Published in final edited form as:

Clin Imaging. 2020 November ; 67: 68–71. doi:10.1016/j.clinimag.2020.05.030.

Isolated urethral metastasis from appendiceal mucinous adenocarcinoma.

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Abstract

We are presenting a compelling case of a 61-year-old female with a history of appendiceal mucinous adenocarcinoma (AMA) with a new complaint of irritative lower urinary tract symptoms. Magnetic resonance imaging (MRI) showed a semi-circumferential, T2 hyperintense, rim enhancing, and lacking restricted diffusion lesion involving the urethra and infiltrating the right perineal and internal obturator muscles. The suspected differential diagnosis was urethral malignancy, based on her cancer history and MRI findings. After interdisciplinary consensus, the patient underwent excision of the lesion, and pathology was consistent with metastasis from the primary tumor. The urethra is a rare site of primary malignancy and metastatic disease. In particular, a non-contiguous metastatic disease involving the urethra is exceedingly rare. To the best of our knowledge, this is the first report of an AMA metastasizing to the urethra.

Keywords

Urethral neoplasms; adenocarcinoma, mucinous; appendiceal neoplasms; magnetic resonance imaging

1. INTRODUCTION

Urethral malignancies, either primary or metastatic, are rare, representing fewer than 1% of all urinary tract malignancies [1]. Women are more commonly affected than men [2], though

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CONFLICT OF INTERESTS: none.

the rarity of urethral malignancies makes exact estimations difficult and men are more commonly affected in some populations [3].

Among primary urethral malignancies in women, the most common histologic subtypes are squamous cell carcinoma (SCC, 70%), transitional cell carcinoma (TCC, 20%), and adenocarcinoma (AC, 10%) [4]. Regarding locations, SCC usually involves the distal urethra and external urethral meatus, whereas TCC and AC tend to compromise the anterior urethra [5]. Secondary involvement by contiguous extension in women can be found in the external meatus mostly from a vulvar SCC [1].

The literature on urethral metastasis is limited to case reports and a few small case series, with most publications focusing on histopathologic and clinical presentations rather than MRI findings. The scant reports of urethral metastasis have described spread from primary cancers such as colonic adenocarcinoma [6–8], prostate adenocarcinoma [9], melanoma [10], high grade ovarian serous cell carcinoma [11], renal clear cell carcinoma [12], and primary lung adenocarcinoma [13], among others [14]. In women, the most common locations of urethral metastasis involved either the external meatus or the whole urethra [1, 5, 6, 8, 10, 15, 16]. Possible mechanisms of metastasis are hematogenous or retrograde lymphatic spread, or possibly instrumentation [15].

We describe, to the best of our knowledge, the first published report of appendiceal mucinous adenocarcinoma metastasizing to the urethra. The following discussion focuses on the MRI features of urethral metastasis to enrich the radiologists' understanding of the imaging appearance as well as clinical and pathological characteristics.

2. CASE REPORT

A 61-year-old female presented with complaints of worsening urinary frequency and urgency, nocturia, and dysuria over the last four months. The physical exam, including palpation, showed a vaginal lesion that was indurated, right-sided, and inseparable from the urethra.

Further evaluation with magnetic resonance imaging (MRI) showed a semi-circumferential lesion involving the urethra and measuring $3.2 \times 2.7 \times 3.4$ cm. On T2-weighted images, the lesion was homogeneously hyperintense. On diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC) mapping, the lesion exhibited a lack of restricted diffusion. On post-contrast images, the lesion demonstrated peripheral rim enhancement and the involvement of adjacent structures. The lesion abutted the vagina superior to the introitus and infiltrated the right perineal and internal obturator muscles (Figure 1). The suspected diagnosis was urethral malignancy based on the imaging features.

The patient also had a history of appendiceal mucinous adenocarcinoma (AMA) diagnosed four years prior. Initially, the diagnosis was moderately differentiated AMA after the patient underwent emergent laparoscopy due to small bowel obstruction secondary to pseudomyxoma peritonei. The patient then had multiple recurrences which were treated with either surgery or FOLFIRI (folinic acid, fluorouracil, and irinotecan) and bevacizumab. The

most recent pathological diagnosis after surgery for recurrent peritoneal disease was poorly differentiated AMA with signet ring cells.

