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Metastatic Cutaneous Prostate Cancer – A case report of a rare presentation.

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Character Summary: This case report explores the rare presentation of cutaneous metastatic prostate cancer, including epidemiology, pathophysiology, and management approaches.

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Abstract

Introduction: Prostate cancer is a leading cause of cancer morbidity and mortality in Australian men. Though prostate cancer is common, rarely does it present with cutaneous manifestations. Metastatic cutaneous prostate cancer represents less than 1% of all cutaneous metastatic disease and occurs in 0.06% to 0.3% of prostate cancer cases. This case report explores the rare presentation of cutaneous metastatic prostate cancer.

Case overview: An 83-year-old male with a history of metastatic castration-resistant prostate cancer presented with nodular chest lesions. The patient had been diagnosed with prostatic adenocarcinoma eight years earlier, and had received a radical prostatectomy, adjuvant radiotherapy, palliative chemotherapy, and androgen deprivation therapy. He was receiving palliative treatment at the time of presentation. The patient reported an eight-week history of firm, fast-growing flesh-coloured nodules over his right pectoral region which were otherwise asymptomatic. A prostate specific membrane antigen positron emission tomography scan demonstrated avidity within cutaneous lesions and was highly suspicious for cutaneous metastatic castration-resistant prostate cancer. The patient declined targeted radionuclide therapy and was managed with palliative superficial radiotherapy. The patient passed away six weeks after diagnosis of cutaneous metastases.

Discussion overview: Metastatic cutaneous lesions can result in diagnostic dilemmas for clinicians due to the rarity of presentations. Most cases will present with a known history of metastatic disease, however, a small number of cutaneous metastases may be the first indication of a clinically silent prostate cancer. Cutaneous metastasis is associated with a poor prognosis as there is often systemic disease present. Treating clinicians, including radiation oncologists, medical oncologists, dermatologists, urologists, and general practitioners, should consider the diagnosis of cutaneous metastasis in the case of skin lesions in prostate cancer patients.

Introduction

Prostate cancer is one of the most commonly diagnosed cancers in Australia and is the second most common cause of cancer-related death in males [1]. Approximately one third of patients with localised disease will progress to locally advanced and metastatic disease, commonly spreading to bone and lymphatics and rarely to cutaneous tissue [2]. Prostate carcinoma is reported to metastasise to skin in 0.06% to 0.3% of cases [3]. The skin lesions are usually asymptomatic involving the lower abdomen, genitalia, thigh, and sometimes chest, head, and neck [3]. Few cases of skin metastases from prostate cancer have been reported in the literature but it usually occurs in advanced disease states and is associated with a poor prognosis [3]. In this report, we discuss an 83-year-old male with metastatic castration-resistant prostate cancer presenting with asymptomatic nodular lesions over his right pectoral tissue.

The case

An 83-year-old male with a background history of castrate-resistant metastatic prostate cancer presented to an outpatient cancer centre due to concerns about nodular chest lesions. Over eight weeks, he had developed multiple lesions circumferentially over his right pectoral tissue. The lesions were 10 mm by 5 mm, firm, raised, flesh-coloured nodules that were non-tender, non-pruritic, and without discharge or necrotic tissue (Figure 1). During this time, the patient also noted a decrease in functionality, including increasing fatigue and dyspnoea. His past medical history included anaemia of chronic disease requiring blood transfusions, right-sided hydronephrosis secondary to extrinsic ureteric obstruction by metastatic lymphadenopathy requiring an intra-uretic stent, lumbo-sacral back pain and lymphoedema of the legs and right arm. The patient was a non-smoker and drank minimal alcohol on social occasions. He was a retired geochemical engineer and widowed father of four children, who lived with his son and required assistance completing activities of daily living. On examination the patient was hemodynamically stable, afebrile, had signs of anaemia (pallor of the skin, palmar creases and conjunctiva) and bilateral pleural effusions. The patient's Eastern Cooperative Oncology Group (ECOG) status was three.

