POSTER PRESENTATION

1. UROLOGICAL PATHOLOGY

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Alfa and beta catenin expression in renal cell carcinoma

KEYWORDS: Renal cell carcinoma; Catenins; Immunohistochemistry

INTRODUCTION

RCC (adenocarcinoma, hypernephroma or Grawiz tumor) is the most common case of kidney tumor with grown-ups. Carcinoma originates in proximal tubules epithelium. The most frequently used RCC classification is according to the cells appearance (Thoenes, 1986), on: lucidocellular, chromophobe, and sarcomatoid type. According to the degree of differentiation , there are few tumor grades-G1,G2 and G3. The tumor grade is of prognostic value, but it is not the only parametar on which RCC prognosis dependes. Cadherins represent the family of calcium-dependent cell-cell adhesive molecules which play an important part in morphogenesis of different kinds of tissues. Despite the continious identification of new cadherin types, little is known about cadherin in the normal kidney tissue, as well as in RCC. N-cadherin exists in proximal tubular cells, whereas E- cadherin is situated in distal tubules epithelium. Alfa, beta and gama catenins are proteins which are bound to the cytoplasmic tail of cadherins. Alfa catenin has first been described as the E-cadherin binding protein but later it has been shown that it binds to other kinds of cadherin such as E- and P- cadherin. Beta catenin binds itself to E-cadherin which is necessary to make E-cadherin function as an adhesive molecule. It has also been found in complex with tumor suppressive protein. Catenin expression studies of adenocarcinomas in different kinds of tissues have revealed changes in these molecules expression.

MATERIAL AND METHODS

10 cases of RCC with different histological appearance and malignancy grades have been examined. In 4 cases granular RCC was identified (twice G2 and twice G3), in two cases chromophobe RCC was identified (G1 and G2), in four cases sarcomatoid RCC was identified (3 times G3 and one G2). Six samples of RCC were taken from male patients and 4 from female patients, aged between 38 and 75. Alfa and beta catenin expression was examined in all samples using immunohistochemical methods. The expression in RCC was compared to the expression in the normal kidney tissue, which was obtained by biopsy from 10 patients.

RESULTS

The expression of both alpha and beta catenins is reduced in granular and chromophobe RCC, compared to their expression in the normal kidney tissue, whereas it remained almost unchanged in sarcomatoid RCC. Beta catenin expression is reduced with the enlargement of the tumor grade. Alfa catenin expression is reduced in all carcinoma types compared to the expression in normal kidney tissue as well as in comparison to beta catenin expression. We observed that in chromophobe and granular RCC alfa and beta catenin expression is higher on the cell membrane along the whole surface of the cell, whereas in sarcomatoid RCC catenins are mainly located in the cytoplasm.

CONCLUSION

RCC cells express both alfa and beta catenin.It has been observed that there is a difference in expression intensity and both catenins distribution in different histological types of RCC, as well as in RCC with different tumor grade. Since the tumor grade is of prognostic importance, the relationship between expression and grade (higher grade-lower expression) can contribute to the prognosis of RCC development in all types, except in sarcomatoid RCC

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Incidence, mortality and regional distribution of kidney, urinary bladder and prostate carcinoma in Serbia, 1990-1999

KEYWORDS: Renal tumors; prostatic carcinoma; bladder carcinoma; incidence

INTRODUCTION

Kidney, urinary bladder and prostate carcinoma are significant medical and social problem in Serbia (1-4). Those carcinoma have different incidence and mortality in various countries. Taking into consideration different epidemiological factors influencing stated carcinomas, it is very important to establish their exact incidence and mortality in different countries (5,6). The aim of the study was to establish the incidence, mortality and regional distribution of kidney, urinary bladder and prostate carcinoma in Serbia in the last decade.

PATIENTS AND METHODS

The study is based on National Statistics data for 1990-1999 period, Cancer Register data from the Institute of Oncology and Radiology in Belgrade, Council Reports, Annual Reports from different clinics and health centers as well as on data from National Health Benefit Center. The descriptive epidemiological method used for this study was based on statistical analysis of trend, standard deviation, standardized rates for different age groups per 100.000 (Segi), and correlation coeficient.

RESULTS

Kidney carcinoma

Incidence. The cumulative incidence rates are estimated to vary between 4.9 and 8.1 for man and 3.1 and 4.2 for women. The Cancer Register from Institute of Oncology and Radiology in Belgrade provides evidence of 50.1 cases of local (node-negative) tumors, 13.3 cases of node-positive tumors and 30.6 of metastatic disease. The five-years survival rate for man is 31-45%, and for woman 37-43%. The analysis depicts higher proportion of incidence and mortality in urban than in rural areas. The youngest group of patient population was 9-19 years of age. There was an increase of incidence with age (over 39) and was highest in the oldest age groups i.e. woman over 60 years and man over 70.

Mortality. Standardized mortality rates for man vary from 2.3 to 3.7 per 100.000 inhabitants, and for woman 1.2 to 2.4. Linear time trend for man is $y=1.7+01x$, and for woman $y=09+02x$, the coeficient of correlation $r=0.74$. The regions of Podrinje, Kolubara and Branicevo show the highest mortality rates for the ten-year period.

