Usefulness of Transurethral Biopsy for Staging the Prostatic Urethra before Radical Cystectomy

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Abbreviations and Acronyms

CIS = carcinoma in situ

PSC = prostate sparing cystoprostatectomy

TUR = transurethral resection

UC = urothelial cancer

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For another article on a related topic see page 325.

Purpose: We determined the likelihood that transurethral resection biopsy of the prostatic urethra adjacent to the verumontanum would detect prostatic involvement of urothelial carcinoma in patients with bladder carcinoma.

Materials and Methods: We compared precystectomy transurethral resection biopsy specimens of the prostatic urethra with those of the matched radical cystoprostatectomy in 272 patients with urothelial carcinoma of the bladder. All prostates were evaluated by whole mount step sections.

Results: Prostatic involvement by urothelial carcinoma was detected by transurethral resection biopsy or radical cystoprostatectomy in 101 patients (37.1%). Transurethral resection biopsy detected urothelial carcinoma in 72 cases with 71.3% sensitivity and 100% specificity. The overall accuracy of transurethral resection biopsy to detect urothelial carcinoma of the prostate was 89% (positive and negative predictive values 100% and 86%, respectively). Invasive prostatic urothelial carcinoma arising from the prostatic urethra was detected by transurethral resection biopsy in 21 of 26 patients (81%) while prostatic carcinoma in situ was detected in 39 of 52 (75%). Transurethral resection biopsy detected prostatic invasive urothelial carcinoma resulting from transmural invasion of a bladder tumor in 4 of 15 patients.

Conclusions: Prostatic involvement by urothelial carcinoma of the bladder was found in 37.1% of patients. Transurethral resection biopsy missed most tumors resulting from transmural invasion of the bladder primary lesion. Carcinoma in situ and invasive urothelial carcinoma arising from the prostatic urethra were detected in most cases. Transurethral resection biopsy of the prostatic urethra can complement staging and support clinical decision making with respect to neoadjuvant chemotherapy and planning for an orthotopic neobladder.

Key Words: prostate, urinary bladder, urothelium, carcinoma, biopsy

It was previously shown that involvement of the prostate is a common finding in patients with advanced urothelial carcinoma of the bladder. Synchronous neoplastic transformation and pagetoid spread of CIS from bladder neck to prostate appear to be the most relevant mechanisms for the development of prostatic urothelial carcinoma while direct transmural invasion of the prostate through the bladder wall accounts for fewer cases.[1]

The clinical significance and prognosis associated with prostatic involvement by urothelial carcinoma are clearly documented in several

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studies.[2–7] Furthermore, the patterns and extent of prostatic involvement affect the outcome in patients with bladder cancer who have prostatic urothelial carcinoma.[5,8,9]

The reported incidence of prostatic urothelial carcinoma in patients with bladder cancer ranges widely from 16% to 48%.[1,2,5,10] Whole mount step sectioning of the entire prostate is associated with much higher sensitivity for detecting prostatic urothelial carcinoma (range 32% to 48%[2–5,11]) than selective sections of the prostate with a detection rate of only 15.6% to 35% of prostatic urothelial carcinomas.[1,6,7,12] A few studies suggest that the transurethral biopsy adjacent to the verumontanum detects most prostatic urothelial carcinomas since this portion of the prostatic urethra has the highest concentration of prostatic ducts.[13–15]

To our knowledge no study to date has described the precise patterns of prostatic involvement detected by transurethral biopsy and its correlation with whole mount step section. Our hypothesis was that precystectomy staging of the prostatic urethra with TUR biopsy is a sensitive method to detect prostatic urothelial carcinoma arising from the prostatic urethra and the prostatic ducts/acini. To determine the accuracy of transurethral biopsy for detecting prostatic UC and its concordance with whole mount specimens we examined prostatic tissue from 272 radical cystoprostatectomy specimens by whole mount sectioning of the entire prostate for the detection of prostatic urothelial carcinoma and correlated this with the final pathology results of the corresponding precystectomy transurethral biopsy.

