CASE REPORT

Management of adenocarcinoma of the female urethra: case report and brief review

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Introduction: *We present a case of a differentiated adenocarcinoma of the female urethra, which caused dysuria and voiding dysfunction.*
Materials and methods: *A 54-year-old female presented with dysuria and the sensation of incomplete voiding.*
Results: *An ultrasound-guided biopsy showed a urethral carcinoma. A magnetic resonance imaging (MRI) scan showed a high-stage tumor. The patient had a pelvic exenteration. The patient was free of disease after 2 years of follow up.*
Conclusion: *Urethral carcinoma is a rare malignancy. A biopsy is necessary to make a diagnosis. MRI is the best imaging for tumor staging. Small tumors are treated with a single modality option including sparing surgery or radiotherapy. Advanced disease should be treated with a multimodality of options including neoadjuvant radiotherapy given concomitantly with chemotherapy followed by surgery.*

Key Words: urethral cancer, carcinoma, radiotherapy, chemotherapy, surgery

Introduction

Carcinoma of the urethra is an uncommon neoplasm, which accounts for 0.02% of all cancers found in women.[1-6] In turn, adenocarcinoma accounts for 10% of these rare carcinomas.[7] There have been only a few published reports of retrospective cases. We describe a case of a urethral adenocarcinoma and discuss it in light of recent data in the literature about management of this disease.

Case report

A 57-year-old woman with dysuria and voiding difficulties was referred to our clinic. A physical examination revealed a pelvic mass at the anterior vaginal wall. The patient had a good general state of health. Laboratory test results showed: hemoglobin, 12 g/dL; white blood count, 6600/mm^3; normal urinalysis, and serum creatinine, 52 µmol/L. Cystography confirmed the voiding dysfunction. A stenosis of the urethral lumen was present at cystoscopy. A fat-saturated coronal MRI revealed a double-compartment (cystic and solid) mass surrounding the urethra from the bladder neck to the distal urethra, Figure 1. The mass was 5 cm long x 3 cm wide with invasion of the bladder neck but no pelvic nodes.

An ultrasound-guided biopsy showed a differentiated adenocarcinoma. Immuno-histochemical staining was positive for cytokeratin (CK) 7, but negative for CK20 and P63. The patient's serum prostate specific antigen (PSA) test result was normal. The patient's cancer was classified as T3N0M0, based on the classification system in the *AJCC Cancer Staging Manual* from the American Joint Committee on Cancer (AJCC), Table 1.

A pelvic exenteration was performed with an en bloc removal of the anterior vaginal wall, urethra, bladder, and uterus with a trans-ileal ureterostomy (Bricker-type uretero-ileostomy) with negative margins. An iliac and obturator lymphadenectomy also had negative margins. At a 2-year follow up examination, the patient was free of disease.

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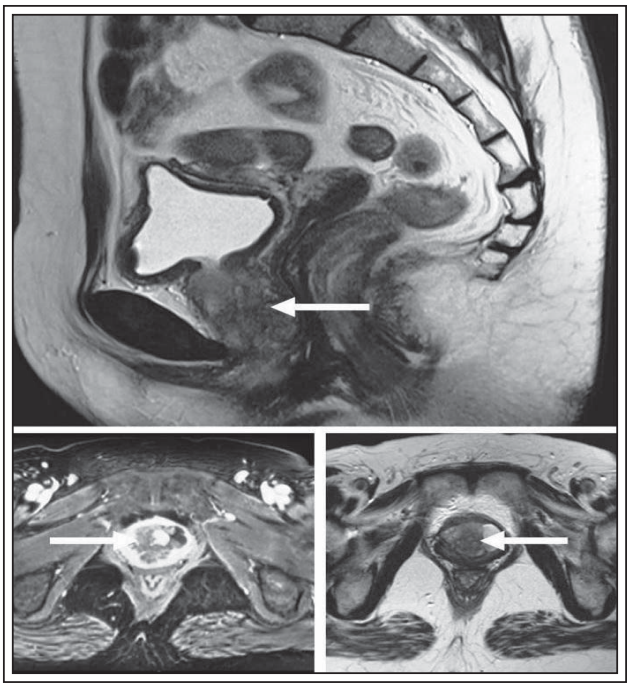

Figure 1. MRI showing the tumor (arrow).

Discussion

Although the urethra is shorter in women than in men, primary urethral carcinoma is four times more common in women than in men. Urethral carcinoma is the only urologic neoplasm that is more common in women than in men.[8] It has been reported that about 85% of urethral tumors occur in white women.[9] However, Swartz et al studied the incidence of the primary urethral carcinomas in men and women in 9 geographic areas that represent 10% of the US using the national Cancer Surveillance, Epidemiology and End Results (SEER) database registries. They found that African Americans were at higher risk of urethral cancer compared with Caucasians.[10]

As was the case with our patient, up to 98% of patients are symptomatic at presentation. Most patients present with obstructive symptoms, dysuria, urethral bleeding, and urinary frequency, and they often have a urethral palpable mass or induration.[2] Up to 50% of patients with proximal or advanced cancers may have palpable nodes.[9] Metastases to the lung, liver, and brain can occur.[11] A physical examination performed under general anesthesia can be useful. For a local tumor extension, a MRI scan is better than a CT scan to evaluate tumor size, location, and the local extension. The accuracy of MRI in the evaluation of local tumor extension has been reported to be up to 90% of cases.[12] An image- guided biopsy or a direct biopsy is necessary to determine the tumor's histological subtype.

