Case Reports in Oncology

Case Rep Oncol 2022;15:1055–1062
DOI: 10.1159/000525842
Received: May 11, 2022
Accepted: June 27, 2022
Published online: November 16, 2022

Case Report

A Rare Case of Castrate-Resistant Prostate Adenocarcinoma with a Unilateral Testicular Metastasis Mimicking a Primary Testicular Tumour

Jun Hee Hong[a] Udit Nindra[a] Rebecca Nguyen[a] Paul Gassner[b] Bavanthi Balakrishnar[a] Tristan Rutland[c]

[a]Department of Medical Oncology, Liverpool Hospital, Sydney, NSW, Australia; [b]Department of Urology, Liverpool Hospital, Sydney, NSW, Australia; [c]Department of Anatomical Pathology, Liverpool Hospital, Sydney, NSW, Australia

Keywords

Metastatic prostate adenocarcinoma · Testicular metastasis · Metastasectomy · Metastatic castrate-resistant prostate cancer

Abstract

Prostate adenocarcinoma with testicular metastasis is rare, present in up to 4% of autopsy diagnoses, and presents symptomatically in less than 0.5% of cases. We report an unusual case of a 55-year-old male who developed a symptomatic testicular metastasis from primary prostate cancer 4 years after initial diagnosis of metastatic castrate-sensitive prostate cancer with nodal and bone-only involvement. The patient had orchidectomy, histologically confirming the metastasis and revealing sparing of the spermatic cord. Prior treatment for his metastatic castrate-sensitive prostate cancer had included androgen deprivation therapy and upfront docetaxel chemotherapy. He had received palliative radiotherapy for symptomatic bone metastasis and managed on enzalutamide for castrate-resistant disease for the preceding 22 months with ongoing PSA response at the time of diagnosis of new testicular metastasis, with a further significant PSA response following his "testicular metastasectomy." At the time of diagnosis of testicular metastasis, he did not have any evidence of other visceral metastases, and his metastatic disease otherwise remained radiologically stable. We describe his disease course, treatment and outline the rare nature of his case of testicular metastasis from prostate cancer.

Correspondence to:
Jun Hee Hong, junhee.hong@health.nsw.gov.au

Case Rep Oncol 2022;15:1055–1062
DOI: 10.1159/000525842

Background

Prostate adenocarcinoma is the most commonly diagnosed cancer in men, accounting for more than 20% of new cancer diagnoses in men [1]. Australia has one of the highest incidences of prostate cancer in the world, ranking 15th for new diagnoses in 2018 [2]. The vast majority of prostate cancers are diagnosed in the early stages; however, up to 5% of patients present with de novo metastatic disease [3]. Common sites of spread are pelvic lymph nodes and bones. Less commonly, other visceral organs may be involved including the liver, lungs, and adrenal glands.

Testicular metastasis from prostate adenocarcinoma is a very rare phenomenon, reported to occur in between 0.18 and 0.5% of cases [4]. Testicular metastases were traditionally found on either post-mortem examinations or orchidectomy for surgical castration, where small deposits of prostate adenocarcinoma are seen [5]. However, as pharmacological androgen deprivation therapy (ADT) emerged in the modern era, incidental detection with surgical castration has become rarer [6]. This case report describes a patient who had a unilateral testicular metastasis from prostate adenocarcinoma which presented as a testicular lump late in the course of his history. A presentation like this is very rare and can pose some challenges in diagnosis.

Case Presentation

A 55-year-old Caucasian male was diagnosed with de novo metastatic prostate cancer after presenting with skeletal pain and elevated prostatic-specific antigen (PSA) of 2,300 μg/L. He was investigated with prostate biopsy, revealing prostate adenocarcinoma, Gleason score of 9 (4 + 5). His computed tomography (CT) of abdomen and pelvis revealed prostatomegaly with para-aortic and para-rectal lymphadenopathy. Furthermore, his whole body bone scan demonstrated wide-spread skeletal metastasis involving the skull, vertebral column, bilateral ribs, and pelvis. He did not have any other medical comorbidities.

