

Adenocarcinoma of the female urethra: Clear-cell variant

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Primary urethral carcinoma is a rare malignancy with an annual age-adjusted incidence rate of 1.5 per million in females in the U.S. The three main histologic subtypes include transitional-cell carcinoma, squamous-cell carcinoma, and adenocarcinoma. Of these, adenocarcinoma is the least common. Female urethral carcinomas are aggressive neoplasms with a generally poor prognosis. We report a case of the clear-cell variant of adenocarcinoma.

Case report

A 59-year-old Caucasian female with a past medical history of hypertension, type II diabetes, and uterine carcinoma, status posthysterectomy, presented to the urologist with hematuria for over one year. She denied any weight loss or constitutional symptoms. A prior evaluation at an outside institution, including several cystoscopies and a CT scan, reportedly failed to reveal any abnormality.

On physical exam, she had a palpable, firm, 3-4-cm mass on the right aspect of the urethra. Bloody drainage was expressed from the urethral meatus on palpation. Cystoscopy revealed extrinsic compression of the urethra.

Gadolinium-enhanced pelvic MRI revealed a 3.4 x 3.3 x 3.9-cm infiltrative mass in the region of the urethra. The mass was T2 hyperintense (Fig. 1), T1 hypointense (Fig. 2), and demonstrated slightly heterogeneous enhancement (Figs. 3 and 4). An incomplete fat plane was identified between the mass and the urinary bladder, with possible vesicular invasion identified on the sagittal images (Fig. 3). No lymphadenopathy was detected.

The patient underwent radical cystectomy and bilateral pelvic lymphadenectomy. Surgical pathology revealed a

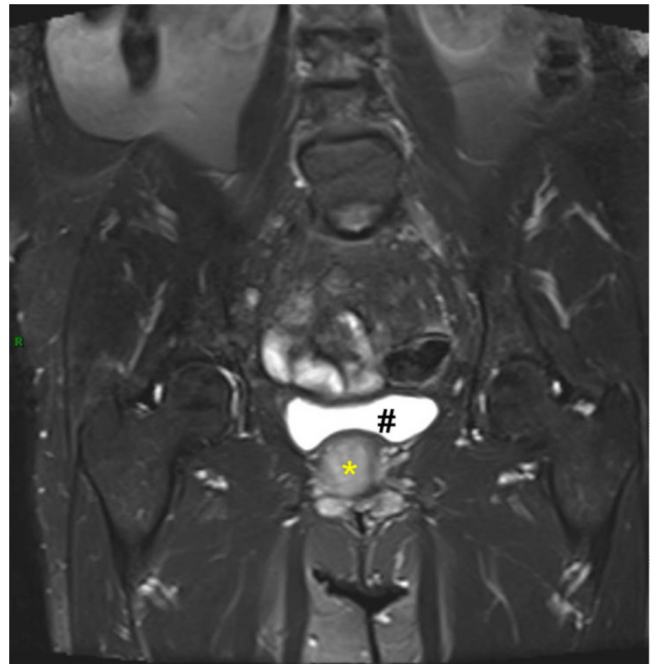


Figure 1. 59-year-old female with adenocarcinoma, clear-cell variant. T2 fat-saturated MR image in the coronal plane demonstrates a mass (*) inferior to the urinary bladder (#).

3.6-cm, poorly differentiated, urethral adenocarcinoma, clear-cell variant (Figs. 5 and 6).

It was the urologist's opinion that the tumor had originated within a urethral diverticulum, due to its location and the fact that the mass appeared to be encapsulated and without any vesicular or urethral invasion. "A diverticulum

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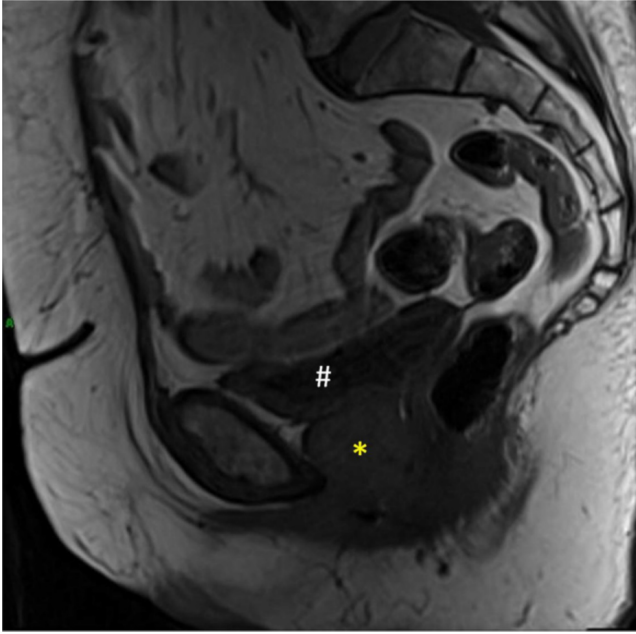


Figure 2. 59-year-old female with adenocarcinoma, clear-cell variant. T1-weighted MR image in the sagittal plane demonstrates a low-signal 3.9-cm mass (*) inferior to the urinary bladder (#).

