exhibits fusion of exon 4 of *ETV6* with exon 14 of *NTRK3* (although fusion of exon 4 of *ETV6* with exon 14 of *NTRK3* has been reported in salivary gland secretory carcinoma).[4,9,13] In the few cases of secretory carcinoma of the thyroid in which the fusion breakpoints have been evaluated, the fusion has involved exon 4 of *ETV6* and exon 14 of *NTRK3*.[2,3] Thus, these findings indicate that even in the presence of an *ETV6–NTRK3* fusion, other morphological features to differentiate PTC from secretory carcinoma must be considered; moreover, the clinical history must be reviewed to ensure that the patient does not have a salivary gland or breast primary.

In summary, we describe a case of primary secretory carcinoma of the thyroid with increased proliferative activity and tumour necrosis. Differentiating secretory carcinoma from PTC is crucial both for prognostication and treatment purposes. Our patient is currently being treated with concurrent chemotherapy (taxol and carboplatin) and external beam radiation; however, therapy with a pan-Trk inhibitor could be considered in the future depending on the clinical course of disease.

Ethics statement

The study has been performed according to the Declaration of Helsinki. The procedures have been IRB-approved (protocol no. 2016P001885). Informed consent was not required for our study.

Conflict of interest

The authors have no conflicts of interest.

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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 associated frequently with

urothelial injury or inflammation. It is reported in virtually all urothelial lined sites, but is found most commonly 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,[3–6] and prostate-specific antigen (PSA) and prostatic-specific acid phosphatase (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 used frequently in the evaluation of prostatic glandular lesions is extremely heterogeneous in nephrogenic adenoma, and a subset of cases may have complete immunohistochemical overlap with prostatic adenocarcinoma.

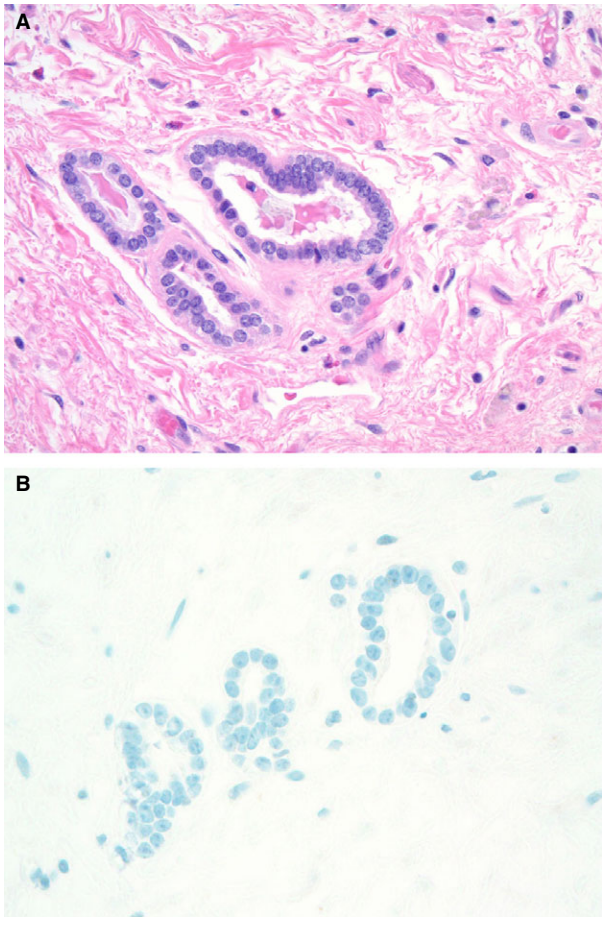

Figure 1. **A**, Tubular pattern of nephrogenic adenoma in a transurethral biopsy specimen. **B**, NKX3.1 immunohistochemistry demonstrated no nuclear reactivity in the lesional cells.

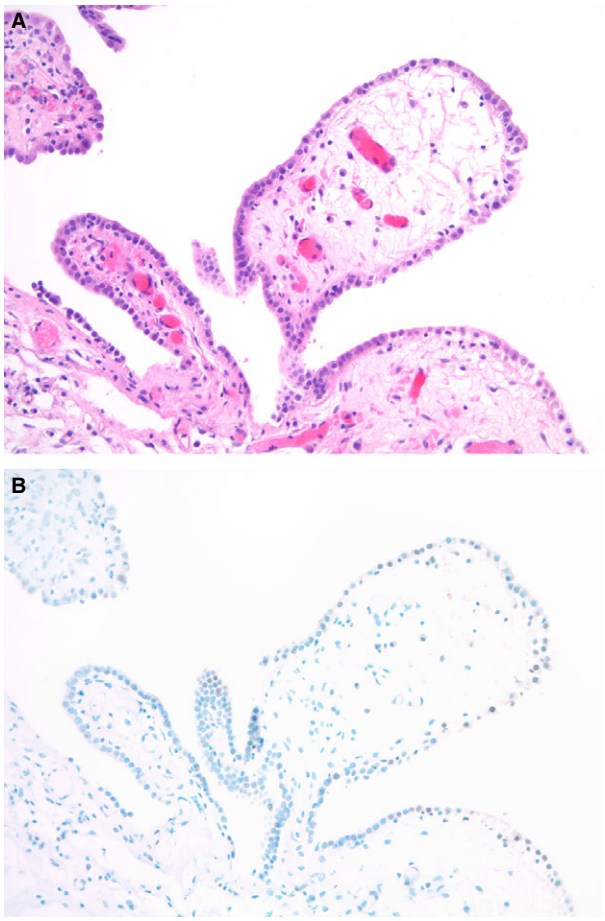

Figure 2. **A**, Papillary pattern of a nephrogenic adenoma in the prostatic urethra. **B**, No NKX3.1 immunoreactivity was present in any of the 35 cases tested.

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.[8–10] In many diagnostic laboratories, 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 tumours. To our knowledge, an immunohistochemical analysis of NKX3.1 has not been reported previously for nephrogenic adenoma.

We selected 35 nephrogenic adenoma cases retrospectively, 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, catalogue number CP422B; Biocare Medical, Concord, CA, USA) on the Ventana Benchmark XT system (Ventana Medical Systems, Tucson, AZ, USA) with appropriate positive and negative controls. The slides were pretreated with pretreatment solution from Ventana at pH 7.5 for 40 min. Brown staining for NKX3.1 protein expression was developed using OptiView DAB polymer (Ventana Medical Systems), with haematoxylin as a counterstain. Strong and diffuse nuclear immunoreactivity was considered as a 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 histological pattern (Figures 1 and 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.

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