

PATHOLOGY

Characterization of minute adenocarcinomas of prostate at radical prostatectomy

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Objectives: To characterize minute prostate cancer seen at radical prostatectomy. With aggressive screening and more extensive biopsy sampling, we have increasingly seen these cancers at radical prostatectomy.

Methods: We examined radical prostatectomy specimens submitted in total for minute cancer.

Results: During the past 1.5 years, 78 prostates (5.2%) had either no cancer (2 cases) or contained between one and six foci of organ-confined carcinoma (76 cases) measuring 6 mm or less, with a Gleason score of 6 or less. The mean prebiopsy serum prostate-specific antigen level was 5.8 ng/mL, and 84.6% of the patients had undergone biopsy because of an elevated prostate-specific antigen level. Of these patients, 40% had had either benign or atypical diagnoses on prior biopsies, and 43% had only minute (0.5 mm or less) foci of carcinoma on biopsy. The radical prostatectomy specimens had a mean of two cancer foci measuring, on average, 3 mm in the greatest dimension. In 85% of the cases, the side of the positive biopsy matched the side of the carcinoma found at radical prostatectomy; 81.5% of cases had high-grade prostatic intraepithelial neoplasia immediately adjacent to the cancer.

Conclusions: The incidence of minute carcinoma of the prostate has increased from 0.5% in 1988 to 5.2% in the current study. The patients often had moderately increased prostate-specific antigen levels and minute foci of carcinoma on biopsy. These small tumors at radical prostatectomy are usually discovered by fortuitous biopsy that is often preceded by other biopsies with noncancerous diagnoses. Patients with the above clinical and biopsy findings should be counseled about the possibility of finding only minute foci of carcinoma at radical prostatectomy and may want to consider watchful waiting.

Editorial Comment

The incidence of “minute” (minimal, insignificant) cancer at radical prostatectomies has substantially increased in the last years. The main reason is aggressive screening and more extensive biopsy sampling. It is important to note that “minute” (minimal, insignificant) cancer in radical prostatectomy does not mean “latent” (dormant, indolent) carcinoma. It represents a low volume (incipient) cancer that can progress either as a “latent” or a “clinical” cancer. It is important to counsel the patients about the possibility of finding only minute foci of carcinoma at radical prostatectomy including the possibility of not finding a tumor at all.

According to the authors of the study, patients having clinical and biopsy findings for minute cancers may want to consider watchful waiting. In this respect, urologists consider age an important variable but the cut point is controversial. Carter et al. (1) informed men older than 65 years that expectant management was a reasonable option for management of cancer regardless of the presence or absence of co-morbidity. The recommended follow-up for those men managed expectantly was semiannual total and free PSA measurement with digital rectal examination, and annual surveillance transrectal ultrasound directed prostate biopsies.

Reference

1. Carter HB, Walsh PC, Landis P, Epstein JI: Expectant management of nonpalpable prostate cancer with curative intent: preliminary results. *J Urol.* 2002; 167: 1231-4.

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Characteristics of insignificant clinical T1c prostate tumors. A contemporary analysis

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Background: The authors examined the cases of men who had undergone radical prostatectomy for low-volume clinical T1c prostate carcinoma that was judged to be “insignificant” on the basis of previously established preoperative clinicopathologic parameters. Pathologic findings subsequently were analyzed for correlations with extent of disease in an attempt to validate the contemporary usefulness of existing parameters for predicting the “significance” of prostate tumors.

Methods: A series of 237 men who had undergone radical prostatectomy for T1c disease between December 2000 and August 2003 was evaluated. Insignificant prostate carcinoma as assessed on biopsy was defined according to the 1994 Epstein criteria, which were as follows: prostate-specific antigen density < 0.15 ng/mL, Gleason score < or = 6, fewer than 3 cores containing prostate carcinoma, and < or = 50% involvement of any core with prostate carcinoma. Postsurgical pathologic findings were analyzed for potential correlations with the Epstein criteria.

Results: According to the Epstein needle biopsy criteria, organ-confined prostate carcinoma was detected in 91.6% of all patients, whereas the remaining 8.4% of patients were found to have non-organ-confined disease. Comparison of pathologic findings and Epstein biopsy criteria revealed that alteration of the original criteria did not improve the detection of non-organ-confined prostate carcinoma.

