Correlation between mast cells and different biological potential of fibrohistiocytic tumors

KEYWORDS: Soft tissue neoplasms; Histiocytoma; Fibrous; Mast cells; Grading

INTRODUCTION

The researches of the mast cells presence in the tumor biology have suggested its potential prognostic significance. Mostly, experimental studies have proposed its potential antitumor activity. Similarly, histological prognostic studies of carcinoma and sarcoma had contradictory results (1,2). Rare histological studies of mast cells in different sarcoma agree that higher number of tumor and peritumor mast cells may have favorable prognostic significance, but in different groups of sarcoma (2,3). AIM: We analyzed the relationship of tumor and peritumor mast cells in fibrohistiocytic tumors with different biological potential as histogenetic homogenous group of soft tissue tumors.

MATERIAL AND METHODS

The presence of tumor and peritumor mast cells was determined by counting them on 10' accidentally selected visual fields, 400 times magnified, in paraffin sections stained by Giemsa method of 121 fibrohistiocytic tumors (FH tumor): 69 benign (BFH), 14 dermatofibrosarcoma protuberans (DFSP) and 38 malignant (MFH), all graded in three degrees of malignancy. The data collected were statistically calculated by means of the Student T test of proportion.

RESULTS

We showed that the average number of peritumor mast cells increased from BFH over DFSP to MFH group with the malignancy G1. While atypical fibroxantomas (AFX) had the highest number of mast cells, in MFH group the number of peritumor mast cells was found to fall down with a further increase of the malignancy grade. The difference in the average number of peritumor mast cells was statistically significant between DFSP and MFH group of the malignancy grade. The average number of tumor mast cells in BFH was 1.3 times as high as the number of mast cells in DFSP and close to their number in all MFH together. However, MFHs of G2 malignancy had the highest average number of tumor mast cells, which was 1.6 times as high as the number of tumor mast cells in BFH, 2.1 times as high as in DFSP and 4.3 times as high as the number of tumor mast cells in MFH of G3 malignancy. As the highest average number of tumor mast cells was evidenced in AFX, it has been concluded that the number of tumor mast cells decreases with increasing tumor malignancy grades.

DISCUSSION

Histological prognostic studies of mast cells in a carcinoma had contradictory results. Lung adenocarcinoma has much higher number of tumor mast cells than the squamous type. Lung adenocarcinoma with a high number of tumor mast cells has a better prognosis. But, patients with the same type but stage I carcinoma have a worse survival than the group with a low tumor mast cell count (4). In breast carcinomas there is a connection between a better survival and a higher number of tumor mast cells, but in the carcinoma of the large bowel a higher number of tumor mast cells was found in carcinomas with nodal metastasis (1,5). A high number of mast cells around the cervical carcinoma is associated with a better survival. Rare histological studies of mast cells in groups of histogenetically different sarcoma agree that a less aggressive sarcoma is associated with a higher number of tumor and peritumor mast cells, irrespective of its histological type (2). When different sarcomas were divided into three grades of malignancy, significantly less mast cells were found in high-grade tumors than in intermediate and low grade groups (3). Considering other inflammatory cells in sarcoma, mast cells have been found to have a significant correlation with the survival. Katenkamp and Hunerbein suggested that the number of tumor mast cells must be a part of the score of the microscopic prognostic parameters for malignant sarcoma (7). We proposed that the activity of tumor and peritumor mast cells is different in carcinomas and sarcomas. These differences, the absence of standardized criteria for researching and the activity of unknown phenomena in tumor and peritumor stroma may be the causes of these contradictory results. Our results are in agreement with those studies which emphasize a favorable prognostic significance of mast cells in tumors pathobiology.

CONCLUSION

The average number of mast cells in tumors were lower than around them. These findings suggest different activity of the tumor and peritumor mast cells and point to a greater significance of peritumor mast cells in the pathology of FH tumors. An increasing number of peritumor mast cells and a falling number of tumor mast cells is connected with an invasive growth of low aggressive FH tumors. With an increasing malignancy grade, the number of peritumor and tumor mast cells falls down. The finding of an increased number of peritumor and tumor mast cells may have direct, independent and favorable prognostic significance for MFH.

REFERENCES

Incidence of gastroschisis

KEYWORDS: Gastroschisis; Amniotic Band Syndrome; Autopsy

INTRODUCTION

Gastroschisis, a rare congenital abdominal wall defect that originates in the antenatal period, with evisceration of abdominal organs, especially intestines in amniotic cavity, occurs almost exclusively in infants of mothers younger than 25 years of age (1). The development of gastroschisis has been attributed to a defect in differentiation of the somatopleural mesenchyme. It has also been proposed that gastroschisis occurs when there is a premature atrophy or abnormal persistence of the right umbilical vein, leading to the mesenchymal damage and failure of the epidermis to differentiate at this site (1). Other investigators have proposed that the condition may result from an intrauterine disruption of the right omphalomesenteric artery (2). It is supposed that gastroschisis can be the result of an antenatal amniotic rupture and amniotic band formation with a direct mechanical influence or fetal compression secondary to oligohydramnios, due to the amniotic fluid leakage or increased resorption (3). The diameter of gastroschisis, located to the right from the umbilicus, between the normal rectus abdominis muscles, is lower than 4 cm (4). In gastroschisis, the extruded organs include, in addition to the bowel, the stomach, urinary bladder, uterus, adnexa, or testicles (1), but the liver is not involved (4). The discolored, edematous intestines are embedded in a gelatinous mass, with fibrin. Associated anomalies are rare, comprising intestinal atresia or malrotation (4), undescended testicles, or lung hypoplasia (1). A birth weight is about 2500-g (1). Because there is no a recurrence of gastroschisis, the parents can expect normal next delivery.

MATERIAL AND METHODS

At the Institute of Pathology, University of Niš, 1356 standard pediatric autopsies were performed from January 1988 to December 2001. This autopsy material was analyzed in this study.

RESULTS

From January 1988 to December 2001, a total of 305 cases with congenital anomalies were registered. Nine babies with gastroschisis were found, three of them in 2001, and one case in 1991, 1995, 1996, 1997, 1999 and 2000 respectively. It makes 0.66% of all pediatric autopsies, and 2.95% of all congenital anomalies.

DISCUSSION AND CONCLUSION

The timing of gastroschisis development is controversial. Most embryologists suggest that the defect occurs between the fifth and tenth week of gestation. Others propose that the actual rupture of the umbilical membrane may occur either between the fifth and tenth week of gestation (antenatal variant), or near the time of birth (perinatal variant) (1). At our Institute, the highest number of patients with gastroschisis was found in 2001, unlike the former period when only one case was registered per year. It is in accordance with an apparent increase in the incidence of gastroschisis, reported by other authors.

REFERENCES

INTRODUCTION

Alpha1-antitrypsin deficiency is an autosomal recessive disorder, occurring only when both alleles at a given gene locus are mutant. The recurrence risk is 25% for each birth, 50% of the offspring are healthy gene carriers. Heterozygots are fenotypically normal, and both sexes are equally involved. Alpha1-antitrypsin deficiency is marked by an abnormally low serum level of this major protease inhibitor. The major function of this protein is to inhibit proteases, particularly neutrophil elastase released at sites of inflammation, resulting in elastine degradation in alveolar walls, and panlobular emphysema. The aim of this investigation was to present pathoanatomic features of two newborns with Alpha1-antitrypsin deficiency.

CASE REPORTS

Case 1. A female infant two months old, with the body weight of 2500 g, and body length of 55 cm. Because of the congenital microcolon and ileal stenosis a surgical intervention was performed. The main causes of death were diffuse peritonitis and bronchopneumonia. Panlobular emphysema, giant cell transformation of hepatocytes, with PAS (periodic acid and Schiff reagent) positive globules, and thymic atrophy were found.

Case 2. A female newborn, with the birthweight and length of 2500 g and 55 cm, respectively, after 40 weeks' gestation. Omphalocele measuring 7 cm, and scoliosis were present at birth. At necropsy presented by congenital bronchiectasies, panlobular emphysema, hyaline membrane disease, hydropic degeneration with extramedullary haematopesis in the liver, with PAS positive globules in hepatocytes.

DISCUSSION AND CONCLUSION

The association of the serum deficiency of alpha1-antitrypsin and chronic obstructive pulmonary disease was first noted in 1963 by Laurell and Eriksson (3). Characteristic globules in hepatocytes are measuring from 2 to 20 μm in diameter, with PAS positivity after diastase treatment, commonly located around portal tracts. In both our patients panlobular emphysema, and characteristic PAS positive globules in hepatocytes were found. Other anomalies were also found, including congenital microcolon and ileal stenosis in case 1, and omphalocoele and scoliosis in case 2.