He was initially treated with ADT and upfront chemotherapy with six cycles of docetaxel 75 mg/m^2 every 3 weeks. He had a PSA nadir of 7.7 μg/L. Also, he had good partial radiological response with significant reduction in size of the nodal disease and near complete resolution of radionucleotide uptake within his bone metastases with only faint activity at T11, right iliac bone, and right 8th rib posteriorly (shown in Fig. 1a). Hence, he was continued on ADT alone for 6 months until he had biochemical progression with PSA of 13 μg/L. At this stage, bicalutamide, an oral antiandrogen agent, was added to his treatment. However, after a year of biochemical stability, his PSA increased further from 10 μg/L to 17 μg/L within a 3-month interval, and bicalutamide was ceased. His PSA further increased off bicalutamide after 3 months to 22 μg/L and enzalutamide 160 mg daily was initiated with ongoing ADT using leuprorelin. Initially, he had very good early response to treatment where his PSA dropped to 2.7 μg/L after 2 months of addition of enzalutamide. However, he became poorly compliant with enzalutamide despite minimal toxicity and had further progressive disease with PSA rising up to 53 μg/L. Throughout his treatment, he has been compliant with leuprorelin. On conventional restaging CT and bone scans, he had a single site of progression with a new skeletal lesion in the sacrum which was treated by local radiotherapy, 25 Gy in five fractions, and enzalutamide continued.

Following this, after 3 years and 9 months from initial diagnosis, he reported a new right-sided testicular lump. He did not report any trauma to his testis, and there was no previous history of testicular or scrotal surgery. It was non-tender and he did not have any significant weight loss or night sweats. Testicular ultrasound revealed a markedly heterogeneous echogenic appearance to the right testicle (shown in Fig. 2). The right testicle was larger in