Urinary bladder carcinoma (7,8)

Incidence. The incidence rates are higher in man than in woman (3:1) showing an increase with age i.e. after the age of 44. The data from Institute of Oncology and Radiology in Belgrade provide evidence of 70% of cases with local (node-negative) tumors, 15% cases with node-positive and 15% with metastastic disease. The 5-year survival rates are 40-60% and 60-70% for man and woman respectively.

Mortality. Urinary bladder carcinoma is responsible for 16.4% in 1995 and 17.1 in 1999 of all uro-genital malignancies in Serbia. The standardized mortality rates range from 2.1-5.8 and 2.2-4.1 for man and woman respectively depending on the region. The highest mortality rates (38%) are registered in rural areas, they are 36% in Belgrade and 26% in smaller towns. The highest mean standardized mortality rates in the regions of Branicevo, Zajecar, Pirot and Pomoravlje. The specific standardized mortality rates for the observed period demonstrate a significant increase in number of death cases both for man ($y=2.9+0.2x$) and woman ($y=1.5+0.4x$). The correlation coeficients are $r=0.86$ for man and $r=0.78$ for woman. The estimated cumulative mortality rates are 8.9-17.1 and 2.2-4.1 for man and woman respectively.

Prostate carcinoma (9)

Incidence. We register 920-980 prostate carcinoma per year. The standardized rates per 100.000 man are estimated to vary between 54.5 in Belgrade and 32.8 in other towns. At the Institute of Oncology and Radiology in Belgrade, the register gives evidence of 96-97.4% diagnosed tumors. Only 50.5% of cases show an early stage of the disease at diagnosis, 12.1% are node-positive and 37.4% patients have metastatic disease. 5-year survival period is 46-67%.

Mortality. The number of deaths from prostate carcinoma was found to be much higher than for any other male genital carcinoma (499 in 1990, 587 in 1995 and 718 in 1999). Within death rates from all malignancies in male population 5.7% stands for prostate carcinoma. Standardized mortality rates for different regions vary from 11.3 to 25.8, the highest being in the regions of Zajecar, Pirot, Pomoravlje, Rasina. A significantly rising pattern of prostate carcinoma mortality has been demonstrated in Belgrade since 1995 ($z=14.3+0.6x$, $r=0.87$).

CONCLUSION

We believe that our study indicate that different factors including heredity could be considered as significant risk factors (10). In the endemic Balkan nephropathy, persistant inflammatory states may be inductive to urothelial kidney pelvis and urinary bladder carcinoma (11). The constant increase of incidence and mortality rates could be attributed to higher proportion of aged population as well as to increasing pollution of the environment.

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Double carcinoma of the left kidney - A case report

KEYWORDS: Renal tumors; Renal cell carcinoma; Urothelial carcinoma

INTRODUCTION

Simultaneous development of pelvic transitional cell carcinoma and clear cell carcinoma in the same kidney is extremely rare. Over 50 cases of double renal carcinoma have been described in the available literature (1,2). We report a case of unusual tumor combination that had been diagnosed using *ex tempore* analysis.

CASE REVIEW

Leading clinical symptoms in this 76 year old female patient were macroscopic hematuria, with dull pain in left lumbal region. Intravenous pyelography and CT scan showed tumor in left kidney. Radical nephrectomy had been performed because of the suspect pelvis tumor, and this material has been examined by *ex tempore* analysis. Two different tumors were described pathohistologicaly: poorly differentiated renal carcinoma,40mm in diameter, and high grade papillary transitional cell carcinoma of pelvis, 42 mm in diameter. Metastasis of clear cell carcinoma has been diagnosed in one lymph node. Uretherectomy also had been done after *ex tempore* analysis. Both tumors were limited on kidney. Patient did not have any postoperative treatment. Postoperatively, six years later, patient is without any symptoms of local or disseminated neoplastic process.

CONCLUSION

Combination of renal cell carcinoma and pelvis carcinoma in the same kidney represent the unusual synchronous development of the high grade double carcinoma. Preoperative and postoperative diagnoses of this carcinomas is very important to estimate the type of surgery procedure in the meaning of how radical it should be, and also these diagnoses are very valuable in making the right decision considering postoperative treatment.

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A case of renal amyloidosis of AA type associated with renal cell carcinoma and symptoms of ulcerative colitis - An etiopathogenetic dilemma

KEYWORDS: Renal cell carcinoma; Renal amyloidosis; Ulcerative colitis

INTRODUCTION

Amyloidosis is a generic term for a group of diseases of different etiologies that have in common accumulation of pathologic proteinaceous substance (amyloid) in the tissues in amount sufficient to impair their normal function. Amyloid is a group of fibrillar proteins of similar ultrastructure, but different chemical composition. Amyloidosis may be systemic (generalized) or localized (affecting single organ, most commonly heart). Clinically 3 major systemic clinical forms are recognized and referred to as: primary (when there is no associated disease), secondary (associated with chronic diseases of inflammatory nature and some neoplasms) and hereditary (unassociated with other disease, with distinctive types of neuropathy, nephropathy and cardiopathy). Long standing tissue destruction and inflammation lead to elevated levels of SAA, which is synthesized by the liver cells under the influence of cytokines. SAA is normally degraded to soluble end products by monocyte-derived enzymes. In individuals with defect of these enzymes, insoluble AA molecules are generated and amyloidosis is developed. Chronic inflammatory (rheumatoid arthritis, connective tissue disorders, ulcerative colitis), infectious (tuberculosis, chronic osteomyelitis, bronchiectasiae) and malignant diseases (renal cell carcinoma, Hodgkin` s disease) are effective stimulators of systemic deposition of AA protein.

