



Case Report

A rare case of isolated castrate resistant bilateral testicular metastases in advanced prostate cancer



Jiarui Su ^a, Edwin Jonathan Aslim ^{a,*}, Hakan Aydin ^b,
Puay Hoon Tan ^c, Henry Sun Sien Ho ^a

^a Department of Urology, Singapore General Hospital, Singapore

^b Department of Anatomical Pathology, Singapore General Hospital, Singapore

^c Division of Pathology, Singapore General Hospital, Singapore

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Abstract Testicular metastasis is rare with the prostate being the most common site of primary cancer. We report a case of a 72-year-old man with castration-resistant prostate cancer (CRPC) and known metastases to bone and lymph nodes, who developed bilateral painful swollen testes 3 years after the initial diagnosis of prostate cancer. He had first presented with lower urinary tract symptoms (LUTS) with suspicious findings on digital rectal examination of the prostate, and an elevated serum prostate specific antigen (PSA) level of 129 ng/mL. Transrectal prostate biopsy revealed Gleason 4 + 5 adenocarcinoma. Radiological staging showed locally advanced prostate cancer with extensive metastases to bone and pelvic and retroperitoneal lymph nodes. He was given hormonal therapy for over 2 years until progression to CRPC. Six months later he developed painful bilateral testicular swellings, and serum markers for testicular germ cell cancer were normal. Bilateral orchiectomy was performed, showing metastatic prostate cancer (Gleason 4 + 5) on histology. One month postoperatively his PSA level dropped to 0.1 ng/mL from a presurgery level of 6.24 ng/mL.

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* Corresponding author.

E-mail address: edwinjonathan.aslim@mohh.com.sg (E.J. Aslim).

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1. Introduction

The testis is a rare site of metastasis from solid organ tumors, with an incidence of 0.02%–2.5% based on autopsy studies [1]. In such cases, the most common primary malignancy is the prostate (15%–43%), followed by gastrointestinal, kidney, bladder and lung cancers [2]. Testicular metastases can present clinically indistinguishable from primary testicular tumors, and bilateral involvement is extremely rare. More commonly, the diagnosis is incidental on routine histology following surgical castration for prostate cancer [1].

Prostate cancer cells are dependent on circulating androgens for survival, at least initially, until they progress to androgen independence following hormonal therapy. The major source of circulating androgens is the testis; hence, surgical castration remains a treatment option in metastatic prostate cancer. Here we report a patient with symptomatic bilateral testicular metastases from prostate cancer, where bilateral orchiectomy was both palliative and therapeutic.

2. Case report

A 72-year-old Malay man presented in August 2011 with lower urinary tract symptoms (LUTS) of poor stream, hesitancy and straining, with a hard nodular prostate on digital rectal examination, suspicious for cancer. His serum prostate specific antigen (PSA) level was 129 ng/mL, and transrectal ultrasound-guided prostate biopsy revealed Gleason 4 + 5 adenocarcinoma. Bone scan found extensive bone metastases. A computed tomography (CT) scan of abdomen and pelvis showed locally advanced prostate cancer invading the left seminal vesicle and mesorectum, with extensive pelvic and retroperitoneal lymphadenopathy.

The patient was diagnosed with metastatic prostate cancer, and started on androgen deprivation therapy (ADT) with a luteinizing-hormone-releasing hormone (LHRH) agonist monotherapy (three-monthly subcutaneous injection of Goserelin 10.8 mg). His serum PSA levels reached a nadir of 0.116 ng/mL within 9 months, but began rising after 18 months (Fig. 1). An androgen receptor antagonist (oral Bicalutamide 50 mg daily) was added for complete androgen blockade (CAB). The biochemical response from CAB lasted 11 months, after which the PSA levels started to rise. The serum testosterone was 0.4 nmol/L, confirming castrate level. The diagnosis of castration-resistant prostate cancer (CRPC) was made on biochemical progression.

Six months later, the patient complained of painful enlarging bilateral testicular swellings. His serum PSA level then was 6.24 ng/mL. An ultrasound scan of the scrotum revealed a heterogeneous mass with increased vascularity in the right testis measuring 1.9 cm, and two ill-defined lesions in the left testis measuring 1.4 cm and 1.1 cm in maximal diameters. A repeat CT scan of the chest, abdomen and pelvis found stable bony metastases, resolved pelvic and retroperitoneal lymphadenopathy, and interval reduction in size of the prostate gland. Serum markers for testicular germ cell tumors (α -fetoprotein, β -human chorionic gonadotropin and lactate dehydrogenase) were normal.

