PATHOLOGY

Positive-Block Ratio in Radical Prostatectomy Specimens Is an Independent Predictor of Prostate-Specific Antigen Recurrence

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Background: Tumor volume has been considered an important variable in determining the probability of disease progression in prostatic adenocarcinoma. There have been many studies that have tried to determine an appropriate method of calculating tumor volume, but no single methodology has been agreed upon. We tested the hypothesis that the ratio of tumor positive tissue blocks to the total number of blocks submitted (positive-block ratio) can be used as an independent prognostic indicator for disease recurrence.
Design: We analyzed 504 patients who underwent total radical retropubic prostatectomy between 1990 and 1998. None of the patients had preoperative radiation or androgen-deprivation therapy. Clinical records were reviewed.
Results: The mean positive-block ratio was 0.44 (median, 0. 43; range, 0.05-1.0). The positive block-ratio was significantly associated with Gleason score, pathologic stage, surgical margin status, extraprostatic extension, seminal vesical invasion, lymph node metastasis, perineural invasion, and preoperative serum PSA level (all $P < 0.001$). Using a multivariate Cox regression model, controlling for pathological stage, Gleason score, and surgical margin status, positive-block ratio was an independent predictor of PSA recurrence (hazard ratio, 2.4; 95% confidence interval, 1.1-5.1; $P = 0.02$). Five-year PSA recurrence-free survival was 67% for those patients with positive-block ratio 0.43, as compared to 42% those with positive-block ratio > 0.43 ($P < 0.001$).
Conclusions: Positive-block ratio is an independent predictor of PSA recurrence and we recommend that this variable be recorded in radical prostatectomy specimens.

Editorial Comment

One of the most controversial aspects of the pathologic assessment of radical prostatectomy specimens is the measurement of tumor volume (1). No accepted standard exists for reporting cancer volume in prostatectomy specimens (2). Some institutions have calculated tumor volume accurately using computer-assisted image analysis systems. Because this method is not feasible for routine clinical practice, other investigators have proposed alternative simpler means of measuring tumor volume including diameter of largest tumor focus, number of tumor foci, number of involved blocks, percentage of blocks involved, use of a grid with 3.0 mm squares, or naked eye examination of the glass slides after the pathologist had circled all microscopically identifiable foci of carcinoma with a marking pen (the pathologist's percentage estimate) (3-7). The method for evaluating tumor extent applied and proposed in the study by Marks et al. is based in the positive-block ratio and is a simple one and accessible to all general pathologists. Actually is easier than the one we proposed based on a point count method (8).

Numerous studies have documented that tumor extent, volume and percentage of prostatic tissue involved by tumor within the prostate gland are important prognostic indicators. Tumor extent has been correlated with histologic grade, clinicopathologic stage, extraprostatic extension, seminal vesicle invasion, metastasis, tumor progression, and patient survival rate (6).

Although most authors agree that tumor size (percentage of carcinoma or tumor volume) in patients with prostate carcinoma should be reported in radical prostatectomies because of its prognostic importance, in some analyses, tumor size has not been considered to be an independent predictor of tumor recurrence (1,9). In the study surveyed, Marks et al. have shown that the 5-year biochemical-free progression was 67% for those

patients with positive-block ratio 0.43, as compared to 42% for those with positive-block ratio > 0.43 ($p < 0.001$) and that the positive-block ratio is an independent predictor of biochemical progression.

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Utility of ALK-1 Protein Expression and ALK Rearrangements in Distinguishing Inflammatory Myofibroblastic Tumor from Malignant Spindle Cell Lesions of the Urinary Bladder

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Inflammatory myofibroblastic tumor of the urinary bladder is an unusual spindle cell neoplasm that displays cytologic atypia, infiltrative growth and mitotic activity mimicking malignant tumors, such as leiomyosarcoma, rhabdomyosarcoma and sarcomatoid carcinoma. The objective of this study was to determine if anaplastic lymphoma kinase (ALK-1) protein expression detected by immunohistochemistry and ALK rearrangements detected by fluorescence in situ hybridization (FISH) were useful in distinguishing inflammatory myofibroblastic tumor from malignant spindle cell tumors of the urinary bladder. In inflammatory myofibroblastic tumor, ALK-1 expression was identified in 13 of 21 cases (62%) and ALK rearrangements in 14 of 21 cases (67%). All cases of inflammatory myofibroblastic tumor demonstrating ALK-1 expression, carried ALK rearrangements.

One case negative for ALK-1 expression exhibited ALK rearrangement. ALK rearrangements were more common in women (P=0.0032). Leiomyosarcoma, sarcomatoid carcinoma, embryonal rhabdomyosarcoma and reactive myofibroblastic proliferations were negative for ALK-1 protein and ALK rearrangements. Immunohistochemistry using markers of muscle, epithelial, neural, and follicular dendritic cell differentiation showed overlap between inflammatory myofibroblastic tumor with and without ALK gene rearrangements, and between inflammatory myofibroblastic tumor and spindle cell malignancies. However, coexpression of cytokeratin and muscle-specific antigens was unique to inflammatory myofibroblastic tumor, observed in approximately half the tumors. This study indicates that detection of ALK protein and ALK gene rearrangements are useful in distinguishing inflammatory myofibroblastic tumor from spindle cell malignancies in the urinary bladder. Additionally, our findings suggest that ALK rearrangement is the primary mechanism for ALK activation and that inflammatory myofibroblastic tumor likely represents a heterogeneous group of spindle cell proliferations with the majority associated with ALK translocations, and the remaining associated with other etiologies.

Editorial Comment

Inflammatory myofibroblastic tumor is a rare lesion occurring at a number of anatomic sites, including the urinary bladder. The vast majority of these tumors behave in a benign fashion, although occasionally tumors can recur following surgical excision. Due to the fact that displays cytologic atypia, infiltrative growth and mitotic activity, the tumor mimics aggressive malignant tumors, such as leiomyosarcoma and sarcomatoid carcinoma.

The differential diagnosis is of utmost importance and particularly difficult for the pathologist. The sarcomatoid variant of urothelial carcinoma is a very aggressive tumor. In a study by Lopez-Beltran et al., 70% of patients died of cancer at 1 to 48 months (mean 17 months) (1). Leiomyosarcoma is a rare malignant mesenchymal tumor that arises from urinary bladder smooth muscle and is the most common sarcoma of the urinary bladder. Although previous reports suggest that 5-year survival after partial or radical cystectomy approaches 70%, the largest recent study indicates that 70% of patients with leiomyosarcoma developed recurrent or metastatic disease, resulting in death in nearly half (2).

The study by Sukov et al. emphasizes the importance of immunohistochemistry as a help for the pathologist in the differential diagnosis of spindle cell lesions of the urinary bladder. In inflammatory myofibroblastic tumor there is a clonal aberration typically involving chromosome 2p (3). This results in rearrangement of the ALK gene which codifies a receptor of tyrosine-kinase and hence over-expression of ALK-1 protein which is disclosed by immunohistochemistry in up of 62% of the cases.

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