated yellowish soft tumor located in the adrenal gland, with a thin rim of macroscopically normal adrenal tissue. Histologic examination showed proliferation of adipocytes which were dissociated from several hemorrhagic foci and myeloid tissue that contained megakaryocytes, erythroid cells and lymphocytes. The surface of the tumor mass was covered with a fibrous capsule. On the periphery there was normal adrenal tissue with no significant changes. Since first described in 1905 by Girke, MLs are arising out as a rare, probably benign adrenal neoplasm. Most of the lesions are small and asymptomatic, incidentally discovered on clinical and CT scan examination, with the size varying from several millimeters to more than 30 cm. The most common complications develop due to pressure upon the neighboring organs. Differential diagnosis of a suprarenal fatty mass includes myelolipoma, renal angiomyolipoma extending from the upper pole, and retroperitoneal lipoma and liposarcoma.

EFFECTIVENESS OF TRANSSPHENOIDAL SURGERY AS AN INITIAL TREATMENT FOR NON-FUNCTIONING PITUITARY ADENOMAS – PERSONAL EXPERIENCE IN CLINICAL PRACTICE

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The vast majority (>80%) of clinically non-functioning pituitary adenomas (NFPAs) are gonadotroph-cell adenomas, as demonstrated by immunocytochemistry. However, they are rarely associated with increased levels of dimeric LH or FSH and usually clinically presented by tumor mass effect, and therefore need to be distinguished from asymptomatic incidentalomas. The aim of this study was to define the impact of surgery on regression of tumor compression symptoms in a series of patients with NFPAs undergoing endoscopic transsphenoidal surgery (TSS) dur-

ing the 2008-2009 period at our Department, which is the Reference Center for Hypothalamus-Pituitary Diseases in Croatia. A total of 31 patients underwent TSS, 11 (35.5%) of them female. The male and female patients were aged 17-84 and 62-76 years, respectively. Twenty-eight (90%) patients had macroadenoma, which was the predominant type of NFA both in men (n=19; 95%) and women (n=9; 82%). After surgery, visual field defects remained in 10 cases. Postoperatively, three (9.7%) patients had hypogonadism, 15 (48%) adrenal insufficiency, one (3.2%) patient hypothyroidism and two (6.5%) patients panhypopituitarism; all of which initially were macroadenomas. Two (6.5%) out of six (19.3%) MRI detected residual masses were successfully reoperated. Postoperatively, the three patients operated on for microadenomas had no residual masses on MRI and no need for hormone replacement therapy or additional treatment. In conclusion, considering that the results of medical treatment with dopamine agonists and somatostatin analogues are disappointing, TSS is the primary therapeutic approach in resolving symptomatic NFAs, especially microadenomas. The strategy of observation for patients with incidentally discovered pituitary adenomas is appropriate, provided that the tumor is well-delimited, small, has no extension with the risk of neurologic or visual chiasm compression, and that a meticulous hormonal work-up has ruled out the possibility of minimal hormonal hypersecretion.

EFFECTIVENESS OF TRANSSPHENOIDAL SURGERY AS AN INITIAL THERAPY FOR PATIENTS WITH ACROMEGALY – PERSONAL EXPERIENCE IN CLINICAL PRACTICE

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Department of Endocrinology, Diabetes and Metabolism, Sestre milosrdnice University Hospital is reference center for hypothalamus-pituitary diseases in Croatia. Acromegaly is a rare chronic debilitating disorder mainly caused by a growth hormone (GH)-producing pituitary adenoma. Acromegaly is associated with a two- to fourfold increase in mortality risk, mainly from cardiovascular disease, unless serum growth hormone (GH) levels are below 2 microg/L and serum insulin-like growth factor (IGF)-I levels are normal following medical treatment. These combined criteria were used to define remission of the disorder in this study. The aim of this retrospective analysis was to evaluate, using the biochemical parameter of remission, the initial outcome in a series of acromegaly patients operated by endoscopic transsphenoidal pituitary surgery (TSS). A total of 21 consecutive patients, 12 (57%) of them female, underwent surgery in 2008-2009. The male and female patients were aged 25-70 and 27-74 years, respectively. Twelve (57%) patients had macroadenoma, which was the predominant type of pituitary tumor in men (66%). In women, the number of micro- and macroadenomas was equal (n=6). None of the patients had ever been treated before. Hormonal assessment was performed at 6 months of surgery. Fifteen (71.4%) patients achieved biochemical remission of acromegaly. The remission rate at 6 months was 100% in patients with microadenoma and 50% in those with macroadenoma. The combined use of TSS and treatment with somatostatin analogues was beneficial for another three (14 %) patients, and two more (9.5%) achieved optimal control of tumor growth and endocrinological normalization by applying gamma knife radiosurgery (GKRS). In one (4.7%) patient, there was no favorable clinical result despite optimal combined therapy. In conclusion, TSS is beneficial and considered as the treatment of choice in the hands of experienced neurosurgeon because for providing rapid cure and normalization of survival in most cases. However, in some patients optimal control of tumor growth and normalization of hypersecretory states are achieved by secondary treatment modalities, including GKRS and somatostatin analogues.

