

A PAX-8-positive Female Urethra Adenocarcinoma: A Case Report with Diagnostic Challenges in Intestinal-Type Adenocarcinoma

Background

- Female urethral carcinoma is rare, representing 0.02% of all women's cancers and <1% of cancers in the female genitourinary tract.
- The most common histologic type is squamous cell carcinoma (70% of all cases), followed by transitional cell carcinoma (20%) and adenocarcinoma (10%).
- The two primary histologic subtypes of adenocarcinoma of the urethra are clear cell and columnar/mucinous ("intestinal"); the latter being extremely rare.
- Female urethral adenocarcinoma (FUA) exhibiting colonic adenocarcinoma features has only been described once previously, to our knowledge.
- Furthermore, PAX-8 immunopositivity in this entity has not been reported.
- Herein, we report an intestinal-type FUA that developed from inflammation-related metaplasia in urethral diverticulum with positive PAX-8 staining.

Case History

- 64-year-old female with a 32-pack-year history of tobacco use was found to have multiple pulmonary nodules on computed tomography (CT) scan (Fig 1A).

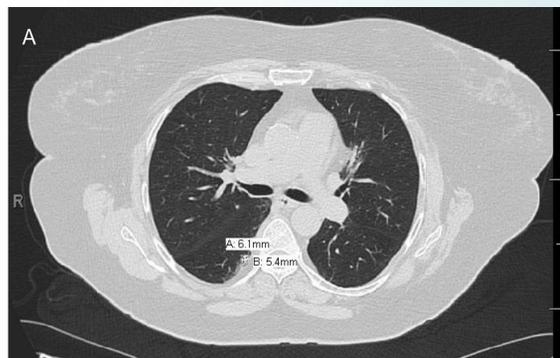


Fig 1A. CT shows multiple small, bilateral pulmonary nodules, the largest measuring 6 mm.

Findings

- Needle core biopsy of pulmonary nodules demonstrated moderately differentiated adenocarcinoma (Fig 2A); the tumor cells were positive for CK7, CK20 (Fig 1B), SAT-B2, and PAX-8 (Fig 1C) and negative for TTF-1/Napsin (Fig 1D) and ER; GATA-3 staining appeared cytoplasmic.
- Diagnostic considerations included gastrointestinal as a primary site, and the positive PAX-8 immunopositivity raised the possibility of a gynecologic/Mullerian primary.
- Subsequent colonoscopy and imaging showed no evidence of colorectal or gynecologic tumors.
- The patient began having hematuria with intermittent urinary retention, and cystoscopy showed a 4 x 3 cm mass involving the bladder neck circumferentially and invading into the vaginal wall.
- Urethral and vaginal tumor biopsies were performed. Morphologic examination of the urethral biopsy demonstrated intestinal metaplasia of squamous mucosa with transition from a mature to dysplastic phenotype (Fig 3A) where the adenocarcinoma originated from. The vaginal wall biopsy showed the same morphology.
- The urethral and vaginal wall biopsies showed a similar immunophenotype as the pulmonary nodule biopsy: positive for CK7, CK20, CDX2 (Fig 3B), b-catenin (membrane stain), CEA, patchy expression of SATB2 (Fig 3C) and PAX-8 (Fig 3D), and negative for TTF-1, p16, ER, Vimentin and GATA-3.

