Detection and Treatment of Primary Prostatic Melanoma

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OBJECTIVE To describe a case of primary melanoma of the prostate gland, then review the published literature of similar cases.

METHODS Presentation of the clinical course of a 42-year-old man diagnosed with primary melanoma of the prostate after presenting with gross hematuria. Review of published literature.

RESULTS Primary melanoma of the genitourinary tract is a very rare disease, representing less than 1% of all melanomas in men. Only 6 cases of primary melanomas have been previously reported in the English literature.

CONCLUSION The current report emphasizes the importance of a multidisciplinary approach and adherence to treatment principles in cutaneous melanoma. With complete surgical extirpation (including extended pelvic lymphadenectomy as needed), close surveillance using 18F-FDG PET/CT, and aggressive systemic treatment in patients with good performance status, cure can be achieved. UROLOGY 123: 16–19, 2019. © 2018 Elsevier Inc.

Primary melanoma of the genitourinary (GU) tract is a very rare disease, representing less than 1% of all melanomas in men.[1] The majority develop from the penis and distal urethra, with fewer cases of primary melanoma originating more proximally along the GU tract. Of the described cases of prostatic melanoma, most are of prostatic urothelial origin or secondary to metastatic disease.[2] To our knowledge, only 6 cases of primary melanomas have been reported in the English literature to have unequivocally originated from the prostatic parenchyma (Table 1).[3-8] We present the diagnosis and treatment course, as well as long term follow-up results of a rare case of primary prostatic melanoma.

CASE REPORT

A 42-year-old man with no medical comorbidities presented for hematuria workup in August, 2008. Digital rectal exam revealed a 30 g prostate, without induration. Prostate specific antigen was 0.6 ng/mL. Cystoscopy and computed tomography (CT) scan were unrevealing, and the patient was started on tamsulosin and finasteride combination therapy for lower urinary tract symptoms by his treating urologist. Due to persistent obstructive symptoms, the patient elected to undergo GreenLight Laser photoselective vaporization of the prostate. Intraoperatively, a dark lesion in the patient's prostatic urethra was noted and biopsied. Histologic analysis was consistent with prostatic melanoma, prompting staging CT of the chest, abdomen, and pelvis, as well as brain MRI and bone scan. Multidisciplinary tumor board also recommended evaluation with ^{18}F-FDG PET/CT scan, which detected a hypermetabolic lesion with SUV of 6.9 to the left and posterior to the prostatic urethra without any other metastatic focus (Fig. 1A). In March, 2009, the patient underwent bilateral nerve sparing radical retropubic prostatectomy and pelvic lymph node dissection encompassing the nodal packets surrounding the external iliac vessels, obturator fossa, and internal iliac vessels.

Pathologic specimen corroborated the diagnosis of primary prostatic melanoma, with 2 distinct melanoma nodules found within the anterior prostate with no intraepithelial malignancy found within the overlying urothelium. The tumor stained positive for HMB-45 and S-100 (Fig. 2B and C) and was negative for cytokeratin. Margins of resection were negative, and the seminal vesicles, vasa deferentia, and 17 pelvic lymph nodes were free of tumor. Due to the R0 resection, no adjuvant therapy was advised and no additional molecular testing was performed. The patient had an uneventful recovery postoperatively.

On routine surveillance, 3 months following surgical extirpation, the patient regained urinary continence and achieved sufficient erectile function for intercourse with the aid of a penile vacuum erection device. However, on repeat PET/CT scan, he was found to have a 2 × 1.2 cm lesion along the right common iliac artery with SUV of 4.1 (Fig. 1B). An additional 1.1 cm pulmonary nodule was noted without significant ^{18}F-FDG uptake. Biopsy of the common iliac lesion demonstrated metastatic

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Table 1. Case reports of primary melanoma of the prostate

Author/year	Age	Presenting Symptoms	PSA (ng/mL)	Local Treatment	Time to Recurrence	Systemic Treatment	Outcome
Berry et al, 1953	38	Lower urinary tract symptoms	n/a	Cystoprostatectomy	7 months	None	Disease specific death at 33 mo
Wang et al, 2001	61	Lower urinary tract symptoms	n/a	TUR		None	NED at 73 mo
Wong et al, 2006	71	Urnary retention	normal	TUR		None	Disease specific death at 5 mo
Doublali et al,2010	75	Lower urinary tract symptoms, recurrent UTI	normal	TUR		None	Disease specific death at 1 mo
Ma et al, 2010	29	Dysuria	0.94	Radical prostatectomy		None	NED at 3 mo
Tosev et al, 2015	37	Hematuria, urinary retention	1.57	Radical prostatectomy, PLND	4 months	Dacarbazine, Ipilimumab, anti-PD1 therapy	Disease specific death at 16 mo
Current case	42	Gross hematuria	0.6	Radical prostatectomy, PLND	3 months	Dacarbazine/ vinblastine/ cisplatin/IL-2/INF	NED at 84 mo

PLND, pelvic lymph node dissection; PSA, prostate specific antigen.

melanoma staining positive for HMB-45 (Fig. 2D) and negative for prostate specific antigen. Unfortunately, insufficient tissue was obtained for molecular testing. Additional PET/CT scans following biopsy revealed progressive disease with enlarging pulmonary metastases and right retrocrural nodal metastases (Fig. 1C).