TABLE 1. **Classification (TNM) of urethral carcinoma[9]**

Primary tumor (T) (male and female)	
TX:	Primary tumor cannot be assessed
T0:	No evidence of primary tumor
Ta:	Non invasive papillary, polypoid, or verrucous carcinoma
Tis:	Carcinoma in situ
T1:	Tumor invades subepithelial connective tissue
T2:	Tumor invades any of the following: corpus spongiosum, prostate, periurethral muscle
T3:	Tumor invades any of the following: corpus cavernosum, beyond prostatic capsule, anterior vagina, bladder neck
T4:	Tumor invades other adjacent organs
Regional lymph nodes (N)	
NX:	Regional lymph nodes cannot be assessed
N0:	No regional lymph node metastasis
N1:	Metastasis in a single lymph node 2 cm or less in greatest dimension
N2:	Metastasis in a single node more than 2 cm in greatest dimension, or in multiple nodes
Distant metastasis (M)	
MX:	Distant metastasis cannot be assessed
M0:	No distant metastasis
M1:	Distant metastasis

Squamous cell carcinoma is the most common histological type of cancer (70%) followed by transitional cell carcinoma (20%) and adenocarcinoma (8%-10%). Other histological types such as sarcoma, melanoma, and lymphoma are rare (less than 1%).

Tumors originating from a urethral diverticulum are most commonly adenocarcinomas.[13] Moreover, the two compartments (solid and cystic) of the tumor in the current patient case suggest that it might have originated from the urethral diverticula. Some investigators suggest that the origin of these carcinomas may be Skene's gland or Mullerian tissue. Prostatic cancer-like histology with positive immunohistochemical PSA and PAP staining, as well as elevated serum PSA can be encountered.[14,15]

The outcomes of patients with urethral cancers have not improved over the past few decades, especially for patients with advanced disease. Reported 5 year overall survival ranged from 30%-50%.[1-6] The most important prognostic factor for survival among patients with urethral cancer is the stage of the disease at diagnosis. Disease-free survival for patients with tumors < 2 cm is 70%-80% versus disease-free survival of 10% to 20% for patients with tumors > 2cm.[1-6]

Location site, lymph node status, and histological subtype do not predict overall survival.[2,4] Some studies[2] suggest that squamous cell carcinoma tends to have a lower recurrence rate compared to adenocarcinoma and transitional cell carcinoma, but case series are too small to yield any statistical significance.

For local and distal disease, surgery consists of local wide excision. A sling procedure can be performed in cases of urinary incontinence. Most authors have reported minimal complications from urethral surgery and rare incontinence. However, Di Marco et al noted de novo or worsening stress urinary incontinence in 42% of patients.[2] Advanced disease is treated with a wide pelvic exenteration with a urinary diversion for advanced tumors.[1-6] However, Hedden et al[16] reported that five female patients with locally advanced urethral cancers with no bladder invasion who were treated with a wide local excision without cystectomy had good local control of cancer (at a median follow up of 42 months). The authors suggested that bladder sparing surgery may be considered for selected locally advanced tumors.

Because of the high morbidity associated with inguinal dissections and lack of improved survival, some authors do not recommend standard ileo-obturator lymphaednectomy.[15] External beam radiotherapy (EBRT) can be neoadjuvant or adjuvant therapy to surgery.[1-6] There is no difference in overall survival rates after surgery versus radiotherapy. Neoadjuvant radiotherapy does not improve overall survival rates, but it improves local cancer-free survival.[1]

Milosevic et al,[3] reported brachytherapy, either alone or with EBRT, resulted in better local control of large tumors compared to EBRT alone. They reported a 7 year local relapse rate of 32% following brachytherapy (with or without ERBT) versus 77% following ERBT alone ($p = 0.005$). However, there were no statistically significant between-treatment differences for cause-specific survival or overall survival. Related complications are urinary incontinence, urethral strictures, fistulas formation, vulvar abscess and celullitis.[9] Gheiler et al[4] reported that a 70% disease-free survival rate was obtained in patients with urethral cancer who were treated with multimodal therapy and who were followed for 43 months. Similarly, a study by Narayan and Konety[8] also reported that survival was higher with multimodal therapy as opposed to surgery alone. They reported a 55% survival rate in patients with advanced urethral carcinoma who were treated with radiotherapy and surgery versus a 34% survival rate in patients who were treated with surgery alone. This suggests that the best treatment outcomes in patients with advanced urethral tumors may be obtained if patients are treated with chemotherapy followed by EBRT and/or brachytherapy and surgical resection. Patients with low-stage cancer did well with either single or multimodal therapy. Conversely, patients with advanced disease seemed to benefit from a multimodal approach.

Conclusion

Urethral tumors are rare. A biopsy is necessary to make the diagnosis. A good physical examination and MRI are needed to stage the tumor. Small and distal tumors are associated with a good prognosis. They are treated with a single modality option, such as sparing surgery or radiotherapy. Advanced disease is associated with poor prognosis, and patients should be treated with a multimodality of options including neoadjuvant radiotherapy concomitantly with chemotherapy followed by surgery. Local cancer recurrence can be treated with radiotherapy. □

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