After interdisciplinary discussion, the consensus was to perform a wide lesion excision to alleviate symptoms and confirm the etiology of suspected metastasis.

The physical examination under anesthesia showed the location of the tumor above and between the pubic bone and the urethra, involving the right side and ventral surface of the urethra, and with a distal margin of approximately 0.5 cm to the urethral meatus. The mass was then dissected free from the urethra distal to the urinary sphincter.

On macroscopic examination, the mass consisted of a fibrous nodule measuring 3.5×3.0 cm. The microscopic examination with hematoxylin and eosin revealed mucinous adenocarcinoma with abundant extracellular mucin involving the urethra wall with positive resection margins (Figure 2). The morphology was similar to prior specimens, and the diagnosis was consistent with metastasis from the primary tumor.

The patient received palliative chemotherapy with FOLFIRI and bevacizumab. Four months later, she was diagnosed with the oligometastatic disease in the lungs and treated with local ablation. She is currently continuing palliative chemotherapy.

3. DISCUSSION

To the best of our knowledge, this is the first published report of AMA metastasizing to the urethra. The disease progression in our patient was from moderately-differentiated AMA to poorly-differentiated AMA with signet ring cells. The latter was initially confined to the peritoneal cavity but subsequently there was metastatic/extraperitoneal spread to the urethra and lungs. AMA is a primary appendiceal neoplasm characterized by the presence of at least 50% of the cross-sectional area with extracellular mucin and infiltrative invasion of the appendix. Histologically, it is further classified into well-differentiated, moderately differentiated, or poorly-differentiated AMA, and if it contains signet ring cells, it is determined to be poorly-differentiated adenocarcinoma with signet ring cells [17]. AMA commonly presents with pseudomyxoma peritonei, secondary to peritoneal spread of tumoral cells and mucin [18]. AMA tends to remain within the peritoneal cavity and seldom metastasizes outside the peritoneal cavity [18]. Metastasis from AMA has been described only a few times in the literature, with case reports reporting spread to the bladder [19], lungs [18], and bones [20].

While a urethral diverticulum is far more common condition that could explain the patient's irritative lower urinary tract symptoms, we suspected malignancy based on the imaging features. Regardless of the etiology, most urethral lesions present with non-specific symptoms [5] such as pelvic pain, urinary frequency, urinary urgency, nocturia, dysuria, and bleeding, and they also predispose the patient to suffer from repeated urinary tract infections [5]. This case report illustrates the importance of pelvic physical examination for women with new-onset irritative or obstructive lower urinary tract symptoms as well as the benefit of MRI in evaluating the various possible etiologies and the extent of potential disease involvement.

Among radiological evaluations, MRI is the method of choice for narrowing the differential diagnosis to a benign or malignant urethral lesion, ultimately aiding treatment planning [14]. To narrow the differential diagnosis in the case of suspected urethral malignancy, it must first be ascertained whether the typical appearance of urethral rings, known as targetoid appearance, is disrupted by any morphologic or signal intensity abnormality. The urethral rings correspond to the T2 hypointense muscular layer, T2 hyperintense submucosa, and T2 hypointense mucosa. Differentiation between primary and secondary malignancies, as well as primary malignancies, is not always possible with MRI due to overlapping morphologic as well as signal intensity characteristics [5, 14]. Therefore, when evaluating a urethral lesion in a patient with known malignancy, it is essential to review the baseline study, if available, to identify the particular features of the disease before attempting to characterize the lesion. Morphologically, urethral malignancies may appear as polyps, nodules, or masses that are usually obstructing or infiltrative [6–13, 15, 16, 21, 22]. Although the signal intensity on MRI is variable and non-specific in regards to histopathologic subtype, there are some signal intensity characteristics which would favor certain subtypes. SCC and TCC tend to have an intermediate to hypointense signal on T2-weighted images as well as heterogeneous enhancement; on the other hand, AC tends to have a hyperintense signal on T2-weighted images, which is even brighter if a mucinous component is present, as well as variable enhancement [23]. Similarly to the above mentioned, the patient we are reporting had a disruption of the normal urethral rings by a had a semi-circumferential mass involving the urethra, which explains the lower urinary tract symptoms she had referred. In contrast to the benign lesions, in our case, there was an infiltration of the adjacent muscles. Since the primary tumor of this patient was mucinous subtype, the signal intensity was high on T2 homogenously, with a lack of restricted diffusion, due to the T2 shine-through effect on DWI with ADC mapping due to the high fluid mucinous content of the lesion, and rim enhancement.

