

**PATHOLOGY****Diffuse adenosis of the peripheral zone in prostate needle biopsy and prostatectomy specimens**

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We have observed a group of typically younger patients with multiple foci of small, nonlobular, crowded, but relatively bland acini on needle biopsy and in prostatectomy specimens. It is unclear whether this architectural pattern, which we have termed diffuse adenosis of the peripheral zone (DAPZ), is simply a crowded glandular variant of normal prostate morphology or whether it represents a risk factor for the development of prostatic carcinoma. We studied 60 cases of DAPZ on needle biopsy in our consult practice from 2001 to 2007. Cases, on average, showed 72% of cores involved by DAPZ. Average patient age was 49 years (range: 34 to 73) and the average prostate specific antigen (PSA) level at the time of biopsy was 5.2 ng/mL (n = 42). Forty-three (72%) men had available clinical follow-up with 35 (81%) patients undergoing rebiopsy and 8 (19%) followed with serial PSA measurements. Patients who were rebiopsied after DAPZ diagnosis had higher PSA levels than those who were followed by PSA levels alone (6.2 vs. 3.1 ng/mL, P = 0.04). Of the rebiopsied cases, 20 (57%) were subsequently diagnosed with carcinoma, with an average of 15 months elapsed between initial biopsy and carcinoma diagnosis. Although the majority of tissue sampled in a typical DAPZ case had no cytologic atypia, in 65% of cases there were admixed rare foci of atypical glands with prominent nucleoli comprising < 1% of submitted tissue. Patients with a subsequent diagnosis of carcinoma were more likely to have had DAPZ with focal atypia, although this did not reach statistical significance (70% vs. 36%, P = 0.08). We histologically confirmed the carcinoma diagnosis in 18/20 cases. In 12/14 radical prostatectomies, we were able to review the slides. Eleven had Gleason score 3+3=6 adenocarcinoma in addition to background DAPZ; 9 showed peripheral zone organ-confined cancer, and 2 had focal extraprostatic extension. In one case of DAPZ misdiagnosed as cancer on biopsy, no carcinoma was found at prostatectomy. DAPZ is a newly described and diagnostically challenging mimicker of prostate cancer seen in prostate needle biopsies from typically younger patients. Our findings suggest that DAPZ should be considered a risk factor for prostate cancer and that patients with this finding should be followed closely and rebiopsied.

**Editorial Comment**

Adenosis is a focal lesion that may be confused with carcinoma in transurethral resection specimens (1) or in needle biopsy specimens (2). Another commonly used term for adenosis is atypical adenomatous hyperplasia (3). Epstein prefers the term adenosis, as prefacing adenomatous hyperplasia with the term atypical has adverse consequences in terms of practical patient management considering that there are little data in support of a relation between adenosis and carcinoma. By designating these lesions as atypical, many patients will be subjected to unnecessary repeat biopsies.

In general this lesion is not reported by the pathologist being only a problem in the differential diagnosis with adenocarcinoma. Immunohistochemistry is useful for the correct diagnosis. Lotan and Epstein report a variant of adenosis that is diffuse and seen in younger patients in prostate needle biopsies. Forty-three (72%) men had available clinical follow-up with 35 (81%) patients undergoing rebiopsy. Of the rebiopsied patients, 20 (57%) were subsequently diagnosed with carcinoma, with an average of 15 months elapsed between initial biopsy and carcinoma diagnosis.

The authors consider this newly described variant of adenosis diagnostically challenging mimicker of prostate cancer seen in prostate needle biopsies from typically younger patients (average patient age 49 years). The findings suggest that diffuse adenosis of the peripheral zone should be considered a risk factor for pros-

tate cancer and that patients with this finding should be followed closely and rebiopsied. Therefore this lesion should be reported by the pathologists.

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### **Positive surgical margins in areas of capsular incision in otherwise organ-confined disease at radical prostatectomy: histologic features and pitfalls**

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Capsular incision (CI) refers to the urologist transecting either benign or malignant prostatic tissue, where the edge of the prostate in this region is left within the patient. Histologic assessment of CI is difficult and its diagnosis varies among pathologists. Between 1993 and 2004, we reviewed 186 radical prostatectomies that were signed out as either: (1) CI into tumor in otherwise organ-confined disease [elsewhere no extra-prostatic extension (EPE), seminal vesicle invasion, or lymph node spread] (n = 143); (2) positive surgical margin in an area difficult to distinguish EPE from CI into tumor in otherwise organ-confined disease (n = 36); or (3) equivocal positive surgical margin in an area difficult to distinguish organ-confined disease with tumor close to resection margins (OC M-) from CI into tumor in otherwise organ-confined disease (n = 7). On review, CI with a positive margin was confirmed in 83.2% of cases. Of cases signed out with margins positive where it was difficult to distinguish CI from EPE, CI was confirmed in 52.8% of cases. Cases with equivocal positive margins with either CI or OC M- were considered CI with positive margins in 57.1% of cases on review. Cases in all 3 groups not considered positive margins with CI were on review equally divided between diagnoses of organ-confined margin negative and EPE with positive margins. The locations of the 39 cases originally misdiagnosed as definitive or questionable CI with positive margins were posterolateral (N = 19, 48.7%), distal (N = 12, 30.8%), posterior (N = 6, 15.4%), and anterolateral (N = 2, 5.1%). Familiarity with different patterns of EPE in different anatomic locations and applying strict criteria for diagnosing CI into tumor can minimize overcalling CI and can provide accurate feedback to urologists to prevent iatrogenic positive margins.

#### **Editorial Comment**

Positive surgical margin (vesical, urethral or circumferential) in radical prostatectomy specimens is a well established adverse finding for biochemical (PSA) progression following surgery. The frequency of this

progression varies from 36% to 72% in the literature (1). In our Institution, the progression in 300 patients was 37% after 5 years of follow-up.

It is important for the urologist the definition and the description of the several kinds of positive surgical margins (2):

- a) Positive surgical margins are defined as cancer cells touching the inked surface of the prostate;
- b) Iatrogenic surgical margin occurs whenever there is a transection of the intraprostatic tumor. If this occurs, one cannot determine whether there is extraprostatic extension in the region of incision into the prostate as the edge of the prostate has been left in the patient. Unless there is extraprostatic extension in other areas of the surgical specimen, the pathologic stage is called pT2+;
- c) Non-iatrogenic surgical positive margin occurs whenever there is an inability to widely excise tumor showing extraprostatic extension.

It is worth mentioning the possibility of positive surgical margins in normal prostatic glands. This is not routinely reported by the pathologist; however, it is very important to report in cases of limited carcinoma in the surgical specimen. In these cases, biochemical (PSA) progression following surgery may be due to normal glands left in the patient. In our Institution, no patient with limited carcinoma in the specimen had biochemical progression, except 3 patients. Reviewing the prostatectomy slides, we found that all 3 patients had frequent and extensive positive surgical margins in normal glands.

### References

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## INVESTIGATIVE UROLOGY

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### **Protein oxidation as a novel biomarker of bladder decompensation**

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**Objective:** To measure the degree to which partial bladder outlet obstruction (PBOO) results in oxidative bladder damage, which subcellular components of the bladder are affected and whether these changes correlate with bladder function.

**Materials and Methods:** In all, 32 rabbits were divided into four groups. Each group underwent PBOO for 1, 2, 4, and 8 weeks, respectively. Bladder tissue from each group was homogenized and separated into subcellular