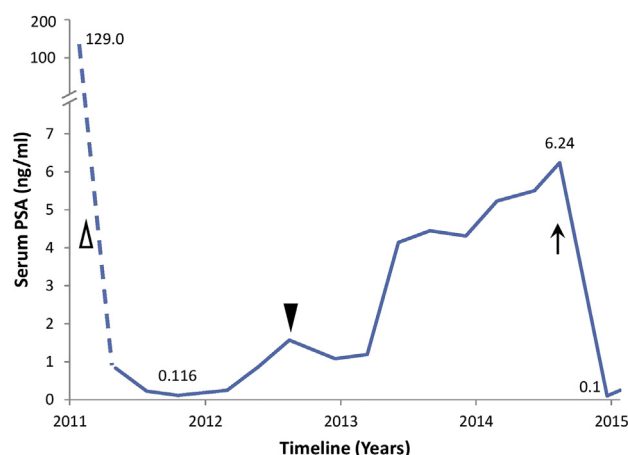


Figure 1 Prostate specific antigen (PSA) trend. Depicted along the timeline are commencement of androgen deprivation monotherapy (open arrowhead), complete androgen blockade (closed arrowhead), and orchiectomy (arrow).

Bilateral radical orchiectomy was performed, and gross sections of the specimens revealed yellowish nodular lesions bilaterally. Histology shows features of high grade prostatic carcinoma in both testes (Fig. 2), with positive PSA staining (Fig. 3). His serum PSA level was 0.1 ng/mL at 1 month after surgery. The patient declined docetaxel chemotherapy.

3. Discussion

Prostate cancer frequently metastasizes to the bones, followed by lungs, liver and the adrenal glands [1]. Testicular metastases from any solid tumors are rare, and the prostate is the most common site of primary tumor. In a series of 26 patients with testicular metastases, Ulbright and Young [2] reported the incidence of primary tumors being: Prostate (43%), kidney (15%), colon (15%), bladder (12%), lung (7%), esophagus (4%) and small bowel carcinoid (4%). Bilateral involvement occurs in 8%–14% of testicular metastases from prostate cancer [2,3]. The proposed mechanisms for testicular metastases include: Retrograde venous extension, arterial embolism, lymphatic spread and direct invasion [1]. Tu et al. [4] found a correlation between prostatic urethra involvement by prostate cancer and testicular metastases. Radiological diagnosis with scrotal ultrasound can be challenging as the findings can mimic primary testicular tumors, particularly mixed germ cell tumors [5].

The true impact of testicular metastases is unknown, and there are no consensus treatment guidelines. From landmark studies, treatment options in advanced prostate cancer with visceral metastases (non-testicular) include docetaxel chemotherapy (good performance status is a prerequisite), or hormonal options such as abiraterone or enzalutamide [6–8]. Our patient had widespread metastases from prostate cancer at diagnosis, with a Gleason score of 9 and PSA level of 129 ng/mL. He received androgen deprivation for 29 months before progression to CRPC, and 6 months later developed testicular metastases. His serum testosterone during treatment confirmed castrate level.