REFERENCES

Borderline ovarian tumors

KEYWORDS: Ovarian neoplasms; Borderline; Pathology; FIGO; Survival analysis

INTRODUCTION

Borderline ovarian tumors were for the first time described by Taylor in 1929; they comprise 10-20% of all epithelial ovarian tumors (1). In contrast to invasive cancers, borderline tumors occur in younger age groups, with lower disease stage and better prognosis (2). Five-year survival for FIGO st. I is over 95%. Earlier reports on the mortality of even 20% in advanced stages were not confirmed in the last decade (3). The relapse rate is still the matter of dispute which influences the degree of radical surgery. However, biologic, epidemiologic and pathologic aspects suggest the association of borderline with invasive ovarian tumors, in spite of the fact that in the clinical practice on large series it was demonstrated that the risk is nevertheless small (4). Chemotherapy administration is still controversial. While some authors think that chemotherapic induces response in a significant number of cases, others dispute the benefit of cytostatic therapy since the mitotic activity in borderline tumors is lower compared to bone marrow cells. We may encounter extreme therapeutic modalities in the clinical practice, from a conservative surgery followed by patients’ observation only, to a radical surgery combined with postoperative chemotherapy. Aiming to contribute to the solution of the problem, a retrospective analysis of the clinical material was performed for the period 1990-2001; through the discussion and conclusion presented are the attitudes of the team performing diagnosis and treatment of malignant tumors of the female reproductive system.

PATIENTS AND METHOD

The group examined included the patients with borderline ovarian tumors treated at the Clinic of Oncology, Clinical Centre Niš, in the period 1990-2001. The data on the age at diagnosis, type of surgery, histologic tumor type, disease stage, postoperative therapy and response to therapy were obtained from patients’ histories, while the data on relapses, treatment of relapses and survival were obtained from the patient documentation planned for tertiary prevention.

RESULTS AND DISCUSSION

At the Department of Gynaecology, Clinic of Oncology, Clinical Centre Niš, 423 patients with malignant ovarian tumors were treated in the period 1990-2001, out of which 344 (81.32%) had epithelial cancers. Borderline tumors were present in 26/344 (7.5%) cases - the lower incidence than in other authors’ reports (1). The question may be asked whether the incidence of borderline tumors is lower in our female population or the patients with this histopathologic form of ovarian neoplasm are not referred to further treatment due to the conviction that surgical intervention would suffice. There is also the problem of precision of primary histopathologic diagnosis since in the clinical practice we have had cystadenoma cases in which progression occurred after a number of years, which corresponds to the borderline tumors clinical picture. There is also the possibility that for insufficiently radical surgical interventions some borderline ovarian tumors are from precaution labeled as invasive by the pathologists. The average age at diagnosis was 50.6 years (minimum 36, maximum 69), one decade more that in other authors’ reports (5). FIGO disease stage was not possible to determine in 11/26 (42%) cases due to insufficiently radical surgery (unilateral or bilateral adnexectomy, classical hysterectomy with bilateral adnexectomy without omentectomy or “blind” biopsies). The disease was diagnosed in the same percent for FIGO st. I, while 2 patients (2/26; 7.6%) had FIGO st. II and 2 (2/26; 7.6%) FIGO st.III. In 5/26 (19.2%) residual tumors (sized 1-3 cm) were identified. In most patients cytostatic therapy was postoperatively introduced (24/26; 92.3%) - 6 mono-chemotherapy cycles with Alkeran (7/24; 29.2%) or 4-6 cycles of polychemotherapy with combined cyclophosphamid (17/24; 70.8%). The reasons for cytostatic therapy introduction were an insufficiently radical surgery, unknown FIGO stage and demonstrated residual tumor. Postoperative radiotherapy of the small pelvis was performed as well in two cases. Irradiation was performed in two patients after cytostatic therapy; they belonged to the group with residual tumors. In spite of the administered therapy, 4 patients died (15.4%), while 1 was lost for follow-up. The remaining patients (21/26; 88.8%) are without the disease symptoms; they are regularly controlled within tertiary prevention measures. The five-year survival for st. I was 91%, which is similar to other authors’ results (7). Relapses have not been observed up to the present.

CONCLUSIONS

In spite of their indolent course, more than 10% of ovarian borderline tumors end fatally. From these reasons, proper intraoperative staging of ovarian tumors and radical surgery are of an extreme importance. The decision on the postoperative treatment should be brought by the council of physicians of appropriate specialties. Adjuvant cytostatic therapy is usually suggested for higher disease stages and the cases where FIGO staging was not possible to perform due to inadequate surgery.

REFERENCES

INTRODUCTION
Numerous reports have shown that administration of MSG during the sensitive early postnatal period results in neurotoxic lesions of the hypothalamus and circumventricular areas with manifestation of endocrine and metabolic abnormalities in adult age (1-3). Conflicted reported results in adult rats, neonatally treated with MSG, are the reason for comparative morphological examination of pituitary and adrenal glands in adult rats.

MATERIAL AND METHODS
20 newborn white rats were injected daily with MSG (5mg/g/TT) sc, on days 1-10 of life. Controls received no treatment. The rats were killed at 10 months of age; the pituitary gland, together with adrenals was removed. The paraffin sections were stained with HE, PAS and Van Gieson methods.

RESULTS
Macroscopically, the treated rats showed: stunted skeletal development, Cushing's obesity of "buffalo type", both pituitary and adrenal glands hypertrophy. Microscopically, basophil cells of the pituitary gland were hyperplastic-of large size, with foamy aspect and infiltrating neurohypophysis. Cortical cells of the adrenals were also hyperplastic, compared to controls.

DISCUSSION AND CONCLUSION
Neurotoxic lesions in the arcuate nucleus and other parts of the brain (3), induced by MSG treatment during early postnatal period, are accompanied by changes in the content of neurotransmitters and neuropeptides produced in hypothalamus. In contrast to our results, the others have reported lower pituitary and adrenal glands weight, but higher plasma corticosterone concentrations (2). The discrepancy in the weight of the examined glands between our results and the reported data (2) could be explained by a longer experiment duration (10 months) in our study. So, we have concluded that the obesity in the MSG-treated rats was secondary to disruption of the hypothalamic-pituitary-adrenocortical axis.

REFERENCES
Urine cytology and the diagnosis of renal allograft rejection - Preliminary experiences

KEYWORDS: Kidney transplantation; Graft rejection; Urine cytology; Histology

INTRODUCTION

Histological finding of allograft biopsy represents the standard in diagnosis of the renal allograft dysfunction. Urine cytology, as the less invasive, quicker and simpler method, showed high accuracy (1,2) in diagnosis of the acute renal allograft rejection, but, there were no systematic investigations of the urine cytology in diagnosis of renal allograft dysfunction of other etiology. This paper presents our first experiences in urine cytology in diagnosis of renal allograft dysfunction that was not caused by the acute allograft rejection.

MATERIAL AND METHODS

From 56 kidney transplanted patients in the period from 1996 to 1999 in Clinic for Nephrology, Military Medical Academy, 23 of them suffered allograft dysfunction. The etiological diagnosis was set up upon the clinical symptoms, histological findings and urine cytology. Biopsy material was analyzed according to Banff classification (3). Urine sediment obtained in cytocentrifuge was air dried and stained with May Grunwald-Giemsa. Cytology finding in urine sediment was interpreted according to Burrows et al. (1) and Schumann et al. (4). The urine cytology monitoring period lasted one year.

RESULTS

Twenty-three patients with renal allograft dysfunction had 20 episodes of acute rejections, 7 episodes of cyclosporine nephrotoxicity, 3 patients had acute allograft infections, 5 chronic nephropathy, one had tubular necrosis, one had allograft infarction, and two patients had recurrent disease. From 7 patients with expressed cyclosporine nephrotoxicity, in 5 of them urine cytology pointed out this etiology, which was also the case in one of two patients with the acute tubular necrosis. The urine sediment of these patients dominated demonstrated the groups of tubular cells with constant presence of erythrocytes, neutrophilic leucocytes, and variable presence of other cells. In two patients with recurrent disease (membranoproliferative and focal sclerosing glomerulonephritis) urine cytology demonstrated dysmorphic erythrocytes, cilin-

dres and mixed cellularity that pointed out the parenchymal damage. From 5 patients with chronic allograft rejection, in 4 patients, occasionally within a year, lymphocytes were present in the urine sediment, neutrophilic leucocytes, monocyte/macrophages, tubular cells, cilindres, without the predominance of one cell type. In three patients with allograft dysfunction urine sediment indicated the infective etiology with findings of bacteria, funges, CMV inclusion bodies in the nuclei of the urothel cells. Out of total 19 episodes of renal allograft dysfunction not caused by the acute rejection, appeared in 12 patients during a year's monitoring period, in 12 episodes urine cytology findings correlated with clinical and histological findings. Thus the accuracy of urine cytology was 78.9%.

CONCLUSION

In the diagnosis of the acute renal allograft rejection, the urine cytology is partially standardized, but there is no appropriate standardization of the urine cytology in renal allograft dysfunction of other etiology. Our results demonstrated that urine cytology could be the alternative to histological findings in diagnosis of the acute tubular necrosis or cyclosporine nephrotoxicity. Also, urine cytology pointed to renal parenchymal damage, while the importance of this method in chronic allograft nephropathy is still to be investigated.