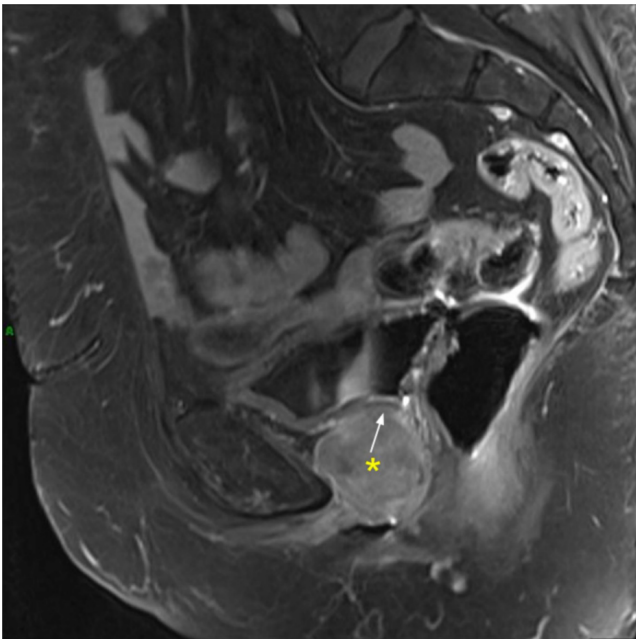


Figure 3. 59-year-old female with adenocarcinoma, clear-cell variant. T1 fat-saturated postcontrast MR image in the sagittal plane demonstrates heterogeneous enhancement of the periurethral mass (*) with possible vesicular invasion (arrow).

replaced with neoplasm” was the urologist’s characterization. This suspicion was not borne out following pathological analysis, which showed invasion through the periurethral muscle and direct extension into the bladder neck.

One left and six right pelvic lymph nodes were submitted, all of which were found to be benign.

Discussion

The female urethra is an approximately 4cm-long tubular conduit lined by transitional epithelium in its proximal third and stratified squamous epithelium in its distal two-

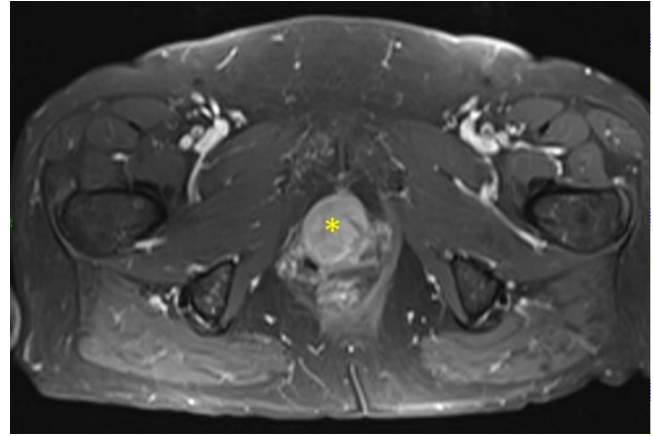


Figure 4. 59-year-old female with adenocarcinoma, clear-cell variant. Axial, T1 fat-saturated postcontrast MR image demonstrates heterogeneous enhancement of the infiltrative periurethral mass (*).

thirds. Urethral carcinomas are rare neoplasms, representing less than 0.02% of all malignancies in women and with an annual age-adjusted incidence rate of 1.5 per million females in the U.S. (1, 2). These neoplasms may present as exophytic, papillary, fungating masses or infiltrating tumors (3). Risk factors include infection with the human papilloma virus and urethral diverticula (1). These malignancies typically affect postmenopausal patients, whose symptoms may include a mass, dyspareunia, dysuria, hematuria, or partial obstruction (4).

Imaging can be extremely helpful in the workup of women presenting with urethral symptoms, as the clinical assessment is often difficult. High-resolution multiplanar magnetic resonance (MR) imaging with phased-array pelvic and endovaginal coils demonstrates the urethral anatomy in detail and provides an accurate road map for surgeons (3). However, imaging features cannot distinguish between histologic subtypes, and histopathologic analysis is required for definitive diagnosis.