CASE REPORT

We present a case of a 43-year old male patient with renal amyloidosis having symptoms of nephrotic syndrome after unilateral nephrectomy due to hypernephroma. The clinical examination of the patient revealed history of ulcerative colitis for years before. Since both accompanying diseases may lead to amyloid deposition, the doctor`s dilemma is the origin of the amyloid. Four months after the nephrectomy and histopathologically confirmed hypernephroma, the patient developed symptoms of nephrotic syndrome, due to which a kidney biopsy was performed. The obtained material was divided in

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two parts: for histological analysis and for electron microscopy analysis. The material for histological analysis was further divided in two parts: for frozen section and for paraffin embedding procedure. The frozen section cuts were stained for immunofluorescence analysis with antibodies for IgA, IgM, IgG, C1q, C3 and Fibrin. The paraffin embedded tissue specimens were stained with standard histological (HeEo), histochemical (Trichrome Goldner-Masson, Silver-methenamine Jones, PAS, Congo red), immunofluorescence (with the above mentioned antibodies) and immunohistochemical (AA amyloid, B2 microglobulin, k and l light chains) stains. Furthermore, the slides from the previously removed kidney were analyzed again and stained with Congo red and AA amyloid.

RESULTS

The light microscope analysis on histochemically stained tissue specimens from the kidney biopsy showed 14 glomeruli with increased volume and reduced cellularity, hyaline thickening of the Bowman membrane and periglomerular fibrosis. The urinary space of all glomeruli was reduced to obsolent due to deposition of amorphous eosinophilic material (PAS positive, fuscinophobic and argirophobic) in the mesangium and glomerular basal membrane. Similar amorphous deposits were found in the walls of the blood vessels from the vascular pole and small arterioles. The amorphous eosinophilic material was positive on Congo red (both on light and polarizing microscope), and immunohistochemically on the staining for AA amyloid. The review of the slides from the removed kidney showed atypical adenoid structures of different size made of polygonal cells with abundant clear cytoplasm and central hyperchromic nuclei, invading the fat capsule, the walls of the collecting system and the urether, and compressing, but not infiltrating the renal vein. Metastatic deposits were also found in the lymph node isolated from the perirenal fat tissue. The neoplasm was poorly differentiated (G3) and clinically in stage III (pT3a, pN1, pMx). An abundant eosinophilic amorphous material was deposited in the tumor stroma, among the atypical adenoid structures, as well as in the mesangium and glomerular basal membrane in the reminder of the glomeruli. These deposits were positive on Congo red, confirming the existence of amyloid. The immunohistochemical typization confirmed the AA nature of the amyloid.

DISCUSSION

The presented case is a rather complicated one in terms of distinguishing the primary cause of amyloid deposition. Both malignant tumors and chronic inflammatory diseases are well known stimulators of amyloid formation. The renal cell carcinoma is established as a malignancy most frequently associated with systemic deposition of amyloid A protein. According to some authors (1), the frequency of secondary amyloidosis accompanying renal cell carcinoma was 2,9% (in a series of 238 postmortem analysis). Inflammatory bowel disease is thought to be another major cause for systemic amyloid A protein deposition. Comparing the literature data, it appears that ulcerative colitis (as in our case) is an entity only exceptionally associated with systemic amyloid deposition. In large series of patients (2) (1341 patient with ulcerative colitis), the reported incidence of amyloidosis was 0.07% (only 1 case). This is in contrast with Crohn`s disease which is more frequently reported to be associated with AA amyloidosis (15 out of 1709 patients - 0.9%) (2). The incidence of secondary systemic amyloidosis in these two entities corresponds with the results of the evaluation of the serum amyloid A protein by the means of immunoradiometric assay. The results of such investigations showed marked increase of SAA in patients with Crohn`s disease, contrary to the modestly raised levels of the same in patients with ulcerative colitis. In absence of histopathological confirmation of the ulcerative colitis in our case, another diagnostic problem to have in mind is the possibility of the amyloid deposits in the large bowel to present with symptoms and roentgenographic findings suggestive of colitis (3).

CONCLUSION

The above reported investigations, as well as the review of the related literature, still leave the mystery unsolved: Which disease is primary to the systemic deposition of amyloid A protein in our case: the ulcerative colitis or the renal cell carcinoma?

