Multiple urinary bladder masses from metastatic prostate adenocarcinoma

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Abstract

We present an unusual case of metastatic prostate adenocarcinoma that manifested with multiple exophytic intravesical masses, mimicking a multifocal primary bladder tumor. Biopsy with immunohistochemical analysis confirmed metastatic prostate adenocarcinoma. The patient was treated palliatively with external beam radiotherapy to prevent possible symptoms from local tumor progression. This case illustrates that when a patient with known prostate cancer presents with multifocal bladder tumors, the possibility of metastatic prostate cancer should be considered.

Case Report

In March 2003, a 60 year-old man was found to have a firm prostate on routine physical exam. Workup revealed adenocarcinoma of the prostate, clinical stage T2b N1 M0, Gleason score 4+3, and a pretreatment serum prostate specific antigen (PSA) level of 106.4 ng/mL. He was treated with androgen ablation therapy (AAT) for 6 years until March 2009, at which time he developed a sign of castration-resistant disease with a progressively rising PSA. Technetium 99m whole body bone scan and computed tomography (CT) scan revealed no evidence of metastatic disease. He enrolled in a phase II randomized clinical trial evaluating an allogeneic whole cell vaccination with or without autologous myeloid dendritic cells. After 12 months of vaccine therapy, his PSA slowly rose to 25.8 ng/mL and restaging studies were performed. In March 2010, a non-contrast CT of the abdomen and pelvis revealed a polypoid mass in the urinary bladder. A bone scan revealed a new focus of increased radiotracer uptake in the right posterior 9th rib, consistent with bone metastasis. A CT urogram revealed multiple nodular filling defects arising from the left posterior bladder wall about the ureterovesicular junction, worrisome for multifocal urothelial carcinoma (Figure 1). The prostate was normal in appearance and there was no suggestion of contiguous involvement between the prostate and the bladder masses. There was no evidence of hydronephrosis. Serum creatinine was 1.0 mg/dL. The patient denied hematuria or urinary obstructive symptoms. Cystoscopy revealed a normal prostatic urethra and bladder neck. On the left bladder wall and left trigone, there were 10-15 spherical superficial masses measuring 1-3 cm in diameter (Figure 2). Biopsy of one of the masses revealed poorly differentiated prostatic adenocarcinoma (Gleason 5+5) (Figure 3). Immunohistochemical stains of the tumor cells were positive for PSA and prostatic acid phosphatase (PAcP) and negative for keratin 903.

The patient was referred to the radiation oncology department for consideration of palliative radiotherapy to the prostate and urinary bladder masses. Clinical exam of the prostate revealed a diffusely firm and nodular gland with extension of induration to the left seminal vesicle, consistent with known locally advanced prostate adenocarcinoma. At the time he was asymptomatic from these lesions; however, there was concern that progressive tumor growth would lead to local symptoms including hematuria, urinary obstruction, irritable voiding symptoms, and/or ureteral obstruction. He was treated palliatively with external beam radiotherapy with a total planned dose of 50 Gy in 20 fractions delivered to the entire bladder and prostate. To reduce potential radiation toxicity, the treatment was delivered in a planned split course schedule of 25 Gy in 10 fractions, followed by a three-week break, and then another 25 Gy in 10 fractions. The patient tolerated the treatment well with only mild increased urinary frequency and diarrhea, which resolved after the completion of radiotherapy. Following the completion of radiotherapy, the patient was initiated on systemic chemotherapy with docetaxel for castration recurrent prostate cancer.

Discussion

The most common tumor occurring in the urinary bladder is a primary urothelial carcinoma.[1] Secondary tumors of the urinary bladder are rare, accounting for 2-13% of all urinary bladder tumors.[1,2] Secondary tumors can involve the bladder through direct extension, as in the case of colon/rectum, prostate, and cervix primaries, or through hematogenous spread from distant organs.[2] The tissue of origin can usually be elucidated by means of immunohistochemical staining characteristics. Positive immunostaining for PSA and PAcP is characteristic of prostate adenocarcinoma and can be used to distinguish from primary adenocarcinoma of the urinary bladder or secondary involvement from colorectal or endometrial adenocarcinoma.[2]

In the era of PSA testing, urinary bladder involvement by prostate cancer is relatively uncommon.[3] Most cases of bladder involve-

