Case Report

Isolated recurrence of prostate cancer to the anterior urethra 5 years after radiation therapy

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Abbreviations
ADT = androgen deprivation therapy
CD34 = cluster of differentiation 34
MRI = magnetic resonance imaging
PSA = prostate-specific antigen

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Introduction: Primary or metastatic urethral tumors are extremely rare. However, treatment strategies differ between primary and metastatic tumors. Therefore, establishing an accurate diagnosis is critically needed for initiating timely and appropriate therapy.
Case presentation: We describe the case of a 79-year-old man with prostate cancer treated with radiotherapy and androgen deprivation therapy. He presented with macroscopic hematuria as a symptom of anterior urethral tumor at follow-up. Endoscopic tumor resection was performed. Hematoxylin and eosin staining showed adenocarcinoma component. Immunohistochemical staining revealed presence of metastatic prostate cancer to the urethra.
Conclusion: Regarding urethral tumors diagnosis, urologists should consider the possibility of metastasis from prostate cancer and perform immunohistochemical examination for establishing accurate diagnosis. Furthermore, if androgen deprivation therapy fails to suppress symptoms, radiotherapy or urethrectomy might be considered.

Key words: adenocarcinoma, androgen antagonists, local neoplasms recurrence, prostatic neoplasms, urethra.

Keynote message

Urethral tumors are rare, and most cases are urothelial cell carcinomas. Few cases of metastatic prostate cancer to the urethra have been reported. However, the metastatic route and appropriate treatment remain unknown. We present the case of urethral tumor detected at follow-up after radiotherapy for prostate cancer.

Introduction

Urethral tumors, whether primary or metastatic, are extremely rare.[1,2] Metastatic urethral tumors usually originate from the bladder. Metastatic prostate cancer to the urethra is rare and only 11 previous cases after 2000 have been reported.[1–9] Common sites of metastases from prostate cancer comprise the bones, distal lymph nodes, liver, and lung. Regarding metastatic penile cancer, it occurs more frequently in the corpus cavernous or foreskin than in the urethra.[3] Herein, we describe the case of metastatic prostate cancer to the anterior urethra. It occurred 5 years after radiation therapy for prostate cancer and developed in absence of PSA elevations.

Case presentation

A 79-year-old man was diagnosed with prostate cancer (Gleason score 4 + 4, cT3aN0M0), with a PSA level of 4.30 ng/mL at diagnosis. He was treated with iodine-125 brachytherapy with a dose of 110 Gy followed by external beam radiotherapy at a dose of 45 Gy in 25 fractions, plus 6-month concurrent ADT with leuprorelin and bicalutamide. His PSA levels

fluctuated between 0.01 and 0.11 ng/mL during follow-up. He presented to our hospital with macroscopic hematuria 5 years after radiation therapy.

Cystoscopy revealed papillary tumor nodule in the anterior urethra. However, no significant findings were observed in either the prostatic urethra or bladder (Fig. 1a). MRI showed a tumor in the anterior urethra (Fig. 1b,c), and computed tomography showed no metastasis.

Endoscopic tumor resection was performed. Histopathological examination of hematoxylin and eosin (HE)-stained slides revealed acinar adenocarcinoma with cribriform pattern (Fig. 2a). Immunohistochemistry for CD34 clearly showed vascular invasion of this tumor (positive staining of capillary endothelium) (Fig. 2b). Since the patient was previously diagnosed with prostate cancer, immunohistochemical staining was performed and revealed strong positivity for both PSA and androgen receptors (Fig. 2c,d).

These findings were suggestive of metastatic prostate carcinoma to the anterior urethra rather than a primary tumor. Restaging imaging showed no metastasis to other organs, and ADT was initiated. Two months after surgery, his serum PSA value was 0.01 ng/mL and cystoscopy showed resection scar tissue and no recurrence despite presence of tumor in specimens biopsied from surgical margin (Fig. 3). The patient has been stable for 3 months since his diagnosis of urethral metastasis with no significant adverse events.