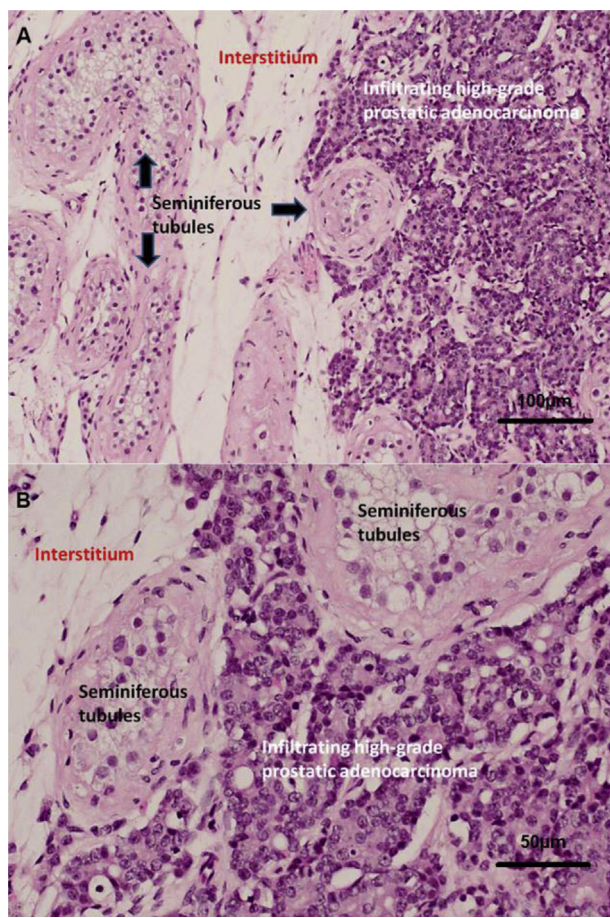


Figure 2 Histopathology of testes. (A) hematoxylin and eosin staining. (B) hematoxylin and eosin staining. Tumor shows infiltrating pattern in-between seminiferous tubules, and is comprised of fused glands, cribriform spaces and solid sheet-like areas which are consistent with high grade prostatic carcinoma (Gleason score $4 + 5 = 9$).

Bilateral orchiectomy was performed, and the patient was offered docetaxel chemotherapy but he declined.

A unique feature in our case was the serum PSA level which dropped to 0.1 ng/mL after surgery, from a baseline of 6.24 ng/mL before operation, on a background of widely metastatic prostate cancer. This, coupled with the observation that the testicular metastases occurred shortly after CRPC diagnosis, might hint that the foci of androgen-independent cancer cells resided entirely within the testes. Thus surgical resection was both palliative and therapeutic; Palliative being symptoms relief and therapeutic being the extirpation of isolated CRPC cells, which reinstated biochemical response to androgen deprivation and maintained castrate level serum testosterone. A possible explanation for this phenomenon could be that the testis is an immune privileged site, thereby preventing the CRPC cells from escaping the testicular confinement. From this experience, perhaps there is a role for surgical orchiectomy in all patients with advanced prostate cancer who develop new onset testicular masses.

From anecdotal reports, testicular metastases are usually found in patients with widespread metastases and

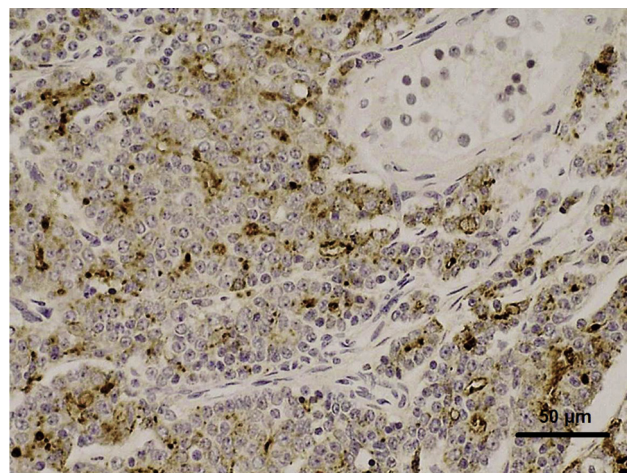


Figure 3 Prostate specific antigen immunostaining is positive while seminiferous tubule is negative.

associated with poor prognosis, although there have been cases of solitary testicular metastases post radical prostatectomies in the literature [3,9–15]. In the latter, the patients were rendered disease free after orchiectomies. The median time from initial diagnosis to clinically detected testicular lesions is 2.5 years (range 1–15 years) [9–15]. Mixed patient characteristics are observed; testicular metastases have been reported in patients with CRPC and androgen-dependent disease, as metachronous or synchronous lesions. Most reported a Gleason score of 9 (range 6–9), and the serum PSA levels ranged from 7.6 ng/mL to 1100 ng/mL [10–15]. From the literature, the risk factors associated with testicular metastases seem to be high PSA levels at diagnosis and high Gleason score.

4. Conclusion

Testicular metastasis from prostate cancer is very rare, and distinguishing it from primary testicular tumors can be difficult even radiologically. Bilateral and multifocal testicular involvement in the setting of metastatic prostate cancer, as in our patient, should place testicular metastases high in the list of differentials. Treatment options need to be individualized, and perhaps surgical orchiectomy should be offered to all men with newly diagnosed CRPC in conjunction with new testicular lumps.

Conflicts of interest

The authors declare no conflict of interest.

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