Conclusions: The findings made in the current study suggest that the majority of patients with T1c prostate carcinoma have insignificant disease. Furthermore, it was found that the Epstein criteria for identifying insignificant prostate carcinoma remained a useful tool in the making of treatment-related decisions.

Editorial Comment

Considering the aggressive screening and more extensive biopsy sampling resulting in higher frequency of stage T1c, criteria predicting “minute” (minimal, insignificant) tumor in radical prostatectomy are of utmost importance.

The Epstein criteria for identifying insignificant prostate carcinoma remain a useful tool in the making of treatment related decisions. In this study prostate-specific antigen density < 0.15ng/mL was included in the criteria. In another study Epstein et al. (1) found a positive predictive value of 94.4% using a free/total PSA of 0.15 or greater and favorable needle biopsy findings (less than 3 cores involved, none of the cores with greater than 50% tumor involvement and Gleason score less than 7).

The involvement of the cores in percentage is controversial. Other authors consider that the extension of the tumor is a better way of evaluation. Noguchi et al. (2) consider that the combination of 1 positive core with cancer length less than 3 mm. that contains no Gleason grade 4 or 5 is probably the best predictor of prostate cancer less than 0.5 cc in men with nonpalpable tumors (stage T1c). These authors also found that PSA or PSA density in combination with needle biopsy findings did not enhance prediction of tumor significance.

References

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- Noguchi M, Stamey TA, McNeal JE, Yemoto CM: Relationship between systematic biopsies and histological features of 222 radical prostatectomy specimens: lack of prediction of tumor significance for men with nonpalpable prostate cancer. *J Urol.* 2001; 166: 104-109.

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INVESTIGATIVE UROLOGY

Androgen receptor expression is inversely correlated with pathologic tumor stage in bladder cancer

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Objectives: To evaluate the expression of the androgen receptor (AR) in transitional cell carcinoma (TCC) of the bladder, and to assess whether its expression correlated with pathologic tumor stage. TCC of the bladder is three times more common in males than in females. The origin of this sex difference in incidence is unknown.

Methods: We evaluated tumor specimens from 49 consecutive patients treated for TCC of the bladder at our institution between July 2002 and June 2003. Immunohistochemistry was performed using a monoclonal mouse anti-AR antibody on paraffin-embedded tissue sections of tumors obtained from transurethral resection, radical cystectomy, or resection of metastases. Specimens were assessed for AR expression, and, in tumors that demonstrated AR staining, the percentage of nuclei that stained positive was recorded.

Results: Of the 49 tumors, 26 (53.1%) expressed the AR. The percentage of tumors that expressed the AR decreased with increasing pathologic stage, from 88.9% of pTa lesions to 0% of pT3 tumors. Overall, 75% of superficial tumors (pTa + pT1 + carcinoma in situ) expressed the AR compared with 21.4% of invasive tumors (pT2 + pT3; $P = 0.002$). In addition, among AR-expressing tumors, the mean percentage of nuclei that stained positive for the AR was significantly greater in pTa tumors (62.5%) than in pT1 (31%) or pT2 (20%) tumors ($P = 0.005$).

Conclusions: We found a decrease in AR protein expression in tumors with increased pathologic stage. Our data suggest that the loss of AR expression is associated with invasive bladder cancer.

Editorial Comment

A previous study that considered smoking and occupational risks showed that the sex-related risk of bladder cancer for men persists independently of other risks (1). Some experimental studies in rats showed that the bladder tumors development is significantly greater in males than in females (2,3), although studies in humans are still scarce. A functional role for the AR in human bladder cancer has been suggested by a recent study that demonstrated that androgen treatment inhibited bacille Calmette-Guérin-induced interleukin-6 expression in bladder cancer cell lines that expressed the AR. The study also demonstrated that pharmacologic androgen deprivation restored bacille Calmette-Guérin-induced interleukin-6 expression (4).

In this present important contribution, Boorjian et al., after evaluating 49 tumor specimens, found a decrease in androgen receptors correspondent to increased pathologic stage. The authors suggest that as a