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Beta-catenin expression in Wilms tumor

KEYWORDS: beta-catenin; immunohistochemistry; Wilms tumor

INTRODUCTION

Wilms tumor (nephroblastoma) is embryonic kidney tumor, which develops from metanephric blastem. It is one of the most frequent tumors among children which appears in 1 out of 10.000 children. Most cases of Wilms tumor are sporadic and unilateral, whereas in 1% of cases it is family tumor and in 7% of cases it is bilateral. There are several histological types of Wilms tumor. Classical (three-phase) type has three components: epithelial, blastemal and stromal, whereas two- phase and one-phase types are not common. Adhesive molecules enable cell-cell and cell-matrix interaction. Cell-cell and cell-matrix interactions influence tissue architecture, changing cell proliferation, differentiation and apoptosis. Cadherins are the family of adhesive molecules which are involved Ca-dependent intercellular adhesion. On the long exstracellular part of cadherin, there are places to which Ca is bound, and in inner cytoplasmic tail there are places to which catenins are bound. Catenins are cytoplasmic cadherin-bounding proteins, and they mediate cadherin-cytosceleton binding. However, it has been shown that cadherin-catenin complex binds actin components of cytosceleton, and in that way it plays an important role in cell-cell adhesion. These molecules together with cadherin molecules are localized in zonula adherens of epithelial cells and they participate in the formation of intercellular connections. There 3 types of catenin and there are marked as α, β and γ catenin. Beta-catenin expression studies have shown that has been a reduction of beta-catenin expression in different types of malignant tumors, as well as beta-catenin gene mutation.

MATERIAL AND METHOD

Examination included 10 patients (8 females, 2 males) with Wilms tumor, aged between 14 month and 11 years, when operated on. It included patients in different stages and with different histological types of tumor. Blastemal component was predominant in 4 cases, stromal component in 2 cases and in 3 cases we had all three components (epithelial, stromal, blastemal), equally distributed. Anaplasia (diffuse) was present in 2 examined cases of Wilms tumor. For comparison we used normal kidney tissue, obtained by biopsy from 10 patients. In all samples of tumor tissue, as well as in normal kidney tissue, beta catenin expression was examined by immunohistochemical method. The results of immunohistochemical staining were obtained by examination with light microscope by two pathologist, who were not previously informed about clinical data nor pathohistological diagnosis.

RESULTS

Beta-catenin was present on tumor cells in all examined cases of Wilms tumor. However, expression of these adhesive molecule was reduced in tumor cases examined, compared to the expression in normal kidney tissue. It was observed that the highest beta-catenin expression was on stromal tumor cells, it was a little lower on the cells of epithelial component, whereas it was the lowest in blastemal component. In 4 cases in which we had blastemal component (2 mixed and 2 with predominant blastemal component) there was no beta-catenin expression. In 2 examined cases with diffuse anaplasia, we observed intensive beta-catenin expression, particularly in epithelial component.

CONCLUSION

There is beta-catenin expression in Wilms tumor and it exists in all component (epithelial, blastemal and stromal). Intensity of expression and distribution of beta-catenin are reduced in tumor tissue compared to normal kidney tissue. The greatest loss of expression was observed in blastemal component, as expected since blastemal component is the least differentiated, and that is why the connections between these cells are the weakest. We have not observed any connections between the reduction of beta-catenin expression and tumor stage.

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Granulomatous prostatitis following bacillus Calmette - Guerin immunotherapy of bladder cancer and secondary MALT lymphoma of prostate - Report of two cases