Regarding treatment planning, MRI provides the ability to localize the lesion as well as to determine the size and extent of disease involvement non-invasively due to its superior soft tissue characterization. It would be more difficult to achieve this level of characterization with other modalities such as computed tomography or ultrasound; moreover, characterization with ultrasound is also dependent on operator expertise. Similarly, characterization would be difficult with conventional radiographic material-enhanced studies, namely retrograde urethrography, voiding cystourethrography, or double-balloon catheter urethrography, which, moreover, are invasive in nature [2, 5, 14]. On MRI, tumoral extension beyond the urethra is best appreciated on T2-weighted images with a high resolution and a small field of view as well as on fat-saturated pre- and post-contrast images. It is helpful to assess the presence of fat tissue plane disruption with possible associated abutment or invasion of adjacent structures such as the vagina, rectum, prostate, bladder, or perineal muscles [14].

The patient presented with a high signal on T2-weighted image and T2 shine-through effect lesion replacing the whole urethra due to the presence mostly of extracellular mucin involving beyond the urethral wall which was best delineated on the post-contrast images. More frequent entities such as urethral diverticulum, skene duct abscess, and urethral

caruncle were not included as differential diagnoses because they do not invade the adjacent structures [1, 5].

We suggest that in complex scenarios such as the one in this case report, the best approach to patient management is interdisciplinary consensus. Cystourethroscopy with biopsy or excision of the lesion is necessary both for pathologic diagnosis and to relieve symptoms. Finally, depending on each patient's metastatic disease burden, in some patients, the mentioned procedures will be enough with a palliative aim, whereas others would potentially benefit from additional palliative systemic therapy [1, 16, 18].

In summary, although rare, radiologists should consider the likelihood of metastatic involvement of the urethra in patients who have a history of malignancy and a new urethral lesion with disruption of the normal signal intensity of urethral rings with possible extension to periurethral tissues and adjacent structures. The signal intensity on MRI will be variable depending on primary tumor histopathology; therefore, it is essential to review baseline studies when available. Radiologists should be familiar with these considerations with the ultimate goal of helping our referring colleagues to decide the best management approach to our patients.

ACKNOWLEDGEMENT:

We thank Joanne Chin for her editorial support of this manuscript.

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- Metastatic involvement of the urethra should be considered in patients who have a history of malignancy and a new urethral lesion with disruption of the normal signal intensity of urethral rings with possible extension to periurethral tissues and adjacent structures.
- Extension to periurethral tissues and adjacent structures is the essential imaging finding to distinguish between benign and malignant diseases compromising the urethra.
- The signal intensity on MRI will be variable depending on primary tumor histopathology; therefore, it is essential to review baseline studies when available.

Figure 1.

MRI of the pelvis with gadolinium-based contrast for characterization and staging of the urethral lesion (long arrows). T2-weighted image on sagittal (A) shows a homogenous high signal involving the whole urethra. T2-weighted image on axial (B) evidences the abutment of the vagina superior to the introitus. DWI (C) with ADC mapping (D) reveals that the lesion does not show restricted diffusion; on the contrary, the lesion shows a T2 shine-through effect. Post-contrast axial images evidences rim enhancement of the lesion (E) and delineates the infiltration of surrounding tissues (F – short arrow).

Figure 2.

Microscopy images with hematoxylin and eosin. 2× magnification (A) delineates mucinous adenocarcinoma (star) involving the muscularis layers of the urethra and periurethral tissue, represented by the overlying benign squamous mucosa (arrow head) and subepithelium (short arrow). 20× magnification (B) evidences that the tumoral cells form nests and trabecula or are floating in pools of mucin (star) involving the muscles bundles of the muscularis layers of the urethra (long arrow).