Discussion

In this case, based on the patient's clinical presentation and cystoscopic findings, our initial diagnosis was urothelial cell carcinoma of the urethra. However, immunohistochemical findings confirmed a diagnosis of prostatic adenocarcinoma. Current epidemiological data suggest that urothelial cell

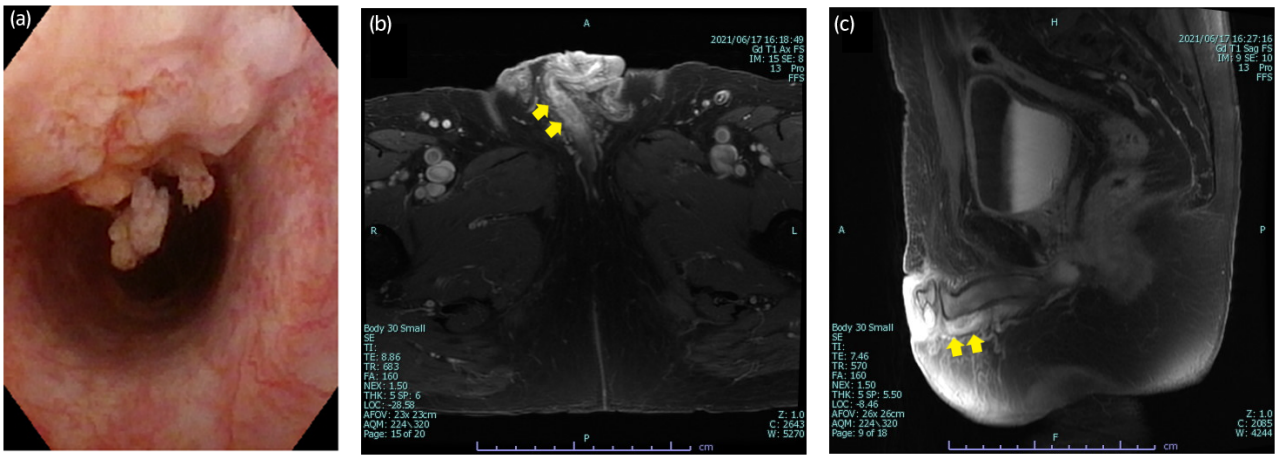

Fig. 1 Cystoscopy of the anterior urethra. (a) MRI showing the anterior urethral tumor (b, c) (yellow arrows).

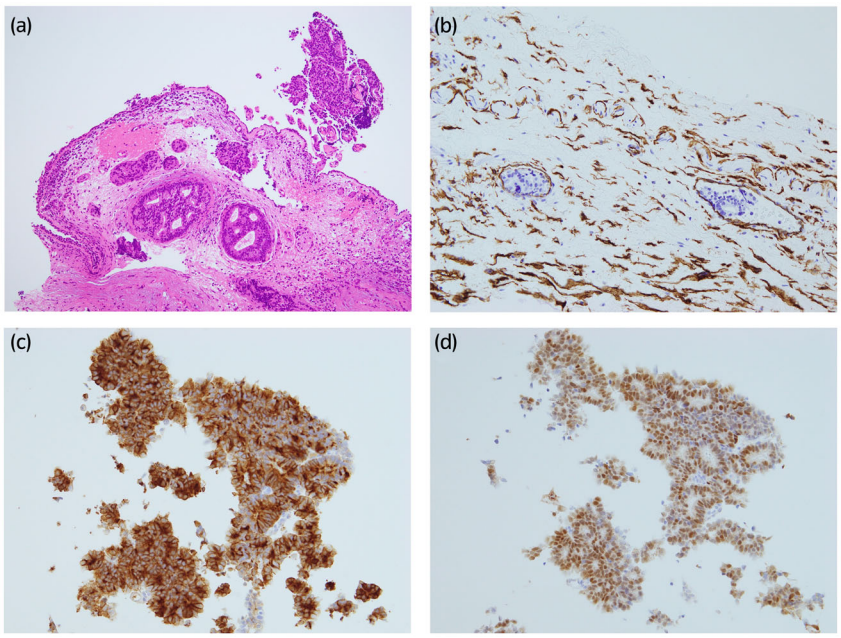

Fig. 2 Biopsy specimen of the urethral tumor. Tumor shows morphology of acinar adenocarcinoma (a) with vascular invasion; (b) immunohistochemistry for CD34 and positive immunohistochemical staining for PSA; (c) and androgen receptors (d).