The patient had a strong family history of prostate cancer and was diagnosed with localised prostate cancer in 2012 after PSA monitoring. A radical prostatectomy and six weeks of adjuvant pelvic radiotherapy were performed due to his high-risk profile and the patient went into remission. In 2015, his PSA levels became detectable and staging investigations revealed the presence of skeletal metastases. The patient was commenced on androgen deprivation therapy (ADT) with degarelix and bicalutamide. Due to continually rising PSA levels, the patient was started on docetaxel for castration-resistant disease. Enzalutamide was trialled but it led to low mood, a recognised adverse effect [4]. In 2017, restaging scans showed extensive bony and lymph node progression for which he received palliative radiotherapy to the lower spine, right humerus, and right axillary lymph nodes.

In light of the patient's prostate cancer history, new skin lesions, and recent functional decline, a prostate specific membrane antigen positron emission tomography (PSMA-PET) scan was performed. The scan revealed extensive nodal PSMA-avid disease both above and below the diaphragm, together with extensive osseous metastatic disease and right chest wall cutaneous lesions (Figure 2). The PSMA PET avidity within cutaneous lesions was highly suspicious for cutaneous metastatic castration-resistant prostate cancer.

The patient received palliative superficial radiation therapy of 900 cGy over two fractions to the right chest lesions to prevent fungation. Though there was improvement with the radiation therapy, the lesion remained. The option of actinium-PSMA (a targeted radionuclide therapy) was discussed, however, the patient's general functional status deteriorated markedly due to progressive metastatic disease in his liver and bilateral lungs, and further treatment was considered too burdensome. The patient received a blood transfusion for symptomatic management of anaemia as an outpatient. The patient passed away peacefully at home with family six weeks later from progressive metastatic liver disease.

Discussion

Cutaneous metastases from visceral malignancies are uncommon, occurring in 2% to 9% of cases [5]. This infrequent phenomenon is more commonly seen in breast, lung, renal, stomach, uterine, and colon malignancies, but rarely seen in prostate cancer [5]. Metastases usually occur in the advanced stage of malignancy and are associated with a poor prognosis [3,5,6]. In recent years, there have been more case reports of cutaneous metastasis of prostate cancer, possibly due to the aging population, new treatment methods lengthening survival, as well as better recognition by clinicians [7]. However, cutaneous metastatic prostate cancer is still very rare, representing less than 1% of all cutaneous metastatic disease and occurring in only 0.06% to 0.3% of prostate cancer cases [6,8].

Clinically, cutaneous metastatic disease presents with abrupt skin eruption which progressively worsens [7,8]. It can occur at any point of prostate cancer progression, with most cases presenting four years after the primary diagnosis [7,8]. The most common presentations include multiple asymptomatic firm flesh-like papules, nodules, or occasionally, sclerodermoid lesions [7-10]. Other variants of the disease include violaceous or erythematous plaques and, rarely, necrotic skin [10-13]. These lesions commonly occur over the suprapubic region, lower abdominal area, medial thigh, and genitalia [3,5,8,10]. Rare sites of cutaneous metastasis include the chest, scalp, and face [6,8,9]. However, a recent literature review has shown that presentations of chest wall metastases are increasing [7].

The pathophysiology of the spread from the primary tumour to the skin is complex and not fully understood [7,8]. The cells must acquire the ability to evade the primary site, enter the lymphatics or the blood stream, survive in the circulation, extravasate to dermal tissue, and proliferate [7,8]. New research has hypothesised that chymotrypsins may be responsible for the spread to cutaneous tissues [3]. Chymotrypsins secrete serine protease, which causes intercellular degradation to adhesive structures of the cornified skin layer, allowing for cutaneous tissue invasion [3,14]. There is a possibility that other receptors, such as androgen receptors, may be part of the metastatic process, however, further studies are required.

Metastatic cutaneous lesions can result in diagnostic dilemmas for clinicians due to the rarity of presentations. Most cases will present with a known history of metastatic prostate cancer. Therefore, if prostate cancer is revealed in the past medical history, it should raise suspicions and aid prompt diagnosis. Interestingly, the literature reports that 15% of undiagnosed prostate cancer present as cutaneous lesions [3]. Differential diagnoses for cutaneous lesions include angiosarcoma, cellulitis, mammary Paget's disease, sebaceous cyst, Sister Joseph nodule, basal cell carcinoma, pyoderma, morphea, and trichoepithelioma [3,7,8,19-21].