KEYWORDS: Prostate; Granulomatous infections; Calmette-Guerin immunotherapy

We present two unusual cases of prostatic lesions, both rare either as a primary or secondary complication, despite the increasing number of reported cases in the past three years. The recent data show a growing evidence of granulomatous prostatitis as a complication during the treatment of transitional cell carcinoma of the urinary bladder with local installation of BCG, and even mycotic aneurysm as a late complication has been reported, so we have to be cautious of granulomas during this type of treatment of transitional cell carcinoma. Malignant lymphoma of the prostate, either primary or secondary, has been reported in a small series or individual cases. Case1: Granulamatous prostatitis followed bacillus Calmette - Guerin immunotherapy of the bladder cancer. Tuberculous infection of the prostate is uncommon and is usually associated with a more obvious infection elsewhere in the genitourinary tract, such as the kidney or bladder. It is sometimes a prostatic manifestation of miliary tuberculosis due to blood-born infection. Most patients have no prostate symptoms, and the infection is documented by culture of the histologic examination. Granulomatous prostatitis, like tuberculous prostatitis, is also induced by bacillus Calmette - Guerin (BCG) treatment for superficial transitional cell carcinoma of the bladder. A 72-years old male was presented with nocturia and Micatin difficulties during the last six to seven years. He was treated conservatively. In 1999 hematuria occurred for several times. During cystoscopy a tumor mass in the urinary bladder was found. Transurethral resection of the tumor was performed for the first time in October 1999. Histopathologically, transitional cell papillary carcinoma grade II was diagnosed. Thirteen months later a recidivant tumor of the urinary bladder was resected and histopathoologically, a similar grade II transitional cell carcinoma was diagnosed. After the second recidivant tumor, a local inoculation of bacillus Calmette - Guerin was performed. In April 2001 the patient was hospitalized because of prostatic difficulties, almost complete retention of urine, so a surgical treatment was necessary. Transvesical prostatectomy-secundum Harris was performed. Macroscopically the prostate weighted 50 grams with clearly distinct unencapsulated lobes. On sagital sections, the lobes showed spongious zones and more solid areas that exhibited necrotic debris on pressure. We took nine samples for microscopic analysis. Benign prostatic hyperplasia was diagnosed. Granulomas with central caseous necrosis surrounded by epithelioid cells and lymphocytes with giant Langhans cells were also found. So, the diagnosis of granulomatous prostatitis-like tuberculosis was established. Because of the previous clinical history of BCG immunotreatment due to the recidivant transitional cell papillary carcinoma of the urinary bladder we conclude that this was a complication of the former inoculation of the bacillus Calmette - Guerin. Case 2: Secondary MALT lymphoma of the prostate. To-date well-documented cases of malignant lymphoma of the prostate (either primary or secondary) are fewer than 100. These comprise single case reports and a few small series. The review of these cases suggests that primary lymphoma of the prostate is much less common than secondary infiltration. Lymphoma is more often a secondary lesion of the prostate than a primary one. Its diagnosis requires either prior recognition of a malignant lymphoma arising elsewhere or identification of a nodal disease in the course of investigation of prostate symptoms. A 73-years old male presented with obstipation and stomach pain, and finally acute abdomen, underwent laparoscopy in November 1999. During laparoscopy 40 cm. of the small intestine was resected. Macroscopically, in the middle of the resected segment intussusception was present, surrounded with hemorrhagic infarction. Another finding was a necrotic lymph node in the wall of the intestine as well as few other enlarged lymph nodes in the vicinity of the intussusception. In the distal (vital) segment of the intestine we observed several oval shaped thickenings of the intestinal mucosa up to 2.5 cm in diameter. Few of these changes are found throughout the whole intestinal wall and exhibit polypoid structures. Several samples were histologically analyzed. The borders of the resection showed normal morphology. Those samples taken from the middle of the resected intestine segment exhibited transmural coagulative necrosis with hemorrhagic infarction. Microscopically, the lymph nodes were completely necrotic thus impossible for further analysis. However, the lymph nodes extracted from the distal (vital) part of the intestine show infiltration of the neoplastic lymph tissue made up of relatively uniform centrocyte-like and small lymphocyte-like cells. Mitotic activity is scant, and the neoplastic process spreads throughout the mucosa, submucosa and the muscular layer. A few dispersed histiocytes were also found. Using immunohistochemical stains the diagnosis of B-cell lymphoma (MALT-lymphoma) was reached. The patient achieved complete remission after a 13-month chemotreatment. In February 2001 the patient was hospitalized in the Clinic of Urology because of a complete retention of urine. Transvesical prostatectomy secundum Harris was performed. The prostatic tissue was made up of two well-defined lobes with a weight of 110 grams. On sagital sections, the cut surface was moist with several foci of soft whitish tissue. Microscopically, the samples exhibited benign prostatic hyperplasia with a diffuse neoplastic lymphocyte infiltration. The lymphocytes were small, relatively uniform, with scant mitotic activity. They invade the smooth muscle and the surrounding collagen tissue. Because of the previously diagnosed MALT-lymphoma of the small intestine, the diagnosis of a secondary MALT lymphoma was established. In March 2002 the patient underwent the sacral bone biopsy for staging the lymphoma, with histopathological findings of normal and slight arrest in maturation of the cellular elements, without any signs of non-Hodgkin lymphoma in the present material. The further follow-up of the patient has showed he has been free of the disease over the last thirteen months. Pathologic evidence of granulomatous prostatitis is a common occurrence after intravesical BCG therapy and its incidence is far greater than the reported incidence of symptomatic granulomatous prostatitis. Intravesical bacillus Calmette-Guerin is generally well tolerated and produces no complication in more than 95per cent of the patients treated. Lymphoma of the prostate, either primary or secondary, is still a very rare disease, so each reported case contributes to an adequate management of this disease. Furthermore, every reported case, including our own, may clarify the differential diagnostic difficulties, which a pathologist encounters during the routine everyday work.

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Primary rhabdomyosarcoma of the epididymis - A case report

KEYWORDS: Epididymis neoplasms; Rhabdomyosarcoma; Immunohistochemistry

Primary tumors of the epididymis are very rare. This is the report of our case: a male patient at the age of 38, with the tumor of the left half of the scrotum and pain during last three months. He was examined by the standard urologic protocol for testicular cancer including: laboratory analyses, tumor markers, and ultrasound. Inguinal orchiectomy performed. The tumor was presented by a pink mass in the left epididymis, 140x10 mm in diameter. The testis was not involved. Microscopically, the tumor is characterized by bundles of spindle cells, with large, polymorph, hyperchromatic nuclei. Stroma is myxoid with foci of hemorrhage. Imunohistochemically, the tumor cells show positive reaction for actin and negative reaction for SMA. On the basis of all obtained results, the tumor was defined as rhabdomyosarcoma of the epididymis.

