PATHOLOGY

Follow up of high grade prostatic intraepithelial neoplasia and atypical small acinar proliferation in a highly screened patient population

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Background: High grade prostatic intraepithelial neoplasia (HGPIN) is the only established precursor for prostate cancer (PCa), with high predictive value as a marker for PCa. About 2% of contemporary needle biopsies contain collections of small acini suspicious for PCa but which fall below the diagnostic threshold. These cases are reported as atypical small acinar proliferation suspicious for but not diagnostic of malignancy (ASAP). Identification of HGPIN, ASAP, or both, warrant repeat biopsy for concurrent or subsequent PCa. PCa has been reported occur in up to 36% of subsequent biopsies for HGPIN and up to 60% for ASAP. We report results of follow up biopsies in a patient population with long term close clinical follow up, a population in which earlier, less advanced lesions are detected.

Design: All patients were from community practices, and had serum prostatic specific antigen studies obtained annually or more frequently. 191 cases with an initial diagnosis of 1) HGPIN 2) ASAP or 3) both HGPIN and ASAP; and at least 1 set of subsequent biopsies were retrieved from the files of Bostwick Laboratories. Cases with concomitant PCa were excluded. Follow up biopsies for each entity were separated into 2 diagnostic categories 1) Ca or 2) Non-PCa.

Results: Repeat biopsies were obtained from 1 week to 14 months after the initial diagnosis. Results are as follows: HGPIN PCa, 23/103 (22%); HGPIN Non-PCa, 80/103 (78%); ASAP PCa, 18/49 (37%); ASAP Non-PCa, 31/49 (63%); HGPIN & ASAP PCa 11/39 (28%); and HGPIN & ASAP Non-PCa 28/39 (72%).

Conclusions: The predictive accuracy for PCa is lower for both HGPIN and for ASAP in a highly screened patient population compared with previously reported unscreened populations. It is still significant compared with historic controls with neither HGPIN nor ASAP. The combination diagnosis of HGPIN & ASAP is an intermediate predictor for PCa, weaker than for ASAP, but stronger than for HGPIN. Other factors that may account for the decline in the predictive accuracies of HGPIN and ASAP for PCa seen here include: 1) more extensive prostate sampling 2) a greater number of biopsies obtained 3) addition of more lateral biopsies.

Editorial Comment

High-grade prostatic intraepithelial neoplasia (HGPIN) and atypical small acinar proliferation suspicious for but not diagnostic of malignancy (ASAP) are timely topics on prostate pathology. Atypical lesions considered to be precursors of prostate cancer had many synonyms. Since 1989 during a consensus meeting in Bethesda sponsored by the American Cancer Society (Urology 1989; 34 (suppl): 2-3) a unified name was adopted for these lesions: prostatic intraepithelial neoplasia (PIN). At that meeting, it was also agreed that only high-grade lesions of PIN should be reported by pathologists (HGPIN). The frequency of prostatic carcinoma in a second biopsy of a patient with HGPIN varies from 23 to 79% (J Urol. 2001; 166: 402-10). It is very significant the trend for a lower frequency of this finding. In this commented paper, the authors found a frequency of 22%. They attribute this decline to: 1) more extensive prostate sampling; 2) a greater number of biopsies obtained; and, 3) addition of more lateral biopsies. This means that a higher number of prostate cancers is diagnosed at the time of the first biopsy. As to the term atypical small acinar proliferation suspicious for but not diagnostic of malignancy (ASAP) it is our opinion that the best term is simply “suspicious but not diagnostic of cancer”.

ASAP may give to the urologist the meaning of a specific entity that this lesion definitely lacks. It happens when the pathologist is not sure of the diagnosis in cases of a tiny focus, absence of nuclear alterations or when the suspicious focus disappears in subsequent sections (Am J Surg Pathol. 1997; 21: 1489-95).

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pT1 Substaging in renal cell carcinoma: validation of the 2002 TNM staging modification of renal tumors

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Background: Tumor size has been used as a criterion to stratify renal cell carcinomas (RCC) into different pT categories. The recent 2002 UICC/TNM classification of malignant tumors is modified to substratify pT1 RCC into pT1a (< 4 cm) and pT1b (> 4 cm ≤ 7 cm). This study aimed to ascertain if this stage modification has prognostic relevance.

Design: 259 consecutive radical nephrectomy specimens from one institution for organ-confined RCC from 1970 to 1997 (156 conventional clear RCC (CRCC), 69 papillary RCC, 28 chromophobe RCC, 1 collecting duct carcinoma and 5 RCC, NOS) with follow-up (mean 7.17 years, median 6.45 yrs) were included in the study.

Results: There were 115 (44.4%) < 4 cm (pT1a), 95 (36.7%) > 4 cm ≤ 7 cm (pT1b) and 49 (18.9%) > 7 cm (pT2) tumors. Disease-related deaths (DD) and disease-related recurrences (DR) occurred in none (0%) and 2 cases (1.7%) of pT1a; 5 (5.3%) and 7 (7.3%) of pT1b, and 12 (24.5%) and 16 (32.6%) of pT2. All analyses were adjusted for age and sex. DR for all histologic subtypes was not statistically different between pT1a and pT1b with a risk ratio (RR) of 3.7 ($p = 0.106$). If only CRCCs were analyzed, DR in the pT1b group was statistically higher compared to pT1a with a RR of 8.54 ($p = 0.047$). The RR for pT2 was significantly higher than pT1a (20.30 for all histologic subtypes and 46.97 for CRCC) ($p = 0.001$). Using size as a continuous variable, the logarithmic change in tumor size was a significant predictor of DR with a risk ratio of 8.62 ($p = 0.001$). Since no deaths occurred in the pT1a category, the combined pT1a and pT1b and pT2 were compared to assess DD; DD in the pT2 group was significantly higher with an estimated RR of 2.2 ($p = 0.002$).

Conclusions: Substaging and staging of RCC into pT1 (pT1a and pT1b) and pT2 yields prognostically important information validating the 2002 TNM modifications for this tumor type. The substratification of pT1 is particularly useful in tumors with CRCC histology.

Editorial Comment

The new proposal to stratify pT1 is also a timely topic on renal pathology. The recent 2002 UICC/TNM classification of malignant tumors was modified to substratify pT1 renal cell carcinoma into pT1a (< 4 cm) and pT1b (> 4 cm ≤ 7 cm). This is a large series based on 259 consecutive radical nephrectomy specimens from one institution for organ-confined renal cell carcinoma. The results of the study yielded prognostically important information validating the 2002 TNM modification for renal cell carcinoma. The authors conclude

that substratification of pT1 is particularly useful in tumors with conventional renal cell carcinoma histology. The conventional renal cell group includes clear and eosinophilic renal cell carcinomas. It is also worth mentioning that the 2002 UICC/TNM classification includes renal sinus (peripelvic) fat invasion as pT3a. In the 1997 edition, only perinephric adipose tissue was considered pT3a. Pathologists must be aware of this modification in order to properly examine the renal sinus.

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