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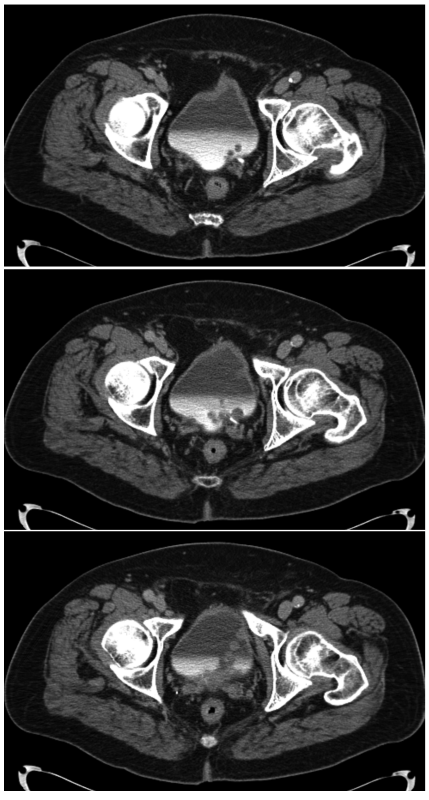

Figure 1. Axial computed tomography urogram showed multiple nodular and spherical filling defects of the urinary bladder.

ment represent direct tumor extension of uncontrolled local disease in either locally advanced prostate cancer at presentation or recurrent local disease after the failure of definitive therapy. Bates *et al*. reported a clinicopathologic series of 282 patients with secondary urinary bladder tumors. Of this cohort, 54 cases were due to prostate adenocarcinoma.[2] A majority of these 54 cases had a solitary mass in the bladder neck or trigone, which likely represents direct tumor extension of uncontrolled local disease into the bladder, based on the location and unifocality of the lesion. Only one patient had multifocal bladder involvement that could indicate a hematogenous spread. In an autopsy study of 1367 patients with metastatic adenocarcinoma of the prostate, urinary bladder involvement was noted in 39% of patients.[4] Others described case reports of isolated tumor recurrence of prostate adenocarcinoma in the urinary bladder several years after radical prostatectomy, which likely typifies a local recurrence of prostate cancer in the region of the vesicourethral anastamosis.[5-7]

Multifocal involvement of the urinary bladder by prostate adenocarcinoma, as seen in our case, is very rare, and presents a diagnostic challenge. It can represent a hematogenous spread, direct local extension, or a combination of both. Recently, Camilot *et al.* described two patients with prostate adenocarcinoma presenting with dysuria who were found to have multiple polypoid lesions in the urinary bladder.[8] The suspected clinical diagnosis was a primary urinary bladder cancer, although biopsy revealed mixed polypoid and diffuse linitis plastica-like infiltration of the bladder wall. As illustrated in this report as well as our case, when a patient presents with multifocal urinary bladder tumors, the diagnosis most often considered is multifocal primary urothelial carcinoma, even in the setting of known prostate adenocarcinoma. Invariably, a cystoscopy with biopsy and immunostaining is required to establish a correct diagnosis of prostatic adenocarcinoma. Systematic biopsy of the bladder neck may be of use in distinguishing contiguous spread from the prostate versus hematogenous spread.

In the previously described cases and ours, multifocal urinary bladder involvement by prostatic adenocarcinoma occurred late in the disease course, thus any potential treatments would be considered palliative in nature.[8,9] While previously reported patients had presented with urinary symptoms, our patient was asymptomatic with the urinary bladder lesions found incidentally on restaging CT of the abdomen and pelvis.[8] We elected to deliver radiotherapy to the prostate and urinary bladder to prevent the development of symptoms from local progression, although the decision to treat this asymptomatic patient could be considered controversial.[9] The radiotherapy was delivered in a split course in order to minimize radiation toxicity. Similar hypofractionated palliative radiotherapy regimens have been successfully used for symptomatic locally advanced prostate adenocarcinoma or urothelial carcinoma with minimal acute toxicity.[10,11] In retrospect, this patient may have benefitted from definitive therapy using a combined treatment of radiotherapy plus AAT at initial diagnosis. Recently, phase III randomized trials have demonstrated improved locoregional control and overall survival with combined AAT and radiotherapy compared to AAT alone for patients with newly diagnosed locally advanced adenocarcinoma of the prostate.[12,13]

In summary, our case represents a rare instance of multifocal involvement of the urinary bladder by prostate adenocarcinoma, mimicking a multifocal primary bladder tumor.