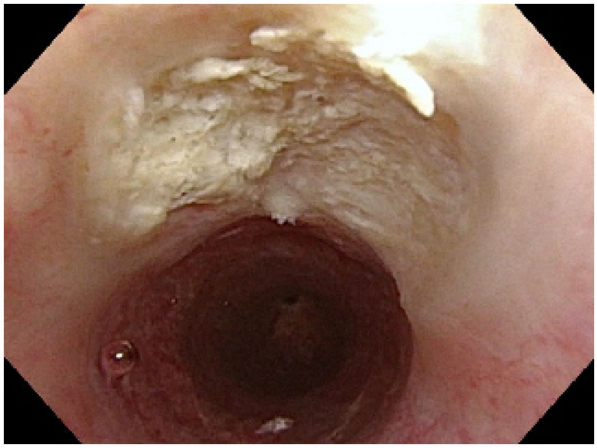

Fig. 3 Cystoscopy of the anterior urethra 2 months after resection.

carcinoma is the most common histological subtype of urethral tumors, and adenocarcinoma is less frequent.[10] Distinguishing between poorly differentiated prostatic adenocarcinoma and urothelial carcinoma is sometimes challenging. Since several cases of cancer have been misdiagnosed as urothelial carcinoma, one patient underwent penectomy due to this misdiagnosis.[11] Clinical features including unusual metastatic sites from prostate cancer, long time from primary diagnosis to metastasis, and poorly differentiated carcinoma result in misdiagnosis. Therefore, clinical and immunohistochemical examination is necessary for establishing accurate diagnosis and optimal treatment of urethral tumors.

Possible metastatic routes from the prostate to the urethra might comprise implantation of instruments such as catheters, arterial emboli, direct invasion, retrograde venous extension, or lymphatic dissemination. Since no single process could describe it clearly due to the complex structure of the urethra, the actual mechanism of metastasis remains unclear.[2,6,11] Vascular invasion of the tumor with an overlying normal urothelium was observed in our case. This suggests that the tumor may have spread from the prostate to the urethra via retrograde venous extension.

Treatment of metastatic prostate cancer to the urethra remains controversial. Most patients underwent ADT with or without transurethral resection,[2,3,6–9] and some cases of prostate cancer metastasizing to the urethra during ADT were treated with chemotherapy.[1,4] Cases of recurrent urethral tumors after achieving remission with ADT have been also reported, and urethrectomy and CyberKnife radiotherapy were performed with good outcomes.[3,6] Kotake et al. reported that patients with penile metastases from prostate cancer had poor prognosis because most of them were diagnosed at an advanced stage. They also reported that 41% of patients had died of cancer within 6 months after diagnosis.[12] However, to the best of our knowledge, patients with urethral metastasis from prostate cancer that have been reported since 2000 had better prognosis: only two patients died within 2 years after diagnosis.[1–9] Compared with penile metastasis, urethral metastasis is more likely to cause hematuria and lower urinary tract symptoms, which may lead to early detection and treatment. Consequently, urethral metastasis has a better prognosis. Therefore, less invasive treatments such as ADT are the first choice. However, if ADT is not effective in suppressing hematuria, more intensive regimes such as radiotherapy and urethrectomy should be considered cautiously. In the present case, the patient has remained stable for 3 months following ADT and local endoscopic resection. If hematuria flares up, we suggest performing radiotherapy.

Conclusion

We describe a case of isolated recurrence of prostate cancer to the anterior urethra. Regarding diagnosis of urethral tumors, urologists should consider the possibility of metastasis from prostate cancer, especially if there is a history of prostate cancer. Immunohistochemical examination should be performed to ensure timely and appropriate therapy. If ADT fails to suppress symptoms, radiotherapy or urethrectomy might be considered.

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Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable.

Informed consent

Informed consent was obtained from the patient for the publication of this case report and accompanying images.

Registry and the Registration No. of the study/trial

Not applicable.

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