REFERENCES

Incidence of multiple tumors in patients with genital tract malignancies

KEYWORDS: Multiple neoplasms; Genital tract malignancies

INTRODUCTION

Multiple organ involvement with cancer is most frequently the consequence of direct spread of the tumor to the surrounding structures or its metastasizing. The diagnosis of two or more tumors in one patient is not a rare event. These processes may be diagnosed simultaneously (most often in the operation tissue material) or several months and even decades after the primary event. Second malignancies may be induced by some therapeutic procedures (radio-, cytostatic or hormonal therapy). In hormonodependent tumors, special attention should be paid to the symptomatology of other normal organs affected by hormones. This especially applies to breast, corpus uteri and ovarian cancer (3,4). We should speak of multiple tumours only if a pathologist clearly confirms two independent malignancies, ruling out metastases. Precise histopathologic diagnosis is of great importance since it determines further therapeutic proceedings. For instance, the presence of ovarian or uterine metastases in primary breast cancer requires quite a different therapeutic approach compared to the treatment of primary cancers of these organs. The responsibility of a clinical pathologist is therefore great, but his positive contribution is even more important - a proper diagnosis will enable appropriate therapy administration. Aim of this paper is to establish the incidence of multiple tumors in women with genital tract malignancies in the region of Niš in the period of four years.

MATERIAL AND METHODS

The information from the Registry for Cancer, Clinic of Oncology in Niš, collected from 1998 to 2001 was used in this work. All new cases of gynaecologic malignancies were registered and out of them multiple cancers were singled out. Based on the data, it was possible for us to establish whether there was the difference in incidence of multiple tumors in cervical, corpus uteri and ovarian cancers, as well as to establish the most common second neoplasms.

RESULTS AND DISCUSSION

In the period 1998-2001 there were 614 cervical, 462 corpus uteri and 254 ovarian cancers (total, 1330 cases). The incidence of cancers of the vulva and vagina was very low so these tumors were excluded from the analysis. Multiple tumors were registered in 36 patients (36/1330; 2.7%). In 35 cases there were two tumors and in 1 case three tumors. Out of 614 cervical cancers, second malignancy was simultaneously diagnosed (or already known) in 9 (1.46%). In 8/9 cases it was planocellular cervical cancer; in one case anaplastic tumor was detected. In 6/9 invasive ductal carcinoma of the breast was previously diagnosed. In 2/9 ovarian tumors were detected in the operative material, 1 cystadenoma serosum and 1 granulosocellular carcinoma. In 1/9 bronchial adenoacarcinoma was diagnosed. Multiple tumors in primary corpus uteri cancer were observed in 15 cases (15/462; 3.25%). In 9/15 cases endometrial adenocarcinoma was verified; in 4/15 patients endometroid carcinoma, in 1/15 adenoacarcinoma papillare and in 1/15 carcinomas of the uterus. Breast cancer was most commonly present as the second independent tumor - in 7/15 cases (6 invasive ductal carcinomas; 1 lobular carcinoma). In 6/15 ovarian cancer was diagnosed (5 cystadenoma serosum; 1 carcinoma endometroides partim mucinosum). Ovarian tumors were diagnosed in operative material and described by pathologists as separate malignancies. Metastatic processes from the uterus to the ovary were ruled out. In one case adenocarcinoma of the colon was diagnosed and in one case planocellular cervical carcinoma. It is worth noting that in addition to the described cases, in 5 other patients with corpus uteri carcinoma CIN-III was diagnosed in the operation material. Multiple tumors in patients with ovarian neoplasms were diagnosed in 13/254 (5.1%) cases. Most common pathology of ovarian tumors is cystadenocarcinoma serosum (7/13). In one case it was endometroid ovarian cancer, 2 granulosocellular carcinomas were detected, 1 dysgerminoma, 1 Brenner and 1 Kruckenberg tumour. Second malignancy was most often verified in the uterus (5 endometrial cancers and 1 uterine carcinomasarcoma). In 2 cases planocellular cervical cancer was diagnosed (in endometriot ovarian cancer and in carcinoma granulosocellulare). Second granulosocellular ovarian carcinoma was diagnosed in 1 patient with adenocarcinoma of the stomach. Stomach was the locus of the primary tumor in one case of Kruckenberg tumor. Brenner tumor was observed in one patient with planocellular carcinoma of the vulva. Invasive ductal carcinoma of the breast was diagnosed in 2 patients. One patient had cystadenocarcinoma serosum ovarii and the other dysgerminoma. In the latter case there is information on medullar carcinoma diagnosed 28 years prior to ovarian cancer.

CONCLUSION

Multiple tumors in patients with gynaecologic malignancies are most commonly encountered in those with ovarian tumours (5.19%); they are least common in those with cervical carcinoma (1.46%). Second tumor is most commonly verified in the breast (6/9 in cervical carcinoma, 7/15 in corpus uteri cancers, 2/13 in ovarian tumours). Association of breast and corpus uteri cancers may be explained by their hormonal dependence, and incidence of cervical and breast cancers probably by the fact that cervical cancer is in incidence second only to breast cancer. In ovarian tumors, a pronounced variability was observed regarding second malignancy presence. Carcinoma of the corpus uteri was observed in a high percent as expected, while breast cancer and digestive tract cancers were observed in a lower percent compared to the literature data.

REFERENCES

Mammary gland tumors of bitches have raised great interest both in human and veterinary medicine, reflected during the last several years in the increased number of the experimental studies in the field. Numerous studies were conducted, among others, in order to find the closest animal model for studying the breast tumor in women. This is also favored by the short life span of the dog, rather rapid progression of the disease and a large number of the potential foci (ten mammary complexes), which make the bitch an ideal model for comparative studies. As for their incidence, mammary gland tumors of dogs are immediately behind the skin tumors, being at the same time the most common neoplasms in the bitches. According to the reports of the majority of authors, these tumors account for 25-50% of all canine tumors with approximately equal malignant and benign neoplasms ratio. Findings of different authors vary mostly due to the disputes related to the classification type. Namely, one of the major disadvantages discouraging the application of the pathohistological method is the fact a precise understanding of the neoplastic cell origin in the tumor tissue hasn't been achieved yet, particularly when the tumor cells are poorly differentiated. Therefore, the histogenesis of a certain number of tumor cells remains unknown, and thus, other methods are used in order to solve the problem. The application of immunohistochemical methods provided for the large amount of data on the roles of different growth factors and hormones in the process of tumorigenesis. The average count and AgNOR area and lower AgNOR - nucleus area ratio have a more favorable prognosis. Pathohistological, cytochemical and immunohistochemical studies were performed on 58 surgically excised mammary gland tumors of bitches. The tissue sections were fixed in 10% neutral formalin and stained by hematoxylin and eosin, Weigert Van Giesson, silver colloid or nuclear fast red. AgNOR counting was performed under immersion (x1000), and each clearly demarcated AgNOR was considered a unit. The silver colloid method was blocked using 3% H2O2 in methanol, while antigen demasking was performed applying protease at 37°C in a thermostat. Visualization of the reaction was achieved by diaminobenzidine (DAB) solution in imidazol with H2O2, while contrasting was performed using hematoxylin. The application of WHO classification on the 58 specimens of the mammary gland tumors of bitches led to the diagnosis of 37 malignant tumors, 17 benign tumors and 4 mammary gland hyperplasias. Out of the total number of 39 malignant tumors in the studied material, simple carcinomas were the most frequent (17 cases), followed by complex carcinomas (12 cases), 5 carcinomas in the mixed tumors and 3 mucinomous carcinomas. The simple carcinomas were composed of only neoplastic epithelial cells forming tubular, papillary, tubulo-papillary or solid structures. However, complex carcinomas were composed of both neoplastic epithelial and myoepithelial cells. Carcinomas in the mixed tumors were characterized by the presence of bone and/or cartilaginous tissue, as well as neoplastic epithelial and myoepithelial cells. Mucinomus carcinomas were composed of the neoplastic cells of the stellate, triangular or dendritic shape and surrounded by a large quantity of basophilic intercellular substance - mucine. The predominant benign tumors in the studied material were benign mixed tumors (10 cases), followed by simple adenomas (6 cases) and complex adenoma (1 case). Complex adenosmas were composed of the myoepithelial and epithelial cells, while simple adenosmas were composed of only a single cell type, either the epithelial or myoepithelial one. Benign mixed tumors are characterized by the presence of the cartilaginous or bone tissue and proliferated epithelial and myoepithelial cells. Out of the total number of 4 hyperplasias, 3 lobular and 1 duct hyperplasia were diagnosed. Cytokeratin found in the simple carcinoma of the tubulopapular and solid structure was diffusely expressed on the prismatic and cuboid uncharged and neoplastic epithelial cells of the alveoli and canals, as well as on the neoplastic epithelial cells in the stroma and lymph nodes. In the complex carcinomas and carci-nomas in the mixed tumor, cytokeratin expression was observed on the epithelial and resting cells, spindle cells and stellate myoepithelial cells. The examination of the mucinous carcinomas evidenced a wide non-reactive band around the cytokeratin-positive neoplastic cells. In all the benign tumors, cytokeratin was expressed exclusively on the epithelial cells, and spindle-shaped and resting myoepithelial cells. In hyperplasias, cytokeratin was expressed only on the epithelial cells of the canals and alveoli. The average AgNOR count per cell was 7.14 in the malignant tumors, 3.73 in the benign tumors and 3.55 in hyperplasias. Based on AgNOR pattern distribution, all the cells in the studied material were classified into six types. Type I is characterized by the presence of 3-6 moderately sized round-shaped AgNOR. As for the type II cells, either centrally or peripherally placed large nucleolus containing a large black colored AgNOR structure is observed. In type III cells, the nucleolus contain 3-7 AgNOR dots. Type IV cells are characterized by the presence of large nucleoli prominently irregular in shape, containing a large AgNOR. Type V cells are distinguished by 5-20 diffusely distributed AgNOR dots. Type VI cells are characterized by relatively large, elongated, sickle- or irregularly shaped nucleoli containing up to 20 AgNOR dots. Cell types I, II and III are predominant in hyperplasias and benign tumors, although in two benign tumors a number of type IV cells was observed as well. In two benign tumors, type IV cells were evidenced, but the examination failure revealed two cell types V and VI. As for the malignant tumors, cell types III, IV, V and VI were the predominant cell population, followed by cell type I, and finally cell type II. Cell types I, II and IV are predominant in the malignant tumors with 5.5-7 AgNOR per cell at the average, while cell types V and VI proved to be dominant in tumors with more than 7 AgNOR per cell at the average.