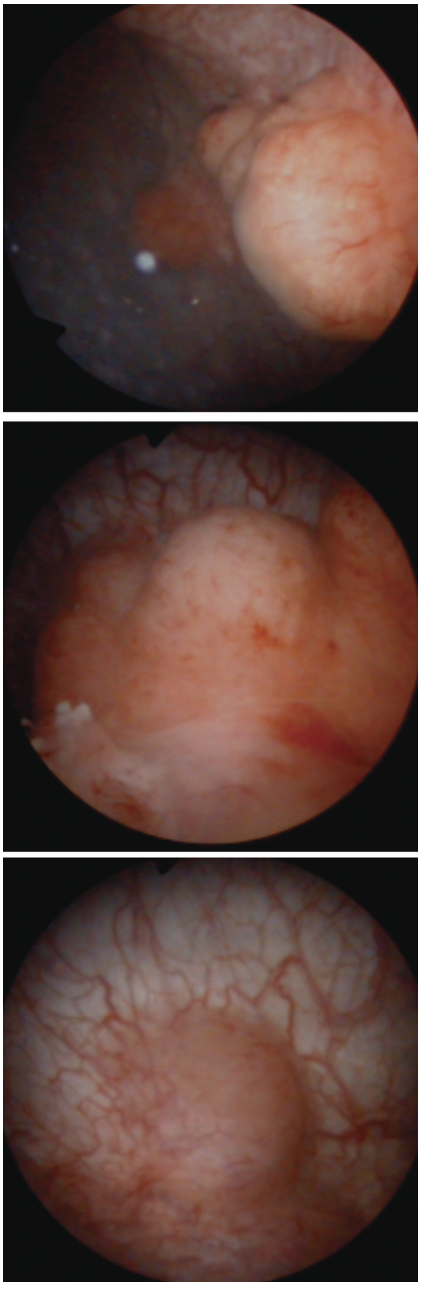

Figure 2. Cystoscopic exam revealed multiple exophytic masses arising from the urinary bladder lumen.

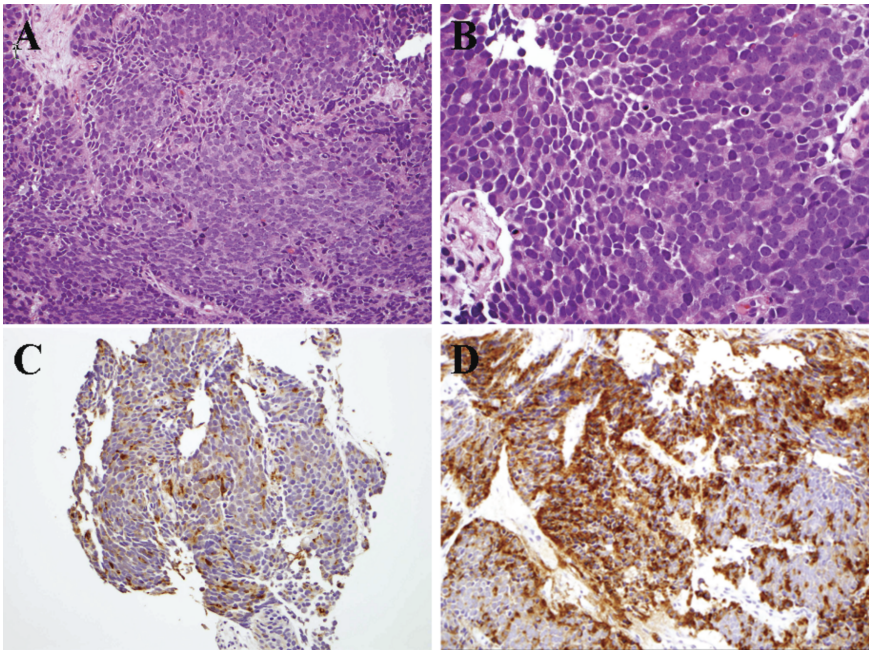

Figure 3. The urinary bladder biopsy showed a poorly differentiated adenocarcinoma characterized by tumor cells showing large pleomorphic nuclei with prominent nucleoli (image A and B). Immunohistochemical stains were performed and the tumor cells were positive for prostate specific antigen (PSA; image C) and prostatic acid phosphatase (PAcP; image D), supporting a diagnosis of metastatic prostate cancer.

This illustrates that when a patient with late-stage prostate cancer presents with multifocal bladder tumors, the possibility of metastatic prostate cancer should be considered. A biopsy with immunohistochemical analysis is necessary to make the correct diagnosis.

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