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Original contribution

The distribution of PAX-2 immunoreactivity in the prostate gland, seminal vesicle, and ejaculatory duct: comparison with prostatic adenocarcinoma and discussion of prostatic zonal embryogenesis

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Summary PAX-2 is a homeogene strongly expressed during development of the genitourinary tract, including the kidney and both wolffian- and müllerian-derived tissues. Expression of PAX-2 by immunohistochemistry has been studied mainly in renal epithelial neoplasms with little attention to the lower male genitourinary tract. We studied PAX-2 expression in epithelium of normal seminal vesicle, normal ejaculatory duct, normal prostatic secretory epithelium, and prostatic adenocarcinoma to define its immunoreactivity pattern throughout the prostate gland and to evaluate its potential diagnostic role in the discrimination of seminal vesicle/ejaculatory duct epithelium from prostatic adenocarcinoma. In addition, given that PAX-2 is highly expressed in tissues of wolffian duct embryologic origin, we also sought to confirm the divergent embryogenesis of the central zone, seminal vesicle, and ejaculatory duct from other regions of the prostate. Prostatectomy specimens from 12 patients were reviewed to identify blocks containing seminal vesicle, ejaculatory duct, periurethral glands, benign prostatic glands, and prostatic acinar adenocarcinoma. A total of 35 blocks from the 12 patients were evaluated. In addition, 2 tissue microarrays representing 15 additional seminal vesicles and 45 prostatic adenocarcinomas, 7 whole sections from prostatic adenocarcinomas of the central zone, and 5 core needle biopsies of seminal vesicle were also evaluated with anti–PAX-2 antibody. In the 12 radical prostatectomy whole sections, nuclear reactivity for PAX-2 was identified in 12 (100%) of 12 of the seminal vesicle epithelium, 9 (90%) of 10 of the ejaculatory duct epithelium, 0 of 12 of the prostatic adenocarcinoma, and 0 of 6 of the high-grade prostatic intraepithelial neoplasia. All 20 total additional seminal vesicles were positive for PAX-2 in the tissue microarray and biopsies; and all 52 additional prostatic adenocarcinomas were negative, including 7 of central zone origin. The staining intensity and percentage of immunoreactive cells in seminal vesicle were both 3+ in all cases. Although the ejaculatory ducts also showed diffuse staining, their staining intensity was less (2+) than that in the seminal vesicles, particularly in the ejaculatory ducts in the periurethral area (1-2+intensity). The smaller glands surrounding the main seminal vesicle duct also showed less intense staining than the luminal

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cells of the main duct. Of the 19 total cases with evaluable central zone glands, 2 (10.5%) had focal nuclear reactivity in normal, benign prostatic secretory cells. All other benign prostatic secretory epithelia from the peripheral and transition zones were negative for PAX-2. In conclusion, nuclear PAX-2 immunoreactivity is typical in epithelium of the seminal vesicle and ejaculatory duct; but the intensity of staining is less in the ejaculatory duct. No reactivity for PAX-2 was seen in prostatic adenocarcinoma or high-grade prostatic intraepithelial neoplasia. PAX-2 has diagnostic utility as a positive immunohistochemical marker of seminal vesicle and ejaculatory duct epithelium. In addition, these data add further support to the proposed embryogenesis of the prostatic central zone, seminal vesicle, and ejaculatory ducts from the wolffian system.

1. Introduction

Numerous morphologic mimics of prostate cancer have been described, including normal tissues such as ejaculatory duct and seminal vesicle [1]. Seminal vesicle epithelium is reported in up to 5% of prostatic needle core biopsies [2]. In core biopsies, the distinction of prostatic adenocarcinoma from seminal vesicle epithelium is usually straightforward based on the presence of scattered pleomorphic nuclei, intracytoplasmic pigment, a large central lumen, and an intact basal cell layer in seminal vesicle. However, occasional examples of seminal vesicle tissue in biopsy specimens may be challenging because of crush artifact, sectioning of the luminal edge with resultant closely packed small seminal vesicle glands, and minimal sampling with only few small glands present. In addition, prostatic adenocarcinoma and benign prostate tissue may contain intracytoplasmic lipochrome pigment [3,4]; and rare examples of carcinoma may have nuclear pleomorphism [5].

PAX-2 is a homeogene that is expressed in the development of the urogenital tract, including the kidneys, wolffian duct system, and mullerian duct system [6-9]. Commercial antibodies for anti–PAX-2 are available, but their application to diagnostic surgical pathology has been limited mainly to renal epithelial neoplasms [10-14]. In this study, we evaluate the expression of PAX-2 in ejaculatory duct, seminal vesicle, prostatic urethra, normal prostate glands, and prostatic adenocarcinoma to address the potential utility of PAX-2 in the distinction of seminal vesicle/ejaculatory duct epithelium from prostatic adenocarcinoma and to address the proposed embryogenesis of these structures.

2. Materials and methods

Twelve specimens of radical prostatectomy performed at the University of Arkansas for Medical Sciences between 2006 and 2007 were identified. All of the slides for each case were reviewed; and slides containing the ejaculatory duct, prostatic urethra, seminal vesicle, normal prostate, and adenocarcinoma were selected. A total of 35 blocks from the 12 prostatectomy specimens were retrieved. An additional 45 prostatic adenocarcinomas, 15 seminal vesicles, and 39 benign prostatic tissues in tissue microarrays (2 additional blocks), 7 central zone adenocarcinomas in whole sections, and 5 additional core needle biopsies of seminal vesicle, all from Stanford University Medical Center, were also studied. "Central zone" origin was based on a dominant carcinoma that was anatomically based in the central zone as determined by complete prostate submission and mapping diagrams. The zonal origin of the benign prostatic tissue was scored as central zone, peripheral zone, or transition zone; and the presence of atrophy and hyperplasia was also recorded. One unstained section from each block was submitted for immunohistochemical staining with anti–PAX-2 (Z-RX2; Zymed, San Francisco, CA; 1:100) using heat-induced epitope retrieval and standard avidin-biotin techniques. The PAX-2–stained slides were reviewed and semi-quantitatively scored for nuclear staining in normal prostate, prostatic adenocarcinoma, high-grade prostatic intraepithelial neoplasia, seminal vesicle, ejaculatory duct, and periurethral glands as follows: negative, 0%; 1, less than 30%; 2, 30% to 60%; and 3, greater than 60%. Nuclear stain intensity was graded subjectively as follows: 1, weak/faint; 2, intermediate; and 3, strong/intense.

3. Results

Immunohistochemical results are summarized in Table 1. In the radical prostatectomy whole sections, nuclear

Table 1 PAX-2 immunoreactivity

Tissue type	PAX-2
Seminal vesicle	32/32 (100%)
Ejaculatory duct	16/17 (94%)
Prostate adenocarcinoma (total)	0/64 (0%)
Central zone adenocarcinoma	0/7 (0%)
Benign prostate epithelium (total)	2/63 * (3%)
Benign central zone	2/19 (10.5%)
Benign peripheral zone	0/54 (0%)
Atrophy	0/32 (0%)
Benign transition zone	0/9 (0%)
Benign hyperplasia	0/9 (0%)

* Sixty-three represents the total number of cases with benign prostate tissue. Multiple benign patterns were often present within the same case.