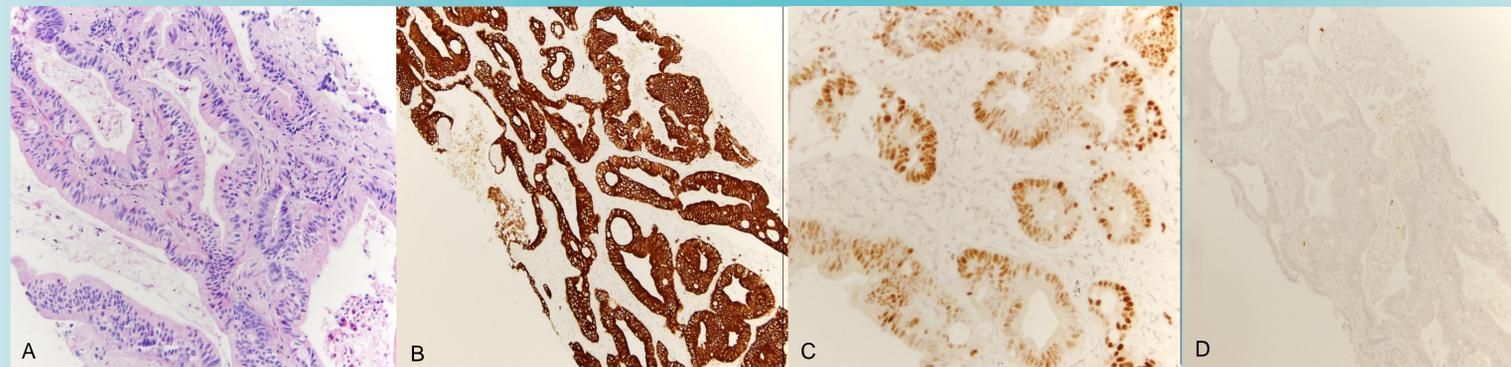


Fig 2. A. Histology showed adenocarcinoma with enteric differentiation. B. CK20 was strongly and diffusely positive. C. PAX-8 was diffusely positive with areas of both weak and strong staining. D. TTF-1/Napsin was negative, ruling out a pulmonary primary.

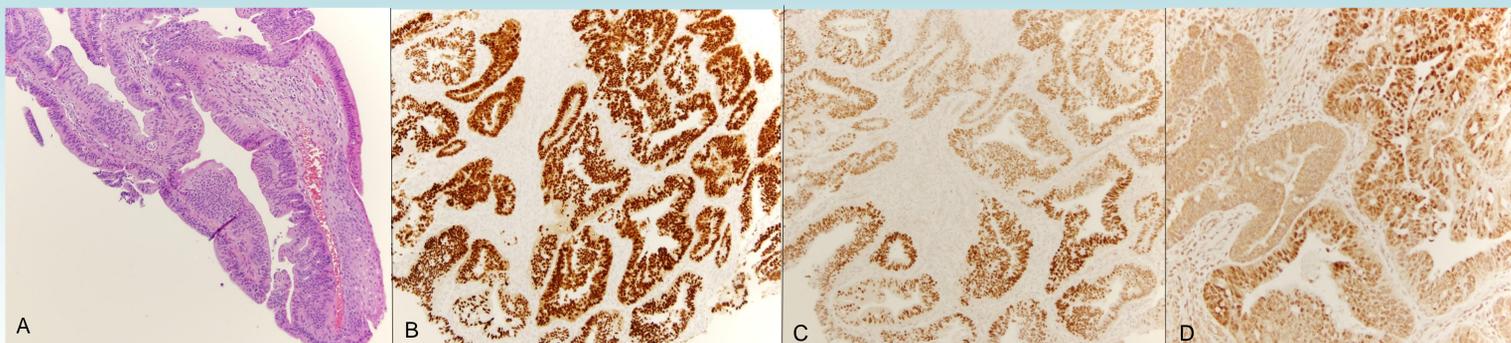


Fig 3. A. Histology showed squamous mucosa with intestinal metaplasia where adenocarcinoma originated. B-C. CDX2 and SATB2, supportive of an intestinal-type adenocarcinoma. D. PAX-8 remained positive on both urethral and vaginal biopsies.

Discussion

- In this case, we describe a rare case of intestinal-type primary urethral adenocarcinoma that developed from inflammation-related metaplasia in urethral diverticulum with PAX-8 expression.
- Because of the immunophenotype, it was prudent that other sites, including colorectal and gynecologic/Mullerian tumors, were excluded.
- The patient presented with advanced disease, with metastasis to the lungs, exemplifying the aggressive nature of this particular entity.
- The patient was started on chemotherapy and eventually underwent palliative radiation for bone metastasis.
- FUA is a rare, aggressive tumor, and the origin remains unclear. Many authors have suggested that FUA originates in Skene's glands; however FUA may arise from other paraurethral structures.
- The vague symptomatology often leads to a delay in diagnosis in most patients, and the prognosis is poor in advanced stage disease.
- Furthermore, because of the disease rarity, there are no strict guidelines regarding treatment modality.

References

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