Accurate diagnosis and prognosis of the mammary gland tumors necessitate a precise determination of the tumor cell origin, as well as the degree of their differentiation. To achieve this, it is necessary to perform additional immunohistochemical and cytochemical studies. The application of cytokeratin antibodies may eliminate, in numerous cases, all the ambiguities related to the tumor cell origin. The information necessary for approximate prognosis of the disease course are obtained applying the silver colloid method. Based on the results of our studies, it may be concluded that the presence of the cell types V and VI is strongly suggestive of the malignant tumor of the mammary gland in bitches.
The peripheral giant cell granuloma (PGCG) is a focal, reactive overgrowth of the oral mucosa. The aim of this study is to present the histopathological features of these lesions. Ninety-one cases of PGCG were retrieved from the files of the Department for Oral Pathology, Faculty of Stomatology Belgrade. The biopsy material was prepared by standard methods, stained by HE, and analyzed by a light microscope. The following parameters were analyzed: the inflammatory infiltrate (localization, contents), bleeding zones, multinucleated giant cells (distribution and types). The inflammatory infiltrate was localized in the superficial layer (60 PGCG, 66%); the focal infiltrate was found in 30 PGCG (33%); the diffuse infiltrate was found in 1 PGCG (1%); 54 PGCG (59%) consisted of the mixed infiltrate (lymphocyte, plasmocyte, and granulocyte). Extravasation of erythrocytes was found in all lesions, while deposits of hemosiderin were found in 86 PGCG (95%). Two main types of giant multinucleated cells were present in all lesions. The distribution of the giant cells was diffuse (94,5%), and focal (5,5%). The peripheral giant cell granuloma is characterized by many multinucleated giant cells distributed throughout the fibrovascular stroma. Due to its specific microscopic features, the PGCG belongs to giant cell lesions of the jaws.

KEYWORDS: Peripheral Giant Cell Granuloma; Jaws; Pathology

During the ordinary medical practice, clinical doctors may have some difficulties in diagnosing a disease and trauma. The possibility of mistakes cannot be excluded, besides the clinical experience and modern technology. The aim of this study is to compare the clinical and histopathological diagnosis of patients who were under the surgical treatment at the Clinic for Maxillofacial surgery, Faculty of Stomatology-Belgrade. The relevant data were taken from ambulatory medical files, histories of diseases and histopathological reports which were completed at the Department of Pathology, Faculty of Stomatology over the period 1999-2001. The total of 5178 biopsies were taken during this period. The biopsy material included the samples obtained from surgical specimens, after the treatment of patients (ambulatory, hospital). We can conclude that a definite diagnosis is the result of an adequate correlation between the clinical and histopathological findings.

KEYWORDS: Differential diagnosis; Clinical diagnosis; Pathology
Cyttoplasmic “budding” and fragmentation is a normal physiological mechanism of platelet formation during the process of thrombocytopoiesis. In pathological conditions it is assumed that this process is connected with acute megakaryoblastic leukaemia (AML M7) and it is also used as its morphological equivalent at the level of conventional microscopy. Pseudoplatelet formation is a very rare pathological condition because there is cytoplasmic budding and fragmentation of other cell types. The exact mechanism is unknown but it is connected with a general disturbance of cellular substruc-

tures. Pseudoplatelet formation can occasionally be seen in other acute leukaemias, preleukaemic states (MDS) and in very severe infections. Cytological and ultrastructural characteristics of 8 patients with acute leukaemia (AML M0, M1, M2, M4 i M6 kao i ALL) and 3 patients with MDS RAEB were analyzed. Leukaemia type was confirmed by standard cytological analysis and by immunophenotyping. In 6 patients ultrastructural analysis was performed. On conventional microscopy, there is vesicular structure formation below the plasma membrane with a tendency to form channels along plasmalema. Sequestration is to be done along this channels. There is also “budding” of cytoplasm, with further sequestration of pseudoplatelets. Cyttoplasmic “budding” and fragmentation is not an equivalent of the megakaryocytic lineage. Pseudoplatelet formation has simillar morphological characteristics as the consequence of the cellular disturbance in a malignant clone. The application of monoclonal antibodies is neccessary to confirm the real cell lineage in acute leukaemias and preleukaemic states.
Squamos cell carcinomas of the oral cavity

The most common malignant neoplasm located in the oral cavity is the squamos cell carcinoma. In European countries this tumor represents 3-5% of all malignancies in the oral cavity. The frequency and distribution of these carcinomas depend on geographic factors, race, sex and of patients' daily habits. The aim of the study is to determine the frequency of squamos cell carcinomas which can be based on localization, age and sex. This study included 100 squamos cell carcinomas diagnosed at the Department for Oral Pathology-Faculty of Stomatology in Belgrade during year 2001 year, which makes 7% (with recidives) of the total number of diagnosed tumors. The most common localization of the squamos cell carcinoma are the lips (54 cases), the lower lip being more frequently involved (44 cases), than the upper one (10 cases). Common localizations are also the tongue (18 cases), maxillary alveolar crest (8 cases), oral cavity base (8 cases), mandibular alveolar crest (5 cases), soft palate (4 cases), hard palate (1 case), paliatoglosal arch (1 case) and retromolar triangle (1 case). The affected age ranges from the 4th to the 9th decade of life, with the peak frequency for the lips in the 7th and 8th decade, for the tongue in the 5th and 6th, for the maxillar alveolar crest in the 6th and 7th, for the oral cavity base in the 7th and 8th, for the mandibular alveolar crest in the 6th and 7th, and for the soft palate in the 7th decade of life. As for the sex, the squamous cell carcinoma is more frequent in males than in females (of 100 patients, 68 were males and 32 females). A considerably higher frequency of these carcinomas in the lower parts of the oral cavity can be explained by a higher sensitivity of the epithelium of this region and its direct contact with cancerogenous agents.

KEYWORDS: Squamous cell carcinoma; Mouth neoplasms; Pathology

Mesenchymal chondrosarcoma - A case report

Mesenchymal chondrosarcoma is an extremely rare tumor composed of sheets of primitive mesenchymal or precartilage cells and interspersed islands of cartilaginous tissue in various stages of differentiation. This report describes a case of a 35-years old female with an extremely aggressive mesenchymal chondrosarcoma of the right upper arm. The patient asked for the medical help because of a rapidly growing tumor in the region of the right upper arm. The X-ray and CT imaging of the arm revealed a tumorous change placed in the biceps without a contact with the humerus. She had the following laboratory test findings: the sedimentation rate of 30/65 and alkaline phosphatase of 161, while other analyses showed normal values. Enucleation of the tumor node was performed. Macroscopically, the node was presented as a lobulated gray-white firm mass, measuring 11x8.5x7cm in size. Microscopically, the tumor was composed of undifferentiated oval and spindle-shaped cells and small nodules of cartilaginous tissue benign in appearance, with central calcification and ossification. The stroma consisted of sinus-like vascular areas. PAS positive material was found in the cytoplasm. Immunohistochemically, the tumor cells revealed S-100 protein positivity. Mesenchymal chondrosarcoma was verified by teleconsultation. The patient received adjuvant chemotherapy. A great number of metastases in the spine and the ribs appeared 8 months after the operation. The patient died 10 months after the tumor had been diagnosed. This rapid clinical course confirmed its extreme aggressiveness.