Case Rep Oncol 2022;15:1055–1062
DOI: 10.1159/000525842

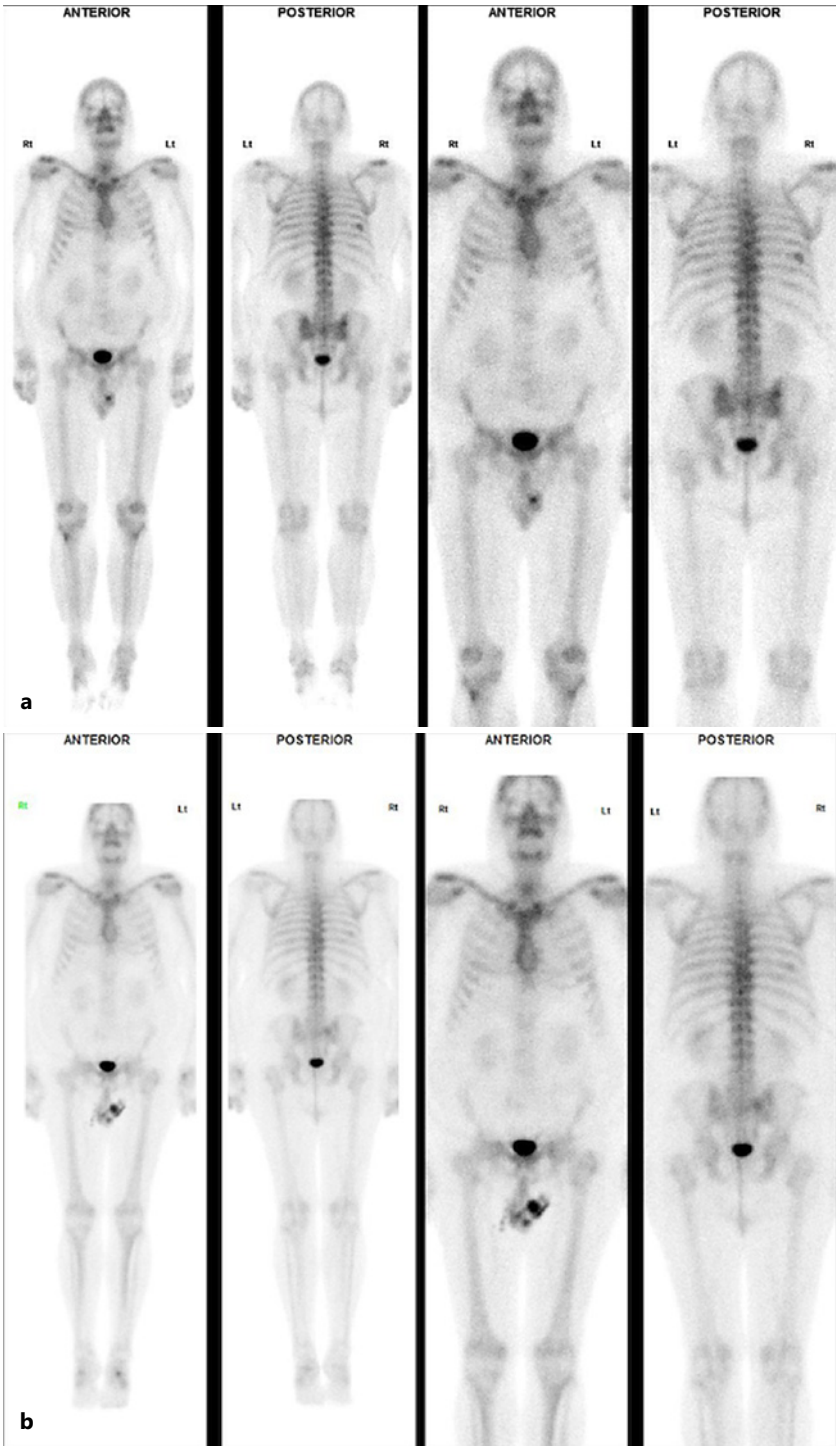

Fig. 1. a Whole body bone scan after the treatment with ADT and upfront docetaxel chemotherapy. Only faint activity demonstrated at T11, right iliac bone, and right 8th rib posteriorly. **b** Whole body bone scan at the time of right testicular metastasis. This demonstrates residual mild uptake at the right sacral ala metastasis previously treated with radiotherapy but otherwise stable disease. The increased uptake in the right pedicle of C3 correlated with a well-circumscribed small sclerotic lesion on CT, favouring benign aetiology.

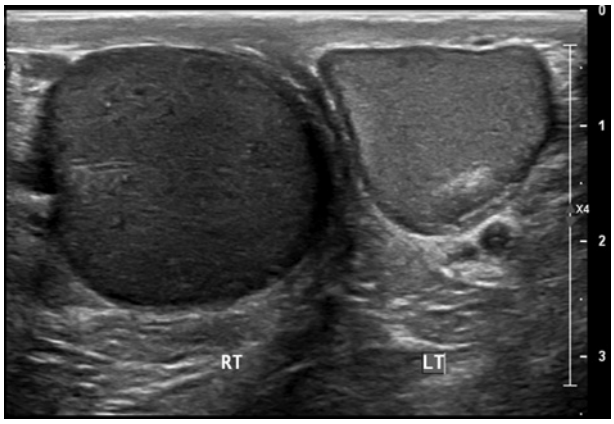

Fig. 2. Scrotal Ultrasound revealing larger volume of the right testicle compared to the left. The heterogenous appearance of the right testicle can be seen.

volume, measuring 4.0 × 2.4 × 2.2 cm compared to the left testicle which measured 3.8 × 1.7 × 1.7 cm. Primary testicular tumour markers including β-human chorionic gonadotropin and α-fetoprotein levels were within normal limits. His testosterone levels were not checked routinely; however, his PSA was 17.9 μg/L, an improvement following better compliance with treatment and palliative radiotherapy for sacral metastasis. Repeat staging whole body bone scan and CT neck, chest, abdomen, and pelvis revealed residual metastasis at the right sacral ala and a new mild uptake within the right C3 pedicle (shown in Fig. 1b) which corresponded to a well-circumscribed small sclerotic lesion on CT favouring benign aetiology. There were no nodal or visceral metastases evident on CT.