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Leydig cell tumor - Case report

KEYWORDS: Testicular tumors; Laydig cell tumor

Leydig cell (interstitial cell) tumors comprise the great majority of all stromal tumors of the testis. Since the first clear description of a Leydig cell tumor in 1895, several hundred cases have been reported. Only rarely are the tumors bilateral, or familial. The neoplastic Leydig cells usually produce testosterone, and, in some well-studied cases, estradiol and progesterone. Either precocious development of secondary sexual characteristics in children or gynecomastia (present in 30 percent of adults) may be the presenting complaint. Lesions may be so small as to be nonpalpable, and ultrasound or spermatic vein catheterization with hormone determinations may be necessary to localize the tumor. The most common complaint, however, is testicular mass. The mean patients' age are the 40s, but the tumor has been reported in children as young as 2 and men as old as 90. We present a case of Leydig cell tumor in a 15 years old male born on 3rd October, 1986 with a long medical history. The first hospitalization was into the Clinic of Pediatric Diseases, Department of Endocrinology on February 17th, 1988 when he was 16 months old, due to mild coughing, loss of appetite, vomiting and extreme sweating. During hospitalization the patient showed signs of acute adrenal crisis with dehydration and infection of the upper respiratory tract, so he was treated accordingly. The following ionogram findings were:obtained:Na=136..120..119 mmol/L, K=4.5..3.8..6.5mmol/L, Ca=2,7..2,4..2,3mmol/L, P=1,29..1,09..1,44mmol/L. A hormone analysis revealed the following: 17 corticosteroids=66.0..45.1mmol/L, 17 ketosteriods=20.4..37.7 mmol/L, pregnantriol=45mmol/L. Finally, because of hyponatriemia, hyperkaliemia, high levels of testosterone and 17OH progesterone, as well as a deficit of the enzyme 21 hydroxylase, the diagnosis of congenital adrenal hyperplasia (CAH), salt loosing type, was established. According to this diagnosis, a classic therapeutical protocol was prescribed: every day substitutional therapy of glucocorticoids and mineralcorticoids for the first 3 years of the patient's life, and after that only glucocorticoids. After the dismissal from the hospital the patient was constantly controlled every 3-6 months. The disease worsened every time the patient was in stress situations, usually infects of the upper respiratory tract. Also this was a case of non-compliance on the part of the patient. These problems led to several adrenal crisis that were treated in the Pediatric Clinic. During the therapy all the parameters were in normal range, with an exception of the levels of 17a hydroxiprogesterone that remained over 20ng/ml high. The patient was constantly checked and the following was determined: first pubic hair appeared when the patient was only 3 years and 6 months old. The beard began to grow when he turned 4 years and 4 months. Three months later an increase in the male genitals (penis was 6 cm long, and the testicles were 2 cm in diameter) was noted. First signs of puber-

ty were noticed when the patient had 7 years and 11 months, with increased genitalia, fully developed pubic, and lower extremity hair. The puberty ended when the patient turned 10years and a half. The patient had oligofrenia with IQ=79. His height growth finished when the patient was 11 years and 11 months old reaching the height of 151cm. When the boy turned 15 years during one adrenal crisis he was admitted to the Pediatric Clinic again. Among other routine investigations, an ultrasound examination of the testicles revealed a change in their normal morphology. A biopsy was taken and sent to the Institute of Pathology for further examination. The biopsy material presented a pink-grayish soft tissue fragment in the size of: 18x15x11mm. The material was completely processed for histological examination. The microscopic analysis revealed a tumor with solid alveolar arrangement, made up of big polygonal cells in most parts with eosinophilic cytoplasm, and centrally placed hyperchromatic nuclei. In smaller parts the cells had a light cytoplasm. The tumor iswas encapsulated with a discrete connective tissue. Peripherally to the tumorous process, there was the testicular parenchyma made up of tubuli seminiferi completely lacking germinal epithelium. The diagnosis of Leydig cell tumor was reached, without mitotic activity. There was no tumor invasion that speaks for the benign nature of the tumor. The differential diagnosis include Leydig cell tumor, Leydig cell hyperplasia and adrenal rests in testis. We eliminated Leydig cell hyperplasia because of an obviously tumorous growth of the lesion. We preferred the diagnosis of Leydig cell tumor. The bilateral nature of the lesion, hormonal status of the patient, bilateral congenital hyperplasia of the adrenals favored the diagnosis of adrenal rests. We have asked our colleagues in Bern, and Switzerland for the second opinion and the answer is yet to come.

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Incidence of testis tumors in the region of Banja Luka - analysis of the bioptic material

KEYWORDS: Testicular tumors; Incidence

Testis carcinomas are the most frequent malignant changes in males at the age 15-35 years, but also the most curable malignancy. The etiology of testis tumors is still unknown, but the risk is 6-10 times higher in genetically predisposed males. The aim of this study is to estimate the incidence of testis tumors in the region of Banja Luka during the period from 1990- 2002. We analyzed 41 patients with testis tumors. Of them, 12% were benign and 88% malignant tumors. According to the histological type of malignant tumors, 44% were seminomas, 14% embryonal carcinomas, 11% teratomas, yolk sac tumor was registered in 1 case, and 28% were mixed tumors (mostly teratocarcinomas). The most frequent benign tumor was mesothelioma. The highest incidence of testis tumors was registered in 25-35 yr age group. The peak incidence occurred in the period from 1993 to 2001. Malignant testis tumors have been increasing.