KEYWORDS: Mesenchymal chondrosarcoma; Case report
Idiopathic giant-cell myocarditis

Idiopathic Giant-cell myocarditis is a disease of relatively young adults, leading to lethal outcome due to cardiac failure and heavy forms of ventricular arrhythmia. Female corps (56 years of age) was delivered to the Institute of Pathology, Medicine School of Belgrade, from Emergency center Clinical center of Serbia, with the following diagnosis: AV block gradus III; status post reanimationem; implantatio pace-maker temporarius; asystolia. For last 6 years the patient was treated for cardiomyopathy (we assume dilative). The anamnesis indicated that the patient had suffered from chest pains, dyspnea, syncope and arrhythmias. Autopsy examination showed significant left ventricular hypertrophy and right atrio-ventricular dilatation. Sections throughout anterior and posterior walls of the left ventricular, septum and apex cordis contained diffuse foci of yellowish colour up to 1 cm in diameter, on the red-brown base of myocardium. Multiple blocks of the heart were taken and formalin fixed, prepared using the standard technique by applying hematoxylin-eosin stains, Elastican Wan-Gieson and Masson (trichrome), and analysed by light microscopy. There were numerous granulomas, composed of giant cells, fibrous tissue and lympho-plasmocytic infiltrate on the sections that were taken from anterior left ventricular wall and septum. We noticed presence of both giant-cells types (Langhans type and foreign body type). The latest from anterior left ventricular wall and septum. We noticed presence of both giant-cells types (Langhans type and foreign body type). The latest

AgNOR distribution and count in T- and B-lymphomas in dogs

Together with mammary gland tumors, lymphomas were the most frequently diagnosed neoplasms in dogs in our sectioned material. They develop in different dogs of all age categories and both sexes. Based on the R.E.A.L. classification (Revised European American Lymphoma Classification), DL were classified into 3 major categories: B-lymphomas, T-lymphomas, NK-cell lymphomas and Hodgkin's lymphomas. Based on the reference data, the prognosis is less favorable in dogs with T-lymphoma in comparison to those with B-lymphoma. AgNOR studies on T and B lymphomas of dogs evidenced that dogs with better prognosis had a smaller number of AgNOR, greater average AgNOR area, greater maximal AgNOR area, smaller distance between the two AgNORs, and smaller AgNOR area-nucleus area ratio. AgNOR pattern distribution in dog lymphoma is relatively insufficiently studied, and based on the results of the study the correlation between the course of the disease and AgNOR distribution pattern was noted. In addition to AgNOR, and for the purpose of as accurate as possible diagnosis of DL, other markers of cell proliferation such as Ki-67 and PCNA are used as well. Due to its similarity with human non-Hodgkin's lymphoma, DL are excellent animal model for studying the new diagnostic procedures and chemotherapeutic agents. The study was performed on the material obtained from 11 dogs of different breed, sex and age, subjected to post mortem examination with a, routine histopathological examination which confirmed the diagnosis of lymphoma. The sections of the lymph nodes, skin, spleen, liver, kidneys, intestines and lungs were fixated for 24-48 hours in 10% neutral formalin and paraffin embedded. After paraffin removal in xylol, rehydration in alcohol and distilled water series, 3-5 μm thick sections were stained by HE, Giemsa, silver colloid method and immunohistochemical methods - peroxidase - antiperoxidase (PAP) and direct peroxidase (DP) in order to verify CD79, CD3 and MAC-387 expression. Colloid silver staining solution was obtained by mixing 33% aqueous AgNO₃ solution (2 parts) and 2% gel in 1% formic acid (1 part). The staining was carried out in a dark chamber for 40 min. at the temperature of 24°C. The sections are thereafter rinsed with distilled water, silver surplus was removed by rinsing with 2% Na₂S₂O₃. One half of the colloid silver stained sections was contrasted using Nuclear Fast Red (NFR). The average AgNOR count per tumor was determined by AgNOR counting in the nuclei of 100 neoplastic cells. The counting was performed under immersion (x1000), and each clearly demarcated AgNOR, regardless of its size and location in the neoplasm was considered a unit structure. As for the peroxidase-anti-peroxidase method (PAP) the sections are previously treated by protease (P8038) at 37°C for 5 minutes. Primary monoclonal antibodies mouse-anti human CD79 (Dako, M7051) to B cell line and mouse-anti human MAC -387 (Dako M0747) to macrophages, monocytes and neu...
trophic granulocytes, were separately applied for 12-16 h at 4°C. Monoclonal mouse antibodies (Contr. T1 - Inst.Vet.Path. Giessen) were used as negative control. Direct peroxidase method (DP) was used for detection of CD3 antigen at T-lymphocytes. The sections are also subjected to proteolytic antigen demasking for 35 minutes at 37°C using commercially available lyophilized trypsin obtained from the cattle pancreas (Dako, S2012). Endogenous peroxidase activity was blocked using 3% H₂O₂ dissolved in distilled water. Commercially available antibody produced on rabbit (Dako epos CD3/HRP, U00026) was used in DP. Dako EPOS negative control was used as negative control. In PAP method, endogenous peroxidase blocking was achieved using 0.3% H₂O₂ in methanol, while pre-incubation was performed in normal 10% rat serum in TBS. Secondary incubation was performed with rat anti-mouse lg, followed after PAP for 3 minutes at room temperature. All dissolutions and washings in the course of reactions were made in TBS. Reaction visualization was achieved in 0.05% 3,3-diaminobensidine tetra-chloride (DAB, Serva) in 0.1 M buffered imidazole HCl, (pH=7.1) with Papanicolaou hematoxylin (Merck) contrasting. LP was diagnosed in three bitches and eight male dogs. According to the anatomical classification, three different forms were observed: multicentric (8 cases), alimentary (2 cases) and skin (1 case). Immunohistochemical studies enabled the diagnosis of eight B-lymphomas and three T-lymphomas. CD79 expression in B-lymphoma was observed in the form of granulated cytoplasmatic brown-colored precipitates. As opposed to it, CD3 reaction was evidenced on the edge of the mature T-lymphocytes or, in the form of the granulated cytoplasmatic precipitate in developmental forms of T-lymphocytes. Based on the histological appearance, count and AgNOR distribution, the tumors were classified to: well differentiated (single T-lymphoma), moderately differentiated (two of each T and B lymphomas) and poorly differentiated (six B lymphomas). The average number of AgNOR was: 7.97 in poorly differentiated, 4.64 in moderately differentiated and 2.91 in well differentiated tumors. The total of 5 different AgNOR distribution patterns, i.e., cell types, were observed. Type I is characterized by a single large centrally positioned nucleolus with a relatively large round-shaped AgNOR in it. Type II is characterized by two to three medium-size nucleoli with a single AgNOR within each of them. Type III is characterized by the presence of mostly 3-6 moderately sized round-shaped nucleoli completely “filled” with AgNOR. Type IV is characterized by the presence of 2-5 irregularly shaped, round or oval nucleoli with 2-5 AgNOR observable in them. The main type V cell characteristic is the presence of the relatively large irregularly shaped nucleoli filled with a large number (sometimes even over 20) of AgNOR. In poorly differentiated DL, types IV and V were predominant, with types I, II and III and types I and II predominating in moderately differentiated and well differentiated tumors respectively. DL immunophenotyping using cell markers CD79 and CD 3 is highly important for the prognosis, since it is impossible to differentiate T and B lymphomas without their application. This is even more important in the light of the already known fact that survival is longer in dogs with diagnosed B lymphoma, while the prognosis is better in dogs with T lymphoma of the same differentiation stage. The average AgNOR number was proved to be a highly reliable prognostic parameter in DL, since, unlike Ki-67 and PCNA markers, it provides the information on the cell cycle duration. However, the differences in thickness, staining solution concentrations, temperature and duration of staining produce great difficulties when correlating the results of different authors. Therefore, the possibility of application of the unique AgNOR distribution pattern as a parameter less liable to biasing is under study.