Given concerns about the possibility of a primary testicular tumour, biopsy of the lesion was not feasible. Subsequently, right orchidectomy was performed, and histopathology revealed poorly differentiated adenocarcinoma with Gleason grade 5 pattern, infiltrating in between the seminiferous tubules (shown in Fig. 3a, b). The tumour had areas of signet ring morphology and clear cells. These findings can confound the histological diagnosis as Sertoli cell tumours can have clear cells and other primary malignancies, especially gastrointestinal cancers, can show signet cells. However, immunohistochemistry showed strong positive staining for the prostate markers NKX3.1 and PSA (shown in Fig. 4a, b). Hence, metastatic prostate cancer in the right testis was confirmed. Almost all of the testis was replaced by the tumour, but the spermatic cord was free of the tumour. After the orchidectomy, his PSA fell to 1.0 μg/L, and the patient remains on leuprorelin and enzalutamide 160 mg daily. This drop in PSA would be due to removal of the tumour without other contributing factors as his treatment remained the same and patient had better compliance.

Discussion

Testicular metastasis has been incidentally detected in up to 4% in surgical castration era and in 0.18–0.5% of cases as ADT became readily available [7]. The rarity of testicular metastasis is thought to be due to lower temperature of the scrotum, which is proposed to be a less favourable environment for tumour proliferation. Also, the Sertoli cells that form the blood-testis barrier may play a role in prevention of haematological spread [8]. Nevertheless, it is interesting to note that prostate cancer was the most common primary tumour to metastasize to the testis, excluding leukaemia and lymphomas [8, 9].

As surgical castration in the management of prostate cancer has been largely replaced by pharmacological castration, testicular metastasis from prostate adenocarcinoma has been

Case Rep Oncol 2022;15:1055–1062
DOI: 10.1159/000525842

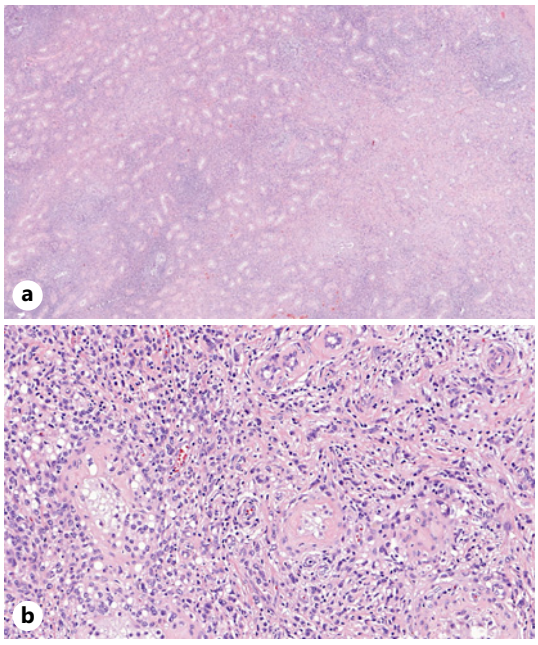

Fig. 3. a, **b** Histology shows a poorly differentiated tumour infiltrating in between the seminiferous tubules.

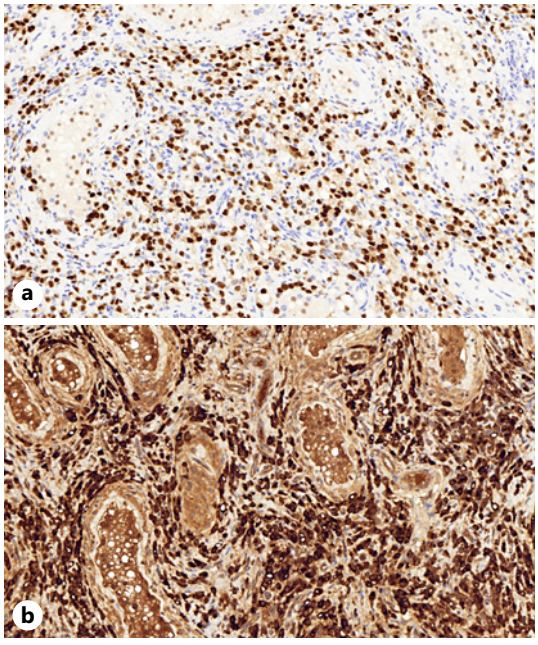

Fig. 4. a, **b** Immunohistochemistry shows strong positive staining for the prostate markers NKX3.1 and prostatic-specific antigen (PSA).