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Correlation between the recidive period in high-grade urinary bladder carcinoma its previous or lower degree of diferentiation, and clinically evaluated TNM staging

KEYWORDS: Bladder carcinoma; Staging

Papillary carcinoma of the urinary bladder is an epithelial neoplasm, often diffuse in appearance. High-grade papillary carcinomas rarely appear as a primary noninfiltrating tumors. They are either preceded by a low-grade carcinoma, or accompanied by an invasive carcinoma. In most cases, they infiltrate the wall of urinary bladder, which is to blame for frequent relapses of the disease, and poor prognosis for those patients. The aim of these study is to fortify the correlation between clinical staging of the previously diagnosed high-grade papillary carcinoma and the degree of histological differentiation of its relapses, observed in relatively estimated period of time. Diagnostic procedures of papillary carcinoma are regularly performed at the Institute of Pathology and Histology, Clinical Center of Novi Sad. All the material for this study has been taken from our Institute, including both biopsy and surgical specimens from 12 patients analysed in this study, who ranged from 53 to 79 years of age (the mean age 69yrs). Byopsy specimens represent electroresected fragments of the urinary bladder papillary carcinoma. Surgical specimens, taken after a radical cystectomy are: the urinary bladder with its intraluminal tumour formation, part of the urethra, prostate gland, seminal vesicles as well as regional lymph nodes. All specimens are treated by a standard histological technique - paraffin framed sections. WHO defined 3 histological grades of the urinary bladder carcinoma, while the clinical evaluation is determined by TNM classification for primary urinary bladder tumours. High-grade papillary carcinoma, after electroresection, appeared in the same, or lower degree of differentiation, most likely in already expected period of time and in correlation with its clinical stage and histopathological classification of the tumour. Once diagnosed, a high-grade carcinoma is confirmed in most of the relapses, less likely to appear in its lower differentiated forms. In terms of TNM classification, clinically evaluated T1 stage of the urinary bladder papillary carcinoma grade III, shows its relapse forms in a period of time between 8 to 12 months, while its infiltrative forms (T2 stage) but also grade III appear again in a shorter period of time - 4 to 8 months, with a predominance of 5 months. Anaplastic forms of these tumours were found in T3 and T4 stages and in those tumors relapses are to be expected in the shortest period of time - 1 or 2 months. Histopathological staging is also a very important parameter. Grade II Papillary carcinoma very rarely turns into an infiltrative form, while grade III tumors often infiltrate the urinary bladder wall representing an indication for radical cystectomy, due to its frequent relapses and differentiations, with no significant treatment benefits for the final outcome of the disease.

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Yolk sac tumor of the testis - A case report

KEYWORDS: Testicular tumors; Yolk sac tumor

Yolk sac or endodermal sinus tumor is one of the most frequent germinative cell tumor occurring in children. We reported a case of a one-year old child with a painless testicular mass localized in left testis.Ultrasound showed tumor mass in testis measuring 26x35mm. Laboratory tests:serum alpha-feto protein levels were 502ng/ml. Macroscopically, tumor was partly solid, yellow and soft, with areas of hemorrhage and partly with cystic spaces contended with mucus. Microscopically, tumor tended to show a irregular tubular arrangement with solid parts and between them numerous small vessels filled with blood and partly hyaline globules. Preoperatively, alpha- feto protein had been 50 times higher than normal, and after chemotherapy decreased to normal. Patient's condition observed during the period of five years is satisfying.

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High molecular weight cytokeratins in diagnostics of well differentiated adenocarcinoma of prostatic gland

KEYWORDS: Prostate Neoplasms; Cytokeratin; Immunohistochemistry

Many histological details may be useful in estimating the degree of malignancy of small well differentiated adenocarcinomas of the prostatic gland. In some cases the well known morphological parameters (architecture and cytology), are not sufficient to make the final diagnosis of well differentiated adenocarcinomas of the prostatic gland , especially from a scanty bioptic material. According to the literature we find that cytokeratin 903 can be used for these cases.. CK 903 marks the basal layer of the prostatic glands epithelium, and allows detection of prostatic gland adenocarcinomas. We used the coctail made of high molecular weight cytokeratins, HMW CK (DAKO) to achieve the final diagnosis. This will be a report of four cases in which the small focuses of well differentiated prostatic adenocarcinomas without intensive cell atypia were diagnosed using the HMW CK, whose presence is confirmed in basal layers, as well as the diffuse appearance in basal cell hyperplasia. Reactivity of HMW CK in basal cells has been checked on normal prostatic tissue, in cases of basal cell hyperplasia, in glands in which reactive atypia is present, in atrophic glands, and also in glands with obvious malignant features. HMW CK may be useful in the diagnostics of prostatic adenocarcinomas.