EFFECTIVENESS OF TRANSSPHENOIDAL SURGERY AS AN INITIAL TREATMENT FOR PROLACTINOMAS – PERSONAL EXPERIENCE IN CLINICAL PRACTICE

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Prolactinomas are the most common hormone-secreting pituitary tumors. Medical therapy with dopaminergic agonists (DA) is the preferred initial

treatment for symptomatic prolactin (PRL)-secreting adenomas. However, in recent years, there has been a renewed interest in surgery. The aim of this retrospective analysis is to report a series of patients operated for prolactinoma in 2008-2009 at our Department, which is the reference center for hypothalamus-pituitary diseases in Croatia. All patients were diagnosed on the basis of neuroradiological imaging and endocrine assessment of pituitary function. A total of 61 consecutive patients underwent endoscopic transsphenoidal pituitary surgery (TSS), 46 (75.4%) of them female. The male and female patients were aged 20-67 and 19-70 years, respectively. Twenty-two (36.0%) patients had macroadenoma, which was the predominant type of prolactinoma in men (73.3%). In women, microadenomas were more common (n=35; 76.0%). None of the patients had ever been treated before. After surgery, normalization of PRL levels occurred in 55 (90.2%) patients. Complete remission was achieved in all microadenoma cases. Six (9.8 %) patients with postoperatively high PRL levels initially had macroadenomas, and were in sequence treated with DA. Four patients resistant to DA and TSS underwent gamma knife radiosurgery (GKRS) with subsequent endocrinological normalization of PRL in two additional patients. The two remaining patients with incomplete remission had follow-up duration of one year that may have underestimated the complete response rate for tumors treated with GKRS. In summary, initial TSS therapy normalized PRL levels and relieved symptoms of hyperprolactinemia in a significant majority of patients, whereas morbidity of TSS is low in the hands of experienced pituitary surgeons. TSS can be offered as a definitive therapy, especially to patients with microadenomas.

ALVEOLAR RHABDOMYOSARCOMA OF FOOT: CASE REPORT

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The clinical and pathologic features of alveolar rhabdomyosarcoma of the left ankle joint in a 73-year-old woman are presented. The patient presented to surgery clinic because of redness and edema in the foot area (she mentioned a possible insect sting), and edema of her left leg. Urgent CD test of arteries and left leg veins was done and vascular events were excluded. On ultrasonography scan, a hypoechoic lesion of solid appearance was subcutaneously verified in the area of the left ankle lateral malleolus. Computed tomography (CT) scan of the pelvis confirmed the test results, showing enlarged lymph nodes of up to 30 mm in diameter parailiacally on the left and in the left inguinal region. Biopsy of the solid formation in the area of the lateral ankle was obtained, later followed by needle biopsy of the left inguinal lymph nodes. Histopathologic analysis of the solid tumor showed tumor tissue composed of fibrous septa covered with small to polygonal, mitotically active atypical tumor cells, and of hyperchromatic nuclei of solid and alveolar growth. Tumor cell mimunohistochemistry showed positive reaction for desmin, vimentin and myoglobin. Histology and immunohistochemistry (desmin, myoglobin, vimentin, CK-PAN, S-100 protein, synaptophysin, CD31) corresponded to alveolar rhabdomyosarcoma. Needle biopsy of lymph nodes was indicative of a malignant tumor of undiferentiated round cells. The patient died two months of the surgery. Alveolar rhabdomyosarcoma of foot is a rare cause of lymphedema of foot in adults. Alveolar rhabdomyosarcoma is a primitive, malignant, round-cell neoplasm that cytologically resembles lymphoma and shows partial skeletal muscle differentiation. The prognosis of alveolar rhabdomyosarcoma is distinctly worse than for the embryonal variety, even with the most recent combined treatment modalities.