reported rarely. Clinically, patients with testicular metastasis can present with testicular pain or lump [4, 8]. Hence, it can mimic primary testicular germ cell tumours. However, patients with primary testicular germ cell tumours are generally younger, and majority of patients with secondary malignancy in the testis are in their sixth or seventh decades of life [10]. Although we had a robust history of prostate adenocarcinoma, cases like this can be diagnostically challenging if there is no previous history of malignancy. There are case reports of visceral carcinomas presenting with testicular metastasis; however, the case report of metastatic gastric signet ring carcinoma highlights the difficulty in making the diagnosis [11]. In particular,

Case Rep Oncol 2022;15:1055–1062
DOI: 10.1159/000525842

metastatic prostate adenocarcinoma can mimic primary testicular tumour, especially Sertoli cell tumour if Gleason grades are low. Histological features that favour metastasis include intertubular growth and lymphovascular invasion. Furthermore, appropriate immunohistochemical studies such as use of PSA and NKX3.1 are useful in diagnosis [9].

In the literature, the timing of testicular metastasis varied significantly. Some patients had isolated testicular metastasis 6 months after radical treatment, whereas some had metastatic disease to testis after 15 years of initial diagnosis [6]. In our case, the patient had already been diagnosed with de novo metastatic prostate cancer involving nodes and skeleton, and this demonstrates that disease progression after conventional treatment could occur in a rare form. Furthermore, it is interesting to note that while the testis is generally regarded as a sanctuary site for chemotherapy, ADT and novel anti-androgens such as enzalutamide would have activity at the level of the testis [12]. Hence, the oligometastatic disease progression in this case represents resistant clone of disease, and in this case, his PSA has declined to a very low level following testicular metastasectomy. Similarly, in the literature, patients with testicular metastasis were managed with orchidectomy with PSA response [1, 8].

Proposed mechanisms to explain prostate cancer metastasis to the testis include arterial embolism and retrograde venous extension or embolism through the spermatic vein [13]. Furthermore, retrograde lymphatic spread or direct invasion of prostate cancer through the vas deferens into the testicle has been suggested in the literature [8]. Interestingly, our patient had no spermatic cord involvement; hence, metastasis via the vas deferens would be less likely. He did not have lymph node disease on the CT scan at the time of testicular metastasis, though previously, he had para-aortic and pelvic lymph node disease. From this, we can postulate that his spread could be lymphatic, but a more likely explanation would be haematological spread.

An area of uncertainty is the prognostic implication of testicular metastasis with evidence limited to case reports and series. One retrospective case series of 3 patients reported survival with testicular metastasis to be less than a year, and all patients had poor prognostic features including high Gleason score of 8 or 9 with bone and lung metastases [14]. In contrast, other case reports indicate survival to be more than 5 years after orchidectomy. This case was also associated with high Gleason score of 9, but the patient only had isolated prostate metastasis in the testis [6]. It is difficult to ascertain the prognostic significance of testicular metastasis in prostate cancer due to the rare nature.

Conclusion

Prostate cancer metastasizing to the testis is very rare in the era of modern treatments, though historically, it was more prevalent as incidental findings in bilateral orchidectomies as part of surgical castration for advanced prostate cancer. Clinical manifestations can mimic primary testicular cancer, and histologically, without awareness of the possibility of metastatic disease in the testis, it may resemble Sertoli cell tumours or other primaries. Furthermore, appropriate immunohistochemistry such as use of PSA and NKX3.1 is extremely useful in making the diagnosis. Although prognostic implications of testicular metastases are unknown, appropriate management with surgical orchidectomy in addition to standard systemic treatments may achieve an adequate PSA response and outcome.