Brown tumor of maxilla in patient with secondary hyperparathyreoidism

Parathyroid osteopathy or brown tumor is a kind of a lesion caused by hyperparathyreoidism. It appears as an expansive bony lesion mostly in mandible, rib, pelvis and femur, but rarely in the upper jaw. Here we present a patient with secondary parathyroidism, terminal renal failure and tumor of the maxilla. 25 years old male, dialyzed for 11 years because of the renal failure, over the last three years suffered of several episodes of facial swelling and nose bleeding, each time successfully managed with nasal decongestives and anterior nasal tamponade. At the moment of admission at the Clinic, he had a massive bleeding from both nostrils and an evident bilateral tumor of the maxilla, deforming the midfacial third. The laboratory finding of PTH = 1050 ng/L indicated the secondary parathyroidism. Splanchnocanal CT scans revealed a spherical, clearly delineated expansive structure sized up to 2 cm, with thick white bony edges outside and partly calcificated soft tissue inside, paramedially on the hard palate. There was also another irregular lobulated lesion into the right inferior nasal cavity with bony edges outside and partly calcificated soft tissue inside, that measured 6 cm, filling with its cranial part both nasal holes, disrupting the medial orbital wall and deforming the right maxillary sinus and ethmoidal cells. Besides the changes at all cranial bones, there were no endocranial pathologic changes. Ultrasonographic examination of the neck described a normal size of the thyroid gland, but the right inferior parathyroid gland measured 64 mm. After a careful preoperative nephrologic and endocrinologic preparations, the patient was operated. Macroscopically, the tumor was distinctive from the adjacent tissues with its bony membrane, inside which was a medulla-like bony mass that could be easily curedt. By partial resection of the right maxilla, the tumor 4x5 cm fulfilling the whole maxillary sinus and penetrating into the orbita and nasal cavity was removed. The histopathologic finding of: the fundament of the lesion consisted of the proliferating connective tissue with small groups of giant multinuclear cells of benign, osteoclastic appearance. There were also areas of bleeding and hemosiderin. All tumors prone to bleeding produce a larger amount of hemosiderin, which contributes to their brownish colour. Besides, there are also areas of ostoid and new bone production. The bone itself demonstrated fibrosis of the bone marrow and osteoclastic resorption of trabecules. Such histopathologic finding is not strictly specific for parathyroid osteopatich lesions, the so called “brown tumors”. Similar histologic structure appears in other gigantocellular lesions of the jaws, such as giant cell tumor, giant cell granuloma and cherubism, histologically characterized with two main components: mononuclear stromal cells and multinuclear giant cells. Chronic renal failure causes renal osteodystrophy due to secondary hyperparathy-
roidism, with the incidence of 18% after one year and 92% after two or more years of dialysis. Bone resorption is a result of the osteoclastic activity due to the increasing parathyroid hormone. This long-term dialyzed patient with chronic renal failure, increasing PTH, decreasing calcium and ultrasonographically enlarged parathyroid glands, obviously suffers from secondary parathyroidism, in whom the bony tumor of the jaws can be ascertained as the BROWN TUMOR. From the surgical point of view, this is considered to be an important fact for operative planning. In these cases, an excessive, mutilating surgery is avoided, but only the tumor reduction or extirpation is indicated, followed by a subsequent parathyroidectomy of the enlarged gland and substitutional therapy, that influence the restructuring of the involved bones.

Oral carcinoma makes 2-5% of all carcinomas. According to the evidence of the Institute of Health Care of the Republic of Serbia, in 2000 malignant tumors of the head and neck appeared in 4% of male and 2% of female patients. The etiology of oral squamouscellular carcinoma (OSCC) is not completely understood. There are several factors that influence its occurrence, such as smoking over 20 cigarettes a day, poor oral hygiene and immune system disturbances. In some patients the predisposition for the OSCC is caused by genetic polymorphism of certain genes that are extremely sensitive to alcohol and cancerogenic substances in tobacco smoke. As an independent risk factor for the onset of another primary malignancy in the oral cavity acts also some genetic predisposition based on chromosomal fragility due to mutagen activity of the tobacco smoke. OSCC appears mostly on the tongue: 75% on the anterior two thirds and 25% on its base. At the moment of establishing the diagnosis, 35% of patients also have regional neck metastases, in 5% bilateral, as a result of cross lymphatic drainage of the tongue. Clinical examination and TNM classification are necessary to determine the stage of the disease, and the histopathological analysis provides histologic and nuclear grades of the disease crucial for selecting the adequate treatment (surgery, polychemotherapy, irradiation or their combinations). They also provide a valid prognostic criterion in the follow-up of the clinical course, remission duration and survival rate. In the spite of better surgical techniques and more efficient postoperative irradiation and/or polychemotherapy, the rate of five-year survival without relapse is still low, accompanied by a high mortality rate. Primary treatment of the OSCC of the tongue and base of the mouth in the first stage (T1N0M0) is surgery - an excision into macroscopic healthy tissue; while in the second (T2N0M0) and the third (T3N0M0, T1-3N1M0) stages the surgery is to be succeeded by postoperative irradiation, except in case of the G4 histologic grade, when the additional polychemotherapy is administered because of its high metastatic potential. In the fourth stage of the OSCC (T4N0-1M0, anyT, N2-3M0), the operability is estimated according to the size of the tumor and adjacent involved structures, taking into account the possibilities for resection and the quality of life after this kind of surgery. If there are distant metastases (any T, any N, M1) surgical treatment is not indicated, but only symptomatic therapy. This retrospective study analyses 30 (26 males and 4 females at the mean 68 years of age) patients who were...
operated at the Clinic for Maxillofacial Surgery of The MMA in period from 1995-2000, because of the OSCC of the tongue and floor of the mouth (second and third stage of the disease, histologic grade G2-3, nuclear grade NG2-3). Postoperatively, they all received additional transcutaneous antitumorous irradiation according to the protocol for this type of carcinoma. It was obvious that the efficiency of both the surgery and irradiation was not the same in all equally treated patients with the same histologic type, grade and size of tumor. The local relapse and/or regional cervical metastases after a certain period of time after the surgery performed according to the radical ablative oncologic surgery principles may result from radioresistance of the tumor, which is defined as an occurrence of the relapse or rest of the tumor of the same histologic type after irradiation. The reason for this event must also be searched for at the genetic level (mutations of the p53 antioncogen). To assess the importance of the histopathologic finding for both diagnostic and therapeutic purposes, it should be correlated to mutations on p53 gene in the tumor tissue of all operated patients by means of the most recent techniques of molecular genetics, aiming to better understanding of cancerogenesis of the OSCC and molecular mechanisms involved in tumor progression and its response to irradiation, as well as better designing of therapeutic protocols specific for certain groups of patients depending on biology of each tumor.

In the area of malignant tumors of the gastrointestinal system, there is an intensified immune response of the organism, including the diffuse and follicular lymphoid tissue. The aim of the work was to compare the number of lymph follicles per unit of the tumors and peritumorous tissue surfaces in the large intestine carcinomas classified after Dukes as the grades B and C, in order to find out if there was a correlation between the immune response of the organism and the tumor aggressiveness. Fifty cases of large intestine carcinomas were analysed, 34 cases being of the Dukes B and 16 cases of the Dukes C grade. The lymph follicles were registered in all layers of the intestinal wall irrespective of the depth of tumor invasion. The investigated area was always a rectangular, whose longer side was determined by the widest tumor propagation. The results were expressed in the number of lymph follicles per sight field, at the magnification of 10x4, of individual tunics collectively in the adenocarcinomas of the Dukes B and Dukes C grades. In the Dukes B adenocarcinomas, there was a conspicuous dispersion of lymph follicles, one follicle occurring per 3.2 up to even 18 sight fields, and in 2 cases they were totally missing. In the Dukes C adenocarcinomas, one lymph follicle occurred per 3.4 to 9 sight fields. The number of lymph follicles in the large intestinal wall invaded by adenocarcinoma does not correlate with the tumor aggressiveness.

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Aggressiveness of the large intestine carcinoma and immune response of an organism

KEYWORDS: Colorectal neoplasms; Immune response; Pathology; Prognosis

In the area of malignant tumors of the gastrointestinal system, there is an intensified immune response of the organism, including the diffuse and follicular lymphoid tissue. The aim of the work was to compare the number of lymph follicles per unit of the tumors and peritumorous tissue surfaces in the large intestine carcinomas classified after Dukes as the grades B and C, in order to find out if there was a correlation between the immune response of the organism and the tumor aggressiveness. Fifty cases of large intestine carcinomas were analysed, 34 cases being of the Dukes B and 16 cases of the Dukes C grade. The lymph follicles were registered in all layers of the intestinal wall irrespective of the depth of tumor invasion. The investigated area was always a rectangular, whose longer side was determined by the widest tumor propagation. The results were expressed in the number of lymph follicles per sight field, at the magnification of 10x4, of individual tunics collectively in the adenocarcinomas of the Dukes B and Dukes C grades. In the Dukes B adenocarcinomas, there was a conspicuous dispersion of lymph follicles, one follicle occurring per 3.2 up to even 18 sight fields, and in 2 cases they were totally missing. In the Dukes C adenocarcinomas, one lymph follicle occurred per 3.4 to 9 sight fields. The number of lymph follicles in the large intestinal wall invaded by adenocarcinoma does not correlate with the tumor aggressiveness.
Congenital heart diseases in adults