MATERIALS AND METHODS

We identified 272 male patients who underwent prostatic urethral biopsy before radical cystoprostatectomy for bladder cancer from 1987 to 2013 from our institutional review board approved database (CAISIS, http://www.caisis.org/) and the pathology database at our private teaching hospital. Patients treated by other surgeons were included in the analysis. However, 204 of the 272 men were treated by a single surgeon (SPL) who performed a total of 278 male cystectomies at the teaching hospital during the study period. Pathological stage after cystectomy was pT0 in 21 cases, pTa/Tis in 62, pT1 in 45, pT2 in 50, pT3 in 63 and pT4 in 31. Transurethral biopsies were performed at the 5 and 7 o'clock positions adjacent to the verumontanum.

For prostatic urethral biopsy the entire specimen was submitted for processing and 3 levels of hematoxylin and eosin stained slides were prepared and examined. For pathological examination of the radical cystoprostatectomy specimen the prostate was separated from the bladder. Whole mount sections of the entire prostate were prepared and examined by at least 1 of 2 urological pathologists (SSS and TMW). The method of whole mount sectioning the prostate using a standard institutional protocol was described previously.[16] Since 2005, we have applied a modified protocol by adding 2 sagittal whole mount sections of the prostate, which are cut along the prostatic urethra, and the remaining bilateral prostate tissue from apex to base is submitted (fig. 1). The specific types and patterns of prostatic involvement by UC that were evaluated included 1) prostatic urethral and ductal/acinar involvement by CIS, 2) lamina propria invasion of the prostatic urethra, 3) stromal invasion of the prostate, 4) periprostatic or seminal vesicle invasion and 5) direct penetrating invasion of the prostate through the bladder wall.

Categorical variables were summarized by the frequency and percent, and quantitative variables were summarized by the median and range. The Fisher exact or chi-square test was used to compare categorical variables among groups. Statistical analysis was done with SPSS® for Windows®, release 12.0. For positive and negative predictive values, and accuracy we defined positive TUR biopsy and negative whole mount as positive so that there were no false-positive results.

RESULTS

Patients with Bladder Cancer with vs without Prostatic Involvement

Prostatic urothelial carcinoma was identified in 101 of the 272 patients by TUR biopsy in 72 and/or whole mount section of the prostate in 78 for a combined incidence of 37.1% (fig. 2). CIS only at bladder tumor TUR was associated with a higher likelihood of prostatic involvement compared to

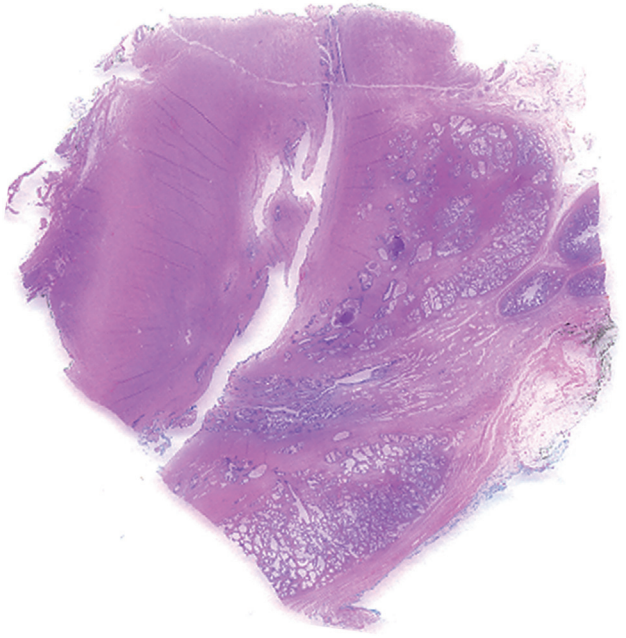

Figure 1. Sagittal section of prostate enables evaluation of urethra in its entire longitude.