Acknowledgments

In addition to the authors listed above, we thank JW Nuclear Medicine in Sydney for providing figures used in this text.

Statement of Ethics

Formal ethics approval was not required for case report composition as per the South West Sydney Human Resources and Ethics Committee. Written and informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

Nil funding was required or sought for this case report.

Author Contributions

Jun Hee Hong, Udit Nindra, Rebecca Nguyen, Paul Gassner, Bavanthi Balakrishnar, and Tristan Rutland were involved in the original manuscript composition and editing aspects of this case report. Paul Gassner, Bavanthi Balakrishnar, and Tristan Rutland were involved in the supervision of the project as the senior members of the team.

Data Availability Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

References

1 Shinn BJ, Greenwald DW, Ahmad N. Unilateral testicular metastasis of low PSA level prostatic adenocarcinoma. Case Rep Child Meml Hosp Chic. 2015 May 20;2015:bcr2015209914.
2 Culp MB, Soerjomataram I, Efstathiou JA, Bray F, Jemal A. Recent global patterns in prostate cancer incidence and mortality rates. Eur Urol. 2020;77(1):38–52.
3 Bernard B, Burnett C, Sweeney CJ, Rider JR, Sridhar SS. Impact of age at diagnosis of de novo metastatic prostate cancer on survival. Cancer. 2020;126(5):986–93.
4 Olorunsola IS, Etonyeaku AC, Lekwa BO, Ojo OS. Bilateral secondary testicular, epididymal and spermatic cords carcinoma of prostatic origin: a case report and review of the literature. J Med Case Rep. 2021;15(1):222.
5 Bubendorf L, Schöpfer A, Wagner U, Sauter G, Moch H, Willi N, et al. Metastatic patterns of prostate cancer: an autopsy study of 1, 589 patients. Hum Pathol. 2000;31(5):578–83.
6 Bonetta A, Generali D, Corona SP, Cancarini G, Brenna SG, Pacifico C, et al. Isolated testicular metastasis from prostate cancer. Am J Case Rep. 2017;18:887–9.
7 Kwon SY, Jung HS, Lee JG, Choi SH, Kwon TG, Kim T-H. Solitary testicular metastasis of prostate cancer mimicking primary testicular cancer. Korean J Urol. 2011;52(10):718–20.
8 Abou Heidar NF, Bustros G, El-Asmar JM, Sabatto BZ, Degheili JA. Isolated testicular metastasis diagnosed more than a decade and a half post primary treatment for prostate cancer. Case Rep Oncol Med. 2019;2019:1–5.
9 Ulbright TM, Young RH. Metastatic carcinoma to the testis: a clinicopathologic analysis of 26 nonincidental cases with emphasis on deceptive features. Am J Surg Pathol. 2008;32(11):1683–93.
10 Turk A, Graff JM, Memo M. Case report of metastatic prostate cancer to testicles: an ominous sign of advanced disease. Urol Case Rep. 2019;26:100935.

Case Rep Oncol 2022;15:1055–1062
DOI: 10.1159/000525842

11 Schaefer I-M, Sauer U, Liwocha M, Schorn H, Loertzer H, Füzesi L. Occult gastric signet ring cell carcinoma presenting as spermatic cord and testicular metastases: "Krukenberg tumor" in a male patient. Pathol Res Pract. 2010;206(7):519–21.
12 James PP, Mead GM. Sanctuary site relapse in chemotherapy-treated testicular cancer. Ann Oncol. 1992; 3(1):41–3.
13 Campara Z, Simic D, Aleksic P, Spasic A, Milicevic A. Metastasis of prostate adenocarcinoma to the testis. Med Arch. 2016;70(4):318–20.
14 Korkes F, Gasperini R, Korkes KL, Silva Neto DCV, Castro MG. Testicular metastases: a poor prognostic factor in patients with advanced prostate cancer. World J Urol. 2009;27(1):113–5.