KEYWORDS: Heart disease; Congenital anomaly

Congenital heart diseases (CHD) most frequently occur in the newborns and children up to 6 months old. There are rare cases in adults without adequate therapy. However, due to the development of new diagnostic and therapeutic techniques in cardiovascular medicine larger number of CHD in adults could be expected (1,2). The aim of the study was to investigate incidence of CHD in adults, types of CHD, characteristic which influence survival rate and life threatening complications in autopsy material of Institute of Pathology, Medical faculty Belgrade. Between 1926 and 2001, 1339 cases of CHD (of total number of 52538 clinical autopsies) were autopsied (153 cases (11.43%) were 18 years and older). Most frequent CHD in adults were: 1. Stenosis aortae (valvularis, sub-et supravalvularis): 31 cases; 2. Defectus septi atrialis (ASD): 18 cases; 3. Coarctatio aortae: 16 cases; 4. Defectus septi interventriculares (VSD): 13 cases; 5. Musculus anomalis ventriculi dextri: 11 cases; 6. Tetralogia et pentalogia Fallot: 6 cases; 7. Valvula bivelaris aortae: 6 cases; 8. Insufficientia valvulae bivelaris aortae: 5 cases; 9. Syndroma Lutembacher: 5 cases; 10. Arteria subclavia dextra aberrans: 4 cases; 11. Ventriculus communis: 3 cases; 12. Anomaliae primariae solitariae arteriarum coronariarum: 3 cases; 13. Morbus Ebstein: 2 cases; 14. Stenosis ostii arteriae pulmonalis: 2 cases; 15. Cor triatriatum: 2 cases. Most frequent localisation of aortic stenosis was on the aortic ostia so called valvular stenosis, usually as bivelar aortic valve. However, bivelar aortic valve is most frequent CHD in general and occurs in 1-2% of population. It can be unmodified in childhood and early adult age but later some secondary changes could occur and cause the calcificant aortic stenosis. Two such cases were operated with implantation of artificial aortic valve and in one case of supravalvular aortic stenosis excision of membrane was done. ASD in oval fossa (ostium secundum type) enables long survival rate due to the late and relatively mild pulmonary hypertension. One of ASD was surgically closed. Adult type of aortic coarctation is not rare. Usually, well developed collateral blood vessels are present. Three cases were operated (3). VSD could decrease or even close spontaneously. Large defects have worse prognosis due to the existence of large left-to-right shunt and development of pulmonary hypertension (4). Tetralogy of Fallot is CHD with very short period of survival time. Only in some mild form of this CHD and co-existing patent ductus arteriosus and strongly dilated bronchial arteries has better prognosis (beter blood oxygenation) (5). Blalock-Taussig anastomosis has the same function as duc-tus. This palliative surgical intervention was done in one case and total surgical correction in two cases (6). Co-existence of congenital ASD with acquired mitral stenosis is called Syndroma Lutembacher. This combination is more severe laesion than congenital ASD alone due to the large left-to-right shunt on atrial level and significant recirculation of blood through lungs with fast development of pulmonary hypertension (7). Rare CHD like Ebstein`s anomaly and common ventricle in some cases with co-existing certain anomalies have better survival rate. Primary anomalies of coronary arteries (left coronary artery is leaving from pulmonary artery, coronary-cameral fistullas) lead to “juvenal angina pectoris”. Cases with musculus anomalis ventriculi dextri without significant obstruction, mild cases of pulmonary artery stenosis and cor triatriatum and aberrant right subclavian artery have very good chances for high survival rate. There are numerous complication of adult CHD. In cases of bivelar aortic valve, valves are slowly thickening due to the fibrosis, hyalinisation and calcification. Modified valves are becoming insufficient or calcificant aortic stenosis occur. CHD with large left-to-right shunt are complicated by pulmonary hypertension due to the development of pulmonary obstructive arterial disease (6). During shunt reversion cyanosis occur and paradoxical embolism is possible. Conoventricular VSD which are in contact with aortic valve might cause insufficient aortic valve (thickening of valves) and subaortic stenosis (due to the fibrotic thickening of endocardium on the down edge of defect). Coarctation of aorta is in approximately half cases associated with bivelar aortic valve which might cause aortic stenosis. Other complications are aortic aneurysms, including dissection of aortic wall (usually cystic degeneration of media is present). Infective endocarditis and vasculitis often occur on anamalnic valves, stenotic places in heart and large arteries. Thrombosis (increased blood viscosity) and infective complications due to the bypass of pulmonary vascular bed (frequent abces of brain) occur in cyanotic CHD. Analysis of observed cases shows that mild CHD with relatively preserved haemodinamics and severe CHD with co-existing cardiovascular anomalies which partially compensate primary disturbance have good survival rate. Also, adequate conservative therapy and palliative and total surgical inter-ventions are very important. However, despite the implemented therapeutic measures further complications are possible. From this reasons adults with CHD need to be often checked and treated by experienced and trained cardiologist.
Triple carcinoma: A histopathologic and clinical rarity - A case report

KEYWORDS: Multiple neoplasms; Breast neoplasms; Cervix neoplasms

The occurrence of two primary malignant tumours of different systems or organs in the same person is relatively rare, so the literature data on the oncologic treatment are scarce and mostly based on personal experiences. However, successive or concomitant appearance of three malignant tumours is a rare event and clinical problem. In the last 15 years at the Department of Gynaecology, Clinic of Oncology in Knez Selo, only 2 such cases were treated, with one of their three tumours localized in one of the gynaecologic organs. We present a case with all three tumours treated with irradiation. Case report: On the account of retromammilar localization of the malignant process opening, upper border of the radiation field passes through IV space L and in March the diagnosis Carcinoma urotheliale vesicae urinarie G1 (in tissue samples there were no muscular tissue elements) was established. Radical combined radiotherapy connoted two complementary ways of administration of total irradiation dose. Transcutaneous radiotherapy was performed on linear accelerator 10 MeV with two opposing fields AP/PA; 40 Gy in 20 sessions was administered to the pelvic region (5 sessions weekly). Lower edge of the radiation field connects lower convexities of the foramina obturatoria, lateral field borders pass 1 cm laterally from the small pelvis radiologic opening, upper border of the radiation field passes through IV space L5-S1. A boost of 10 Gy in 5 sessions was given on both sides parametrially. Intracavitary radiotherapy was administered in 5 weekly fractions (simultaneously with the latter part of transcutaneous radiotherapy) with application of radiation source carriers (Cs137) intracervically to the uterine fundus (oscillating source) and two ovoids to the lateral vaginal fornices (static sources). Extremely serious clinical picture (dysuria, haematuria, acute radiation proctitis and enteritis symptoms) as the consequence of two pelvic tumours, anatomic position of the bladder (whole of it within the radiation field), as well as the clinically expected survival did not indicate additional transcutaneous irradiation of the bladder with lateral fields. Radiotherapy, in spite of the radical dosage and combined approach, remained palliative intervention in this case. After radiotherapy completion there were no periods without clinical signs of the disease or irradiation sequellae. After six months, due to intense pains refractory to analgetics, control CT scan of the lumbo-sacral region was taken. Except for the old degenerative skeletal changes there were no other pathologic processes, including malignancies. In December 1998 the patients was referred for sonographic examination for the last time - hydronephrosis of the right kidney IIIb was observed, ballooned uterus with liquid content and left inguinal lymphatic conglomerate sized cca 9.5 cm. Histopathologic diagnosis after the biopsy was short: Carcinoma adenosquamosum metastaticum in lymphphonodo. The disease ended lethally at the beginning of 1999, with signs of local progression, cachexia and disturbed most biochemical and haematologic parameters. Morphology and biologic behaviour of malignant tumours are well known. The mechanisms of cancerogenesis and molecular basis of most malignant neoplasms are insufficiently understood. Genetic, hormonal and environmental factors play a role in breast cancer occurrence. It is thought that some types of human papillomavirus (HPV) are responsible for cervical cancer, as well as that chemical agents play a role in bladder cancer. The presence of three different tumours in this female patient could not be associated with an influence of the same or similar etiologic factors. Anamnestic and heteroanamnestic inquiries did not render the data on possible malignancies in close or distant relatives.
Pyoderma gangrenosum: A clinico-pathological problem - A case report

Pyoderma gangrenosum (PG) is a very rare destructive, necrotizing, non-infectious type of the skin ulceration. We want to report the case of a 38-years old male patient, with a four-years history of an unrecognized skin disease. The first changes appeared in January 1999 on the skin of the inside part of the right thigh, in the shape of very clear erythema, followed by itching and pain as well as supplemental appearance of a subcutaneous nodus. In the further evolution of the disease, very deep painful ulcerations developed in the same areas, accompanied by a very high fever, myalgia, arthralgia and an excessive body-weight loss in its later course. During the diagnostic procedure which included specialists in different fields, a long list of working diagnoses was made: Thrombophlebitis, Erythema nodosum, Tinea profunda, Status febrilis, Vasculitis. The histopathological biopsy findings of the skin lesion were unspecific, but they doubtlessly confirmed lymphocytic vasculitis and mainly lobular panniculitis were involved here. The histopathological findings of the colon and ileum suggested a chronic non-active colitis and ileitis, as well as a superficial destructive colitis. The clinical features and course of the disease were crucial for establishing the definite diagnosis, since all clinical and laboratory examinations were negative or in the range of normal values. The immunosuppressive therapy with cyclosporine A in the daily doze of 5 mg/kgbw was initiated. The aim of this work is to call our attention to this so rare but very serious disease and also to point out the differential - diagnostic, clinical and pathological dilemmas and difficulties in establishing the definite diagnosis.

