INVITATION LECTURES

1. UROLOGICAL PATHOLOGY

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Nodal metastases of prostate cancer - Analysis of 49 cases

KEYWORDS: Prostatic carcinoma; Nodal metastasis; Radical prostatectomy; Staging

INTRODUCTION

Node-negative (p N0) prostate cancer is the best result after radical prostatectomy. Radical prostatectomy is indicated in patients with localised prostate cancer. The aim of the study is to find nodal metastases of prostate cancer after radical prostatectomy.

MATERIAL AND METHODS

We analyzed 49 cases of radical prostatectomies due to localized prostate cancer in the period 1996-2000 in Clinic of Urology in Clinical Center of Serbia, Belgrade. In analysis we included: nodal metastases (stage of disease), average age of the patients, grade and Gleason score of tumors and premalignant lesions. Material was stained histochemicaly and immunohistochemicaly and histopathologicaly analyzed. We used statistical analysis $\chi 2$ test.

RESULTS

The average age of the patients was 65,6 years (range 44-76, pick 61-70). The most cases 25(51%, $p<0,001$) we found in pT2a N0M0, in pT2b N1M0 9 (18,36%), in pT3bN0M0 10 (20,4%), in pT3bN1M0 3(6,12%) and in pT4aN0M0 2 (4,08%). Nodal status positive was: iliac 4 (right 3, left 1), obturatory 6 (right 1, left 5). Grade 1 of tumors we found in 9 cases (18%), grade 2 in 11 (22%), grade 3 in 29 (60%), $p<0,001$. Gleason score 3 was in 6,1%, 4 in 12,2%, 5 in 8,1%, 6 in 16,3%, 7 in 24,5%, 8 in 26,6%, 9 in 6,1%. HG PIN was in 18 cases (36,7%), LG PIN in 10 (20,4%).

CONCLUSION

Pelvic lymphadenectomy is necessary for staging purposes in adenocarcinoma of the prostate. Radical prostatectomy is most adequate method in surgical treatment of localized prostate cancer.

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Mucinohystochemical and immunohystochemical characteristics of prostatic carcinoma and prostatic intraepithelial neoplasia

KEYWORDS: Prostatic carcinoma; PIN lesions; PSA; Ki-67; p53 protein

INTRODUCTION

Prostatic adenocarcinoma (PCa) is the most important malignancy of the male genitourinary system. Mucinous differentiation is common in prostatic adenocarcinoma, although it seldom involves more then 25% of the volume of any cancer. Normal and hyperplastic prostatic acini produce mucosubstances, but these do not typically stain with the standard stain (1-2). Severe differentiation (PSA) and proliferation abnormalities (Ki-67) occur during malignant transformation of the prostatic epithelium. Prostatic intraepithelial neoplasia high grade (HG PIN) is considered the most likely precursor of clinically significant prostate cancer (3-5). The loss of heterozygosity and abnormalities in structure and function of the p53 gene are present in prostate adenocarcinoma (3).

MATERIAL AND METHODS

Research was performed in 80 patients with PCa, at the Institute of Pathology Clinical Centre Niš. Multiple high and low grade foci of PIN were analyzed in the PCa. Normal tissue and benign prostatic hyperplasia were used as control group. In this study several histological techniques like classic HE method, hystochemical methods (PAS, HID/AB pH 2,5) and immunohistochemistry with ABC (PSA, Ki-67, p53), were used. Statistical analysis was performed by applying $\chi 2$ and Fisher's test.

RESULTS

Applying the hystochemical methods, predominantly intraluminar localization of mucins in neoplastic glands was found, while in 7/80 cases of PCa mucin content was observed not only in duct lumen, but also in surrounding stromal tissue. Mucin presence was detected in Gleason grade 1-4A, while in grade 4B, 5A, and 5B secretion was not verified. Mucin secretion was predominantly focal. Neutral mucins were detected in 33/80 cases (41.25%) with prostatic carcinoma. The presence of neutral-fucomucins decreases, with decrease of malignant glands differentiation ($p<0,05$). Acid secretion was found in 51/80 patients (63,75%), with predominance of sialomucins. Strongly acidic sulfomucin was present in 7 cases. Sulfomucins were verified in Gleason grade 4A and 3 with statistically significant higher secretion in 4A ($p<0,05$). Secretion of acidic mucins decreases with rise of Gleason score. PCa most often showed mixed type of mucinous secretion. Mucino-hystochemical finding was negative in 36% of patients. The analysis of PSA indicated an immunoreactivity in all prostate adenocarcinoma (except particular fields of Gleason grade 5B). The largest number of analysed tumor(s fields have been shown trace or medium reactivity. Hyperplastic epithelial cells almost always showes intensive staining to PSA troughout the entire cytoplasm. A statisticaly significant difference in PSA content was observed between neoplastic and hyperplastic tissue ($\chi 2 = 29,05$ $p<0,001$). The lowest proliferative activity was found in well differentiated cancer glands while areas with Gleason grade 5A and 5B had the highest proliferative activity. Overexpression of p53 protein is present in 60% specimens of PCa. Nuclear accumulation of the altered p53 protein has shown prostate cancer of Gleason grade 4 and 5. Intraepithelial prostatic neoplasm (PIN) was found in 32/80(40%) in surrounding of prostatic carcinoma. Mucinohystochemical examination detected presence of neutral mucins in lumen of low grade PIN lesions in 10 cases (52, 63%), while acidic secretion could not be detected. High grade PIN lesions showed presence of neutral and acidic mucins in 5/24(20, 83%) and 8/24(33, 33%) respectively. Sialomucin type of secretion predominated in 25%, while sulfomucin foci were registered in 8, 33%. The increase of degree of displasia is followed by increase of the production of acidic mucins ($p<0.01$) while production of fucomucin decrease ($p<0, 05$). PIN low grade showed higher activity of PSA ($p< 0,005$), while Ki-67 and p53 activity was higher in high grade PIN ($p< 0, 05$). Hyperplastic and normal prostatic tissue had scant PAS + material and strong PSA + immunoreactivity.