A definitive diagnosis is achieved with skin biopsy sent for histopathology and staining. The histopathology is often similar to the primary tumour, with undifferentiated cells diffusely infiltrating the dermis and gland-like structures in the case of adenocarcinoma [3]. Typically, immunohistochemistry staining is positive for PSA and/or prostatic acid phosphatase (PAP) [3]. Another key investigation is a raised serum PSA level, which in this case was markedly elevated at 174 ug/L. Other investigations may include a restaging scan, such as a computer tomography (CT) chest, abdomen, and pelvis and/or PSMA-PET scan, to check for distant metastases. In this case, the patient decided against biopsy. Therefore, the team made the likely diagnosis of cutaneous metastatic castration-resistant prostate cancer based on the PSMA PET avidity within cutaneous lesions and the patient's clinical history. Given the uncommon features of this presentation, a biopsy would have been useful for definitive

diagnosis and could have guided treatment of variant histology which may only respond to certain treatments.

Cutaneous metastasis is associated with a poor prognosis as there is often overt systemic disease present [3,7,8,22]. The mean survival time after diagnosis of cutaneous metastasis has been calculated to be between six to seven months [3,7,8,22,23]. Treatments are mostly palliative, including local excision, chemotherapy, or radiotherapy [3,7,8]. As most patients have advanced disease, the efficacy of management options has not yet been evaluated. Most patients are treated with a conservative approach, including palliative care and local radiation therapy, in an attempt to treat symptoms and improve the patient's quality of life [3]. In patients receiving more aggressive treatment for cutaneous metastases, chemotherapeutic agents have been utilized without much improvement [17,26]. Other systemic therapies, such as androgen deprivation therapy, have shown encouraging results with resolution of lesions [17,22].

There is PSMA targeted radionuclide therapy (TRT), which binds and emits radiation to PSMA-expressing tissues, destroying the prostate cancer cells [27]. Prostate specific membrane antigen TRT may also be offered as treatment for metastatic prostate cancer and is predominantly used when other treatments fail [27]. Targeted radionuclide therapy is an advancing area of oncology treatment and has shown some promising outcomes in metastatic prostate cancer; however, there is limited research available regarding the efficacy of TRT in cutaneous metastatic prostate cancer [28].

Learning Points

1. Although cutaneous metastatic lesions are rare, their presence warrants prompt assessment. These lesions are associated with dedifferentiated pathology, high burden of the disease, and poor prognosis. Therefore, prompt diagnosis and treatment are necessary to minimise associated morbidity and mortality.
2. Biopsy of lesions allows for definitive diagnosis and can guide treatment in variant histology which may respond to certain chemotherapies. Other useful investigations include PSMA-PET scans, restaging CTs, and PSA markers.
3. Prostate specific membrane antigen TRT is a relatively new therapy that may be offered as treatment for metastatic prostate cancer and is predominantly used when other treatments fail.

Conclusion

This report presents the case of an 83-year-old man with cutaneous metastases of prostate carcinoma. Although prostate cutaneous metastasis is an uncommon presentation, it remains an important diagnostic consideration in patients with unrecognised and advanced disease. Treating clinicians, including radiation oncologists, medical oncologists, dermatologists, urologists, and general practitioners, should consider the diagnosis of cutaneous metastasis in the case of skin lesions in prostate cancer patients. The presence of cutaneous metastatic lesions should prompt further assessment as they are associated with dedifferentiated pathology, high burden of the disease, and poor prognosis.

Conflict of interests

The author of this case report declares no conflict of interest.

Author Contributions

The content of this case report was written by Dr. Madison Boot and was reviewed and edited by Dr Elias Nasser. The first author is Dr. Madison Boot and the second author is Dr. Elias Nasser.

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Consent

Written informed consent was obtained from the patient, prior to his death, for publication of this case report and accompanying images.

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