Tumor histology depends on the site of origin within the urethra. Transitional-cell carcinoma occurs more commonly in the proximal one-third. Squamous-cell carcinoma and adenocarcinoma are more common in the distal two-thirds. Squamous-cell carcinoma is the most common sub-

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type overall; however, adenocarcinoma is the most common type to arise from diverticula (1).

Adenocarcinomas account for approximately 10% of female urethral carcinomas, and clear-cell variant represents approximately 40% of these cases. Amin et al report that approximately 56 cases of this rare malignancy have been reported in women, and three cases have been reported in men (1). Histologically, clear-cell carcinoma displays tubulocystic, tubular, papillary, or diffuse patterns, frequently in combination. The cytoplasm is usually moderate to abundant and varies from clear to eosinophilic (1).

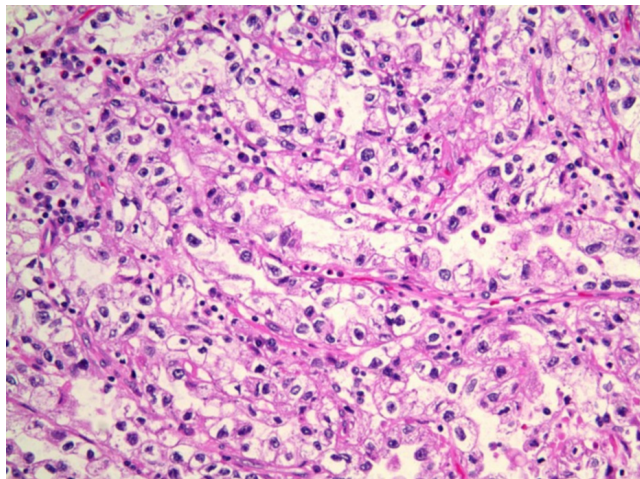


Figure 5. 59-year-old female with adenocarcinoma, clear-cell variant. H&E stained photomicrograph at 40x magnification demonstrates clear-cell adenocarcinoma in a tubular pattern. Note the clear cytoplasm.

At imaging, adenocarcinoma typically appears as an exophytic, heterogeneously enhancing tumor. On T2 MRI, these tumors show high T2 signal with a low-intensity peripheral rim and variable contrast enhancement, findings that were demonstrated on this case (4).

Unfortunately, carcinoma of the female urethra carries a poor prognosis. Up to 50% of women present with metastatic disease (1). Prognostic factors include tumor location (proximal, distal, or entire), depth of invasion of the urethral wall, and size of the tumor. In DiMarco's series of patients at the Mayo Clinic, pathologic stage and positive lymph nodes were predictors of recurrence and cancer-specific survival (5).

Surgical resection is the treatment of choice. Urologists classify female urethral tumors as either "anterior" or "posterior or entire," as this system has significant prognostic value. Anterior tumors are limited to the meatus or distal one-third, and posterior or entire tumors involve the proximal two-thirds or the entire urethra (1, 4). The neoplasm that we present affected the patient's entire urethra. Overall survival rates are approximately 50% for anterior tumors and 6% for entire tumors (1). Due to the rarity of these neoplasms, more data on radiotherapy is needed (6).

Indications are that disease specific survival may be improved with a multimodality approach that uses surgery and adjuvant concurrent chemoradiotherapy (4, 6).

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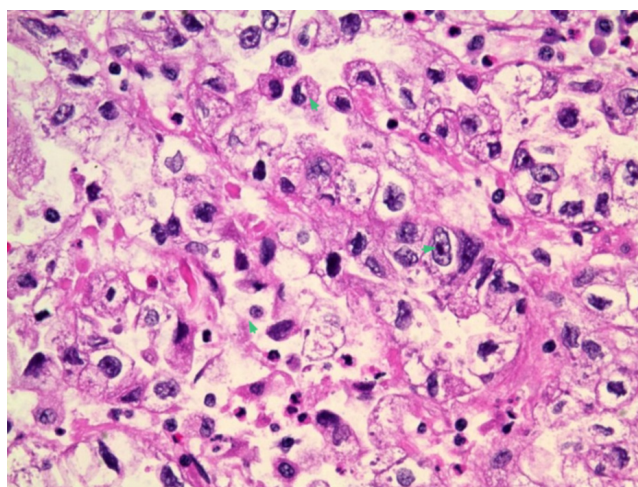


Figure 6. 59-year-old female with adenocarcinoma, clear-cell variant. At 60x magnification, hobnail cells with nuclear hyperchromasia, pleomorphism, and nucleoli are visible (green arrowheads).

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