Comparison of local antiphrotic effects of capecitabine and 5-fluorouracile combined with standard therapy in trabeculectomized conies

Glaucome surgery - trabeculectomy represents the creation of a new channel (fistula) for aqueous outflow to subconjunctival space forming the so called bleb. Fibrovascular proliferation of the episcleral tissue closing the newly formed fistula is the main cause for this procedure to fail. The experimental animals (conies) were treated during the procedure with two substances: CAPECITABINE and 5-FLUOROURACIL, whose inhibitory effect on fibrosis were compared by histological analysis of the bleb tissue two weeks after the procedure. The method of quantification of the cellular elements and extracellular matrix is used to compare the effects of these two substances. In our preliminary results this method proved to be appropriate in this kind of research and suitable for future testing of other substances that could be applied during the glaucoma surgery.
In the course of the year 2002 when Yugoslav pathologists organise their X Congress, three famous pathologists have their biographic anniversaries. It is an occasion for us to remember their versatile contribution to the World, European and Yugoslav pathology and to give them credit for that. The oldest of them, the German pathologist Rudolf Virchow (1826-1901), the founder of both the cellular pathology and a new medical field - oncology was a very versatile physician and at the same time an important politician, archeologist and ethnologist who died a hundred years ago, namely on September 5, 1902 in Berlin. Coming from Beodra in Banat, the Serbian pathologist Đorđe Joannović (1876 - 1932), born in Vienna, was a full-time professor at the Faculty of Medicine in Vienna. In 1920 he came to Belgrade where, together with Vojislav Subotić and Milan Jovanović-Batut he set up the Faculty of Medicine and was also the dean of it. He established the Yugoslav Association for the Fight Against Cancer in Belgrade and founded the Institute of Pathology, one of the most modern ones in Europe of that time. Unfortunately, 70 years ago he tragically died in Belgrade on January 30, 1932. The youngest of them, the Novi Sad pathologist Vladimir Plavec (1922-1976) the founder of the Novi Sad and Vojvodina pathology, the first professor of pathology and the head of the Department of pathologic anatomy at the Faculty of Medicine in Novi Sad was born 80 years ago, namely on February 7, 1922 in Novi Sad. The aim of our work was to remind our colleagues of the pathologists who obligated us with their great and important deeds.

In conclusion, we keep thinking about the fact that all three pathologists made their pioneer deeds by initiatives and self-sacrificing work in even more severe conditions than are those in which we work.

Endometrial neoplasms are a heterogenous group of tumors which consists of three basic types: epithelial, stromal, and mixed. These basic types are divided into a large number of histological types and subtypes of different biological behaviour and prognosis. 101 cases of EN were analysed in the period between January 1999 and December 2001. The World Health Organization classification of EN, and architectural-nuclear grading system have been used. Myometrial invasion and the involvement of the uterine cervix and the other structures have been used as the parameters of the disease dissemination. The age of the women with EN ranged from 28 to 82, with the peak incidence between the ages 65-69. The most frequent tumors were of the epithelial origin (95%), while the neoplasms of stromal and mixed types were extremely rare. Endometrioid adenocarcinoma was the most frequent histological type (69.7%). 66.7% of the cases were endometrial carcinomas of the favourable prognosis (type I), while 33.3% of the cases were endometrial carcinomas of the unfavourable prognosis according to the histological type and grade. At the moment of the diagnosis 11.4% women were at Ia, 29.1% at Ib, 35.4% at Ic, 10.3 at IIa, 7.2% at IIb and 6.6% at IIIa stage of the disease according to the FIGO classification of the endometrial carcinoma. There were 3 cases of carcinosarcomas and 1 of the high-grade stromal sarcoma of the endometrium. Most of the cases were neoplasms of the histological type and grade with favourable prognosis, but at the advanced stage of the disease.
Review of the stage of the colorectal carcinoma at two centres: Sremska Kamenica and Podgorica

KEYWORDS: Colorectal neoplasms; Staging; Pathology; Comparative studies

Adenocarcinomas represent 95% of malignant colon tumors and according to incidence of malignant diseases they are in the third place in men and in the second place in women. Numerous epidemiological, histomorphological and genetic factors influence the prognosis, but certainly the most important one is the stage i.e. the degree to which the disease has already spread at the moment of diagnosis. Several systems of staging are used, but the Astler-Coller classification is most commonly applied. The aim of the work was presentation and comparative analysis of the stage of the disease in patients with colon carcinoma at the Institute for Oncology, Sremska Kamenica and Centre for Pathology of the Clinical Centre of Montenegro. 64 cases of colon carcinoma were analyzed at the Institute for Oncology, Sremska Kamenica, and 44 cases in the Centre for Pathology of the Clinical Centre of Montenegro in the period between January and December 2001. After detailed macroscopic and histopathological analyses of the material, the stage of the disease was determined according to the Astler-Coller classification. At the Institute of Oncology, Sremska Kamenica, 34 patients (53%) were men, and 30 were women (47%). The patients' age ranged between the fourth and the ninth decade, with the highest incidence in persons older than 50 (95%). The most frequent localization of tumors was the rectum (56%), then sigmoid colon (23%), cecum (6%), descending colon (5%), transverse colon (5%) and ascending colon (5%). At the moment of the operative treatment 1 (2%) case was in A stadium, 15 (23%) were in B1 stadium, 25 (39%) were in B2 stadium, 2 (3%) cases were in C1 stadium, 19 (30%) cases in C2 stadium and 2 (3%) cases were in D stadium. In the Centre for Pathology of the Clinical Centre of Montenegro 28 patients (64%) were men, and 16 (36%) were women. The age of patients ranged from the fourth to the eighth decade of life, with the highest incidence in persons older than 50 (89%). The most frequent localization of tumors was the rectum (56%), then sigmoid colon (23%), cecum (6%), descending colon (5%), transverse colon (5%) and ascending colon (5%). At the moment of the operative treatment 1 (2%) case was in A stadium, 15 (23%) were in B1 stadium, 25 (39%) were in B2 stadium, 2 (3%) cases were in C1 stadium, 19 (30%) cases in C2 stadium and 2 (3%) cases were in D stadium. In the Centre for Pathology of the Clinical Centre of Montenegro 28 patients (64%) were men, and 16 (36%) were women. The age of patients ranged from the fourth to the eighth decade of life, with the highest incidence in those older than 50 (89%). The most frequent localization of the tumor was the rectum (52%), then sigma (14%), descending colon (14%), cecum (9%), ascending colon (9%) and transverse colon (2%). At the moment of the operative treatment 2 (4.5%) cases were in A stage, 4 (9%) cases in B1 stage, 19 (43%) cases in B2 stage, 17 (39%) cases in C2 stage and 2 (4.5%) cases in D stage. The comparative analysis of the above stated data showed that colon carcinoma occurs in both populations in older age, somewhat more often in men. The most frequent localization of the tumors is the rectum and sigmoid colon, which are treated operatively in an advanced stage of the disease (B2 and C2 stage).
In the preembryonal and early embryonal periods and during the embryonal folding, the umbilical cord is being formed in continuity with the yolk sac on one side and placenta on the other. The yolk sac wall, allantois and embryonal stalk, which later become part of the umbilical cord, are built in the time of formation of the embryonal connective tissue, mesenchymal tissue. The mesenchymal tissue is well vascularised, with high mitotic and developmental potentials, and it represents the source of the primary extraembryonal hematopoiesis and the first host of germinative cells. The histologic structure of 50 umbilical cords from fetuses aged 26-40 weeks, being compared with the bioptic specimens of skin and knee menisci showing mucoid degeneration, was light microscopically analysed after staining with HE, PAS alcian, toluidin, orcein and Mallory. In the connective tissue of the umbilical cord, there were typical histologic signs of mucoid and cystic degeneration of the same histopathologic characteristics as in any other connective tissue, with respect to the character and quantity of the intercellular substance, connective fibres and cells. The comparison was with the mucoid degeneration in the dermis and knee meniscus fibrocartilage. There is no ground to consider the Wharton’s jelly of the umbilical cord as a separate mucoid tissue; there is mucoid degeneration possibly accompanied by a cystic change in the area of the only embryonal connective tissue - mesenchymal tissue. The mucoid degeneration of the mesenchymal tissue is a regressive, i.e. involutive change in the embryonal and fetal development.

KEYWORDS: Urachal cyst; Degeneration; Pathology; Retrospective studies

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Fine-needle aspiration (FNA) is one of the most useful methods in the diagnosis of Hashimoto’s thyroiditis (HT). This is an additional procedure in examination of the thyroid lesion, and it supplements the hormone analyses, the antibody detection and the ECHO sonography. Six hundred aspirates were stained with HE and MGG and cytologically analysed. The main cytological criteria for HT are: 1. lymphocytic cellularity of smears, 2. oncocytic follicular cells, 3. abundant cellular debris Of 600 analysed aspirates, 35 (3.5%) were diagnosed as HT. A high significance of both the sex and age for the genesis of HT ($\chi^2=24.02; p<0.005$) was statistically confirmed. We analysed the correlation between the clinical and cytological diagnosis: in 82 cases, the initial clinical diagnosis was “thyroiditis”, and 46 (56%) of them were cytologically confirmed. Of 35 patients with FNA diagnosis of HT, it was clinically suspected in 23 cases (66%). Several authors noted a high incidence of thyroid carcinoma in patients with HT. We researched the association of HT and thyroid tumors, and we did not confirm that HT is a premalignant lesion ($\chi^2=1.22, p>0.05$). HT and its association with other lesions could be clearly diagnosed with FNA, a very useful method in both the diagnostic and therapeutic clinical treatment.

KEYWORDS: Thyroid gland; Thyroiditis; Pathology; Needle biopsy, Retrospective studies