DISCUSSION

Mucinohystochemistry found that neutral mucins production had following features: normal and hyperplastic prostatic tissue (57.5%), prostatic carcinoma (41.25%), low grade PIN (52.63%), high grade PIN (20,83%). Progressive increase of amount of acidic mucins was found in areas with high grade PIN and prostatic carcinoma in 33.33% and 63.75% respectively, while it was absent in low grade PIN and hyperplastic prostatic tissue. Immunohystochemical analysis showed presence of distorted cellular differentiation in premalignant phase of prostatic cancerogenesis (2-4). Statistically significant difference in PSA activity was recorded between low grade and high grade PIN and prostatic carcinoma. PSA activity was much higher in former than in high grade PIN and prostatic carcinoma. Ki-67 proliferative activity in PIN increases with increasing the intensity of dysplasia. Significant difference of Ki-67 activity was found between carcinoma and low grade PIN, while there was no difference between carcinoma and high grade PIN. p53 accumulation was found only in high grade PIN but without difference comparing to prostatic carcinoma (3-5). It could be concluded that secretion of acidic mucins in high grade PIN and prostatic carcinoma could be considered as their principal mucinohystochemical feature. Immunohystochemical analysis showed presence of distorted cellular differentiation in premalignant phase of prostatic cancerogenesis.

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Parameters for early prostate cancer biochemical failure after radical prostatectomy

KEYWORDS: Prostatic carcinoma; Radical prostatectomy; Staging

INTRODUCTION

Prostate cancer (PC) is the most frequent male neoplasm after skin cancer. Determination of serum prostate-specific antigen (PSA) has resulted in a major proportional increase of early-diagnosed patients with clinically localized PC. Radical prostatectomy (RP) is the most successful therapy for localized PC. Biochemical relapse of PSA is present in 20-53% of patients after RP in 5-10 year period (1). The relative risk for PSA progression depends on different clinical and histopathological parameters. The aim of this study was to correlate the preoperative serum PSA level, pathologic PC stage, status of tumor margins and prostatectomy Gleason score with the dynamics of biochemical PSA progression in RP material.

MATERIAL AND METHODS

A total of 55 PC patients treated with bilateral pelvic lymphadenectomy and RP were followed for 13 to 73 months. We didn't include the patients who had undergone preoperative or postoperative neoadjuvant hormonal or radiation therapy before the evidence of PSA elevation (N=19). The validation group of 36 patients were followed up after surgery, performing a digital rectal examination and serum PSA determination in 3.6-12 month intervals. Biochemical progression (bP) was defined as a PSA level greater than 0.2 ng/ml in two consecutive measurements. The macroscopic pathological analysis was performed with the method of complete prostate tissue sampling with routine sections. The prostate, seminal vesicles and lymph nodes were examined histologically in the standard fashion for determination surgical margins status and seminal vesicles involvement. Microscopic analysis included quantifying the cancer volume, Gleason differential and tertiary Gleason grade. Distribution of the midrange Gleason score was assigned and closely presented in the form of modified Gleason score, based on the primary and secondary Gleason patterns of tumors growth collectively. The

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Kaplan-Meier method was used to estimate biochemical progression - free survival time for each risk group. The Cox proportional hazards regression analysis was the model for bP time using pathological and clinical variables.

RESULTS

The total of 23 (64%) patients developed bP of the disease after RP. The average time for bP was 16 months. Pathological staging confirmed that 23 (64%) of patients had the organ-confined (pT2) disease and 13(36%) of patients the locally advanced (pT3) one. The preoperative PSA serum level range of ≤ 10ng/ml was established in 52% of the patients. We detected pT3 stage, tertiary Gleason grade and spread over surgical margins of tumors for the highest number of patients with bP of the disease. There was a small number of patients with the preoperative PSA serum level greater than 10ng/ml and modified Gleason sum score >1. Tertiary Gleason grade ($p=0,01$), cancer volume ($p<0,05$) and pathological stage ($p<0,05$) significantly affect the level of postoperative PSA progression. The multivariate analysis revealed the tertiary Gleason grade ($p<0,05$) represents a unique significant predictor of bP after RP.

DISCUSSION AND CONCLUSIONS

Biochemical progression of PC represents a poorly defined parameter after RP and no criteria are uniformly accepted for its implications for the treatment of these patients. The results of initial studies indicated that bP of the disease could precede the clinically manifested disease by several months to several years. The more recent studies do not confirm utility of bP of the disease after RP in 10-years survival period. In 64% of our patients bP of the disease is higher than reported in other studies. These studies found that 20-53% of patients had an elevated serum PSA level five years after RP(1). Recent evidence suggests that the percent of tertiary Gleason grade in the RP specimen is one of the strongest predictors of early bP of the disease (2). Our results show that prostatectomy specimens tertiary Gleason grade, cancer volume and pathologic stage can be used to predict the PSA progression risk group of PC patients.

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