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Progression of prostatic adenocarcinoma classified according to Gleason score in sextant biopsies and after radical prostatectomy

KEYWORDS: Prostatic adenocarcinoma; Gleason score; Radical prostatectomy; Biopsy

In the Department of Pathology and Histology of the Clinical Center in Novi Sad, the daily assessment of possible adenocarcinoma in prostate sextant biopsies and after radical prostatectomy is carried out. The evaluation is made according to the Gleason score, as one of the most important prognostic factors of the disease.The aim of this study was to determine the Gleason score correlation in prostate sextant biopsies and after radical prostatectomy in order to evaluate eventual progression. We analyzed morphological characteristics of adenocarcinoma in preoperative sextant biopsies and prostatic material after radical prostatectomy in 30 patients. Material was prepared after the standard methodology and light microscopically analyzed always by the same pathologist since this method is relatively subjective. Patients were divided into two separate groups according to the progression of Gleason score. In first group there were patients without any Gleason score progression from the first into the second biopsy specimen, while the patients with the progression were included into the second group.The mean age at the diagnosis was 67 years (range 49 - 79), and the time period between the first and the second biopsy was from 19 to 123 days (mean 61.06). In 12 (40%) patients we detected the adequacy of Gleason score of sextant biopsies and postoperative material, from which eight scored 4, and four other patients scored 6, which indicates that prostatic adenocarcinoma rarely changes its grade in well differentiated tumors of this organ. In the second group there were 18 (60%) patients with progression for one or more grades, 14 (46.67%) patients with the progression for one point and 2 (6.67%) for two points. Two (6.67%) patients from the same group had the progression from 6 to 9 Gleason score in whom radical prostatectomy followed sextant biopsy after 112 and 123 days. Considering that the mean time after the primary diagnosis of prostatic adenocarcinoma was two months, we found out that well differentiated carcinoma rarely in that period of time progress to a higher grade, whereas in the same period of time poorly differentiated tumors were progressing into an adverse histological type. We may conclude that the Gleason score of well defined prostatic adenocarcinoma corresponds to the same score on biopsy specimens after radical prostatectomy, whereas a grade progression is evident in the low grade diagnosed tumors, depending on the time interval between the primary diagnosis and radical surgery of this neoplasm.

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Undifferentiated testicular sex cord - gonadal stromal tumor with myofilaments - A case report

KEYWORDS: Testicular tumors; Sex-cord stromal tumor

Testicular sex cord-gonadal stromal tumors (SCGST) are rare, the majority of them differentiate into Sertoli, Leydig or granulosa cell tumors. Unclassified sex cord-stromal tumors of the testis composed predominantly of spindle cells can be difficult to classify. Only two cases of undifferentiated SCGST with myofilament have been teported so far. In our case a spindle shaped, hypercellular, highly mitotic, and smooth muscle actin (SMA) positive tumor was diagnosed. In the differential diagnosis, a malignant mesenchymal tumor - a leiomyosarcoma must also be considered. Additional confusion might be brought up in SMA positive but desmin negative cases. The ultrastructural observation of delicate myofilament is generally consistent with mesenchymal origin of the tumor. However, the presence of desmosome-like intercellular junctions as well as some lipid droplets, also found in our case, and the positivity for (-subunit of inhibin, favor the diagnosis of SCGST. Regarding the prognosis, a sharp distinction between undifferentiated sex cord-gonadal stromal tumor and malignant mesenchymal tumor should be emphasized, the former being completly benign. Careful histological examination, electron microscopy and immunohistochemical reaction for (-subunit of inhibin can be helpful in establishing the diagnosis of SCGST.

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Primary localization of nonHodgkin lymphoma in the testis (Case description)

KEYWORDS: Testicular tumors; NonHodgkin lymphoma

Tumors of testis represent up to 2% of malignant tumors in men. In about 95% of cases, primary tumors are of germinative epithelium origin. Testis can often be places of secondary deposits in lymphomas and leukemias, while primary lymphomas of testis are possible, but very rare. The aim of the paper is to present the incidence of primary malignant tumors of testis diagnosed in the Centre for Pathology of the Clinical Centre of Montenegro, where were immunohistochemicaly and clinically confirmed primary Non-Hodgkin lymphomas of testis. 36 cases of malignant tumors of testis diagnosed in the period 1993-2001 in the Centre for Pathology of the Clinical Centre of Montenegro were analyzed. For immunophenotyping of the lymhomas was used cell presentation of LCA, CD20, CD79α, CD3 and CD43 antigens. Out of 36 cases of malignant tumors, 42% are seminomas of testis, 25% embryonal carcrinoma, 5,5% teratoma, 8% embryonal carcinoma + teratoma, 5.5% choriocarcinoma + teratoma, 5,5% embryonal carcinomas + seminomas and 3% teratoma + seminoma. In 2 patients (5,5%), of 61 and 77 years of age, primary B lymphocytic NonHodgin lymphoma of testis was diagnosed and clinically confirmed. Primary lymphomas of testis are rare, B lymphocytic phenotype, they occur mainly in patients older than 60, of high degree of malignancy with a poor prognosis.