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Nephrogenic Adenoma Does Not Express NKX3.1

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Sir: Nephrogenic adenoma of the urinary tract is a benign lesion that is frequently associated with urothelial injury or inflammation. It is reported in virtually all urothelial lined sites, but is most commonly found in the urinary bladder (75-80%) and the urethra (12%), including the prostatic urethra.[1,2] When identified in this latter site, it may be confused with prostatic adenocarcinoma because of its pseudo-infiltrative small gland-like pattern of growth. In some cases, adjunctive immunohistochemical testing may be needed to aid in this differential diagnostic distinction. Previous studies have demonstrated that the prostate cancer-associated marker α-methylacyl-coenzyme A racemase (AMACR) is expressed in 35%-100% of nephrogenic adenomas,[3,4,5] and PSA and PSAP can be focally positive in 36% and 50%, respectively.[2] Additionally, the commonly utilized basal cell markers high-molecular weight

cytokeratin (CK34βE12) and p63 may be negative in nephrogenic adenoma.[4] Although immunohistochemical testing may provide invaluable ancillary assistance, the expression of markers frequently used in the evaluation of prostatic glandular lesions is very heterogenous in nephrogenic adenoma and a subset of cases may have complete immunophenotypic overlap with prostatic adenocarcinoma.

NKX3.1 is a prostate-specific androgen-regulated homeobox gene.[7] Numerous studies have now documented that NKX3.1 immunohistochemistry can serve as a highly sensitive and specific marker for carcinomas of prostate epithelial origin.[8,9,10] In many diagnostic labs, NKX3.1 has become the prostatic secretory epithelial marker of choice because of its crisp nuclear pattern of immunoreactivity and high sensitivity even in high grade tumors. To our knowledge, an immunohistochemical analysis of NKX3.1 has not been previously reported for nephrogenic adenoma.

We retrospectively selected 35 nephrogenic adenoma cases identified from the Pathology Departments of the Cleveland Clinic and the University of Michigan. All cases were reviewed to confirm diagnoses and a single block was evaluated with NKX3.1 immunohistochemistry. We utilized the prediluted rabbit polyclonal NKX3.1 antibody (1:50 dilution, Catalog number CP422B, Biocare Medical, Concord, CA) on the Ventana Benchmark XT system (Ventana Medical System, Tucson, AZ) with appropriate positive and negative controls. The slides were pretreated with pretreatment solution from Ventana at pH 7.5 for 40 minutes. Brown staining for NKX3.1 protein expression was developed using OptiView DAB polymer (Ventana Medical System) with hematoxylin as a counterstain. Strong and diffuse nuclear immunoreactivity was considered as positive reaction for NKX3.1, and prostatic adenocarcinoma and benign prostate glands were utilized as positive internal and external controls. NKX3.1 was non-reactive in all 35 of the nephrogenic adenoma cases tested, regardless of specific histologic pattern (Figure 1 and Figure 2).

In conclusion, in our series of 35 nephrogenic adenomas, NKX3.1 expression was completely absent. This suggests that, unlike other immunohistochemical antibodies used as surrogates of prostatic secretory lineage, NKX3.1 has potential utility as a prostate specific marker in the differential diagnostic distinction between nephrogenic adenoma and prostatic adenocarcinoma.

Figure Legends

Figure 1: A) Tubular pattern of nephrogenic adenoma in a transurethral biopsy specimen. B) NKX3.1 immunohistochemistry demonstrated no nuclear reactivity in the lesional cells.

Figure 2: A) Papillary pattern of a nephrogenic adenoma in the prostatic urethra. B) No NKX3.1 immunoreactivity was present in any of the 35 cases tested.

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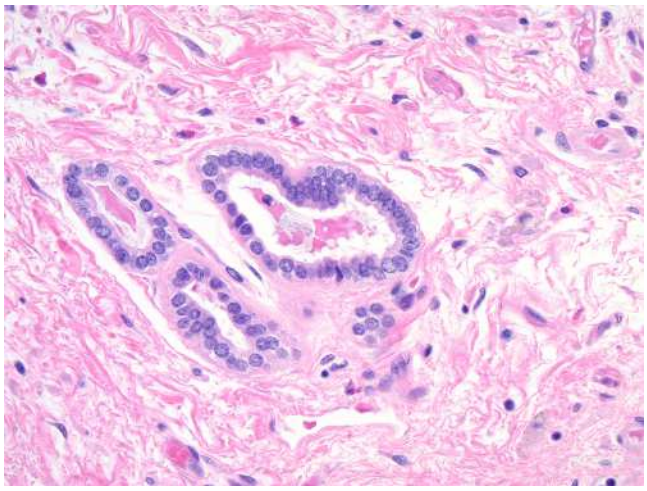

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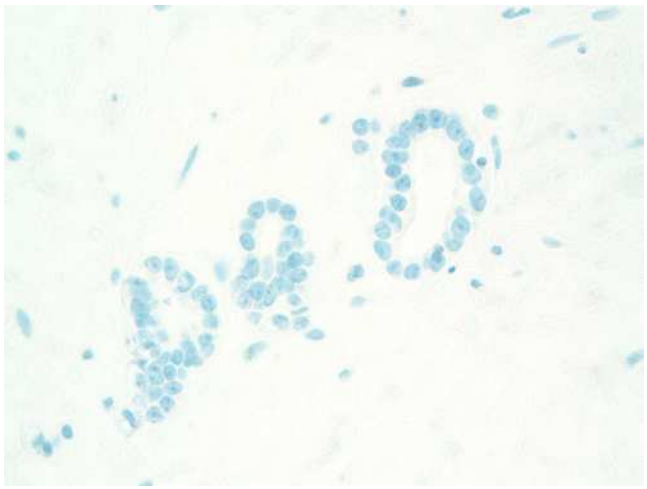

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