Approximately 7 months following surgery, the patient was initiated on biochemotherapy consisting of dacarbazine 800 mg/m^2 × 1 dose, vinblastine 1.5 mg/m^2 × 4 doses, cisplatin 20 mg/m^2 × 4 doses, continuous IL-2 9 × 10^6 units/m^2 × 4 doses, and 5 × 10^6 units/m^2 × 4 doses. Therapy was well tolerated with minimal capillary leak and mild renal function impairment. After dose adjustment, the patient proceeded to receive a total of 6 cycles of treatment. PET/CT scan after the completion of biochemotherapy demonstrated resolution of all metastatic lesions. On follow-up just short of 7 years after completion of biochemotherapy, the patient remains free of disease.

DISCUSSION (JOHN F. WARD)

We report the first successful treatment of metastatic melanoma originating from the prostatic parenchyma with surgical extirpation followed by salvage biochemotherapy. In addition, ^{18}F-FDG PET/CT was found to be an ideal imaging modality for diagnosis and surveillance after treatment.

Melanoma of the prostate is an exceedingly rare disease that can be misdiagnosed as blue nevus or prostatic melanosis. They are speculated to arise from melanoblasts that become entrapped ectopically within the prostate during migration from neural crest cells to more superficial sites.[2] Diagnosis is confirmed with positive HMB-45 staining on immunohistochemistry. Due to its rarity, much remains unknown. From the 7 existing reports including ours, an aggressive disease course seems to be the norm, with cancer specific death occurring 1-33 months after initial diagnosis in 3 of the 5 patients with sufficient follow up[3,4,6] On the other hand, long term survival has been documented with surgical resection alone[7] and with aggressive biochemotherapy after metastatic spread.

While prognosis of cutaneous melanoma is closely correlated with the depth of invasion,[9] little is known regarding how T staging should be stratified in prostatic melanoma. Interestingly, 1 of the 2 nodules noted within the pathologic specimen may represent a satellite lesion, a known poor prognostic factor in cutaneous melanoma.[9] The decision to perform pelvic lymph node dissection aligned with treatment principles of cutaneous melanoma, which has a high propensity for lymphatic spread. Indeed, local control was achieved, as evidenced by all recurrences being limited to outside of the template of dissection. Whether metastasis could have been prevented with extending the dissection beyond the true pelvis is unknown.

With sensitivity ranging from 68%-87% and specificity ranging 92%-98%, PET/CT has been shown to outperform CT scans in staging Stage III-IV cutaneous melanoma.[9] Furthermore, additional information derived from PET/CT impacted treatment decisions in up to 30% of patients. We report the first use of PET/CT to diagnose and surveil primary melanoma of the prostate. Traditionally, PET/CT was regarded as a poor imaging modality for cancers of the GU tract as signals may be masked by tracer excretion along the GU tract. However, as melanoma of the prostate is separate from the urothelium, the lesion can be easily detected on PET/CT. Furthermore, PET/CT was invaluable in the detection of metastatic disease as well as the assessment of response to systemic therapy.

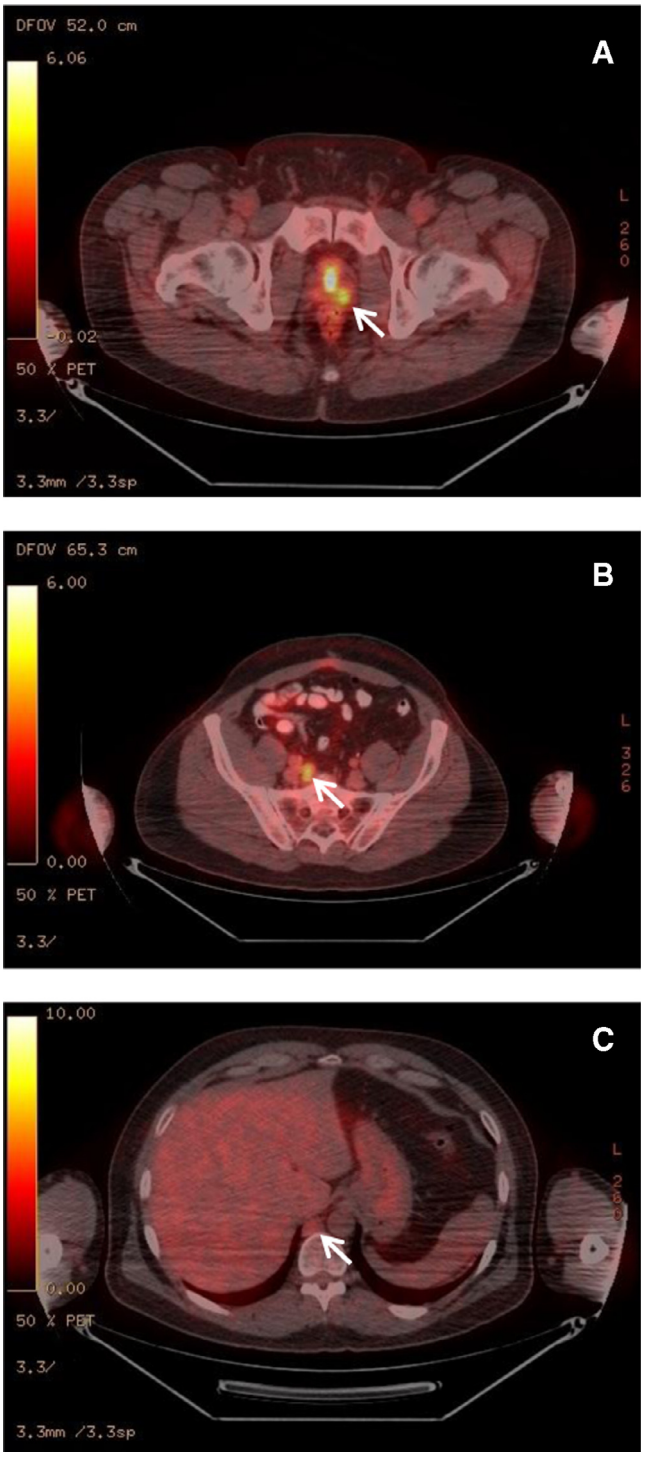

Figure 1. ^{18}F-FDG PET/CT scan images of (A) the primary lesion arising from the prostatic parenchyma; (B) metastatic focus along the right common iliac artery subsequent to local treatment; and (C) progressing metastatic lesion in the retrocrural space. (Color version available online.)

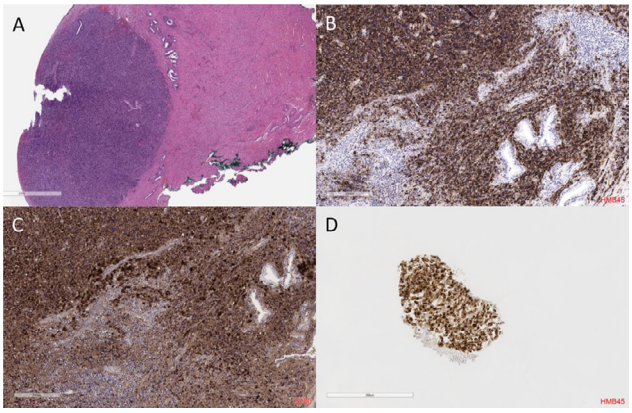

Figure 2. (A) H&E section of the radical prostatectomy specimen demonstrates diffuse tumor growth pattern with adjacent benign prostatic glands. Immunohistochemical staining showed tumor cells positive for HMB-45 (B) and S-100 (C), confirming the diagnosis of melanoma. (D) Biopsy specimen from the common iliac lymph node 3 months after radical prostatectomy stained positive for HMB-45, consistent with metastatic melanoma. (Color version available online.)

Prior to the approval of Ipilimumab for the treatment of metastatic melanoma in 2011, biochemotherapy using a combination of IL-2, interferon-α2b, and cytotoxic chemotherapeutic agents had demonstrated the highest overall response rate (21%-64%), leading to complete response rates between 7.5%-21%.[9] Because of the patient's age and excellent performance status, aggressive biochemotherapy was pursued and led to cure. In contrast, another report documented failure to treat metastatic disease arising from prostatic melanoma with single agent dacarbazine, with further progression after second-line Ipilimumab and third-line anti-PD1 inhibitor.[6] To our knowledge, the current report documents the only case of cure for metastatic disease originating from primary prostatic melanoma.

CONCLUSION

Prostatic melanoma is rare disease with only 7 cases reported in the English literature. The current report emphasizes the importance of a multidisciplinary approach and adherence to treatment principles in cutaneous melanoma. With complete surgical extirpation (including extended pelvic lymphadenectomy as needed), close surveillance using ^{18}F-FDG PET/CT, and aggressive systemic treatment in patients with good performance status, cure can be achieved.

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