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Isolated, PSMA-negative penile metastasis from castration resistant prostate adenocarcinoma, identified by FDG-PET

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ABSTRACT

Penile metastases are a rare entity and are associated with widespread metastatic disease. It is associated with significant morbidity with a poor prognosis. There have been few case reports about metastatic prostate adenocarcinoma to the penis. Diagnosis is often clinical, however, the use of PSMA PET has a high sensitivity. We report the first case of metastatic castration resistant prostate cancer with an isolated penile metastatic site. This was not identified on conventional staging or PSMA PET, but using FDG PET. A radical penectomy was performed with ongoing survival.

1. Introduction

Penile metastases are rare and can result in significant morbidity and mortality. These are usually secondary to genitourinary malignancies, in particular prostate and bladder malignancies.[1] Emphasis on quality of life is preferential over radical therapies given its terminal nature, with a mean survival of 9 months. Few case reports have documented prostate cancer metastasising to the penis, with prostate cancer more commonly involving other sites such as bone, lymph nodes, liver and thorax.[1] Early detection of metastatic disease can be aided through the use of prostate-specific membrane antigen positron emission tomography (PSMA- PET).[2] We present a rare case of non-PSMA-avid, castration resistant prostate cancer metastasising solely to the penis.

2. Case presentation

A 75 year old man with a background of castration resistant prostate cancer (CRPC) presented to a tertiary Urology service with malignant priapism.

7 years prior, he was treated for localised, high volume, Gleason 4 + 5 = 9 prostate cancer, with adjuvant androgen deprivation therapy (ADT), Goserelin with Bicalutamide, followed by conformal radiotherapy and high dose rate brachytherapy, with an initial response indicated by PSA nadir of 0.01. He developed a complex urethral stricture which failed conservative management 4 years after initial diagnosis, and subsequently managed with a perineal urethrostomy. Cystoscopic evaluation at the time showed no evidence of malignant invasion to the urethra or bladder. 1 year after formation of perineal urethrostomy, he demonstrated biochemical recurrence (BCR), with his PSA rising to 85, whilst on ADT. Therapy was changed to Cyproterone acetate, with no significant improvement.

Staging computerised tomography (CT) and bone scan were performed that did not identify metastatic disease (including the penis). 2 staging 68Ga-PSMA-PET scans, 6-months apart, showed no avid disease. His ADT was changed to Leuprorelin acetate given rising PSA to 354, with plans to use both Leuprorelin and cyproterone acetate if no response was observed. As there was no evidence of relapse site and his comorbidities, the multidisciplinary team (MDT) consensus was against systemic chemotherapy or other ADT. He remained asymptomatic.

18-fluorodeoxyglucose (18F-FDG)-PET was organised for non-PSMA excreting prostate cancer. It identified diffuse abnormal moderate-high intensity heterogeneous 18F-FDG uptake throughout almost the whole penile shaft (Fig. 1). No other areas of 18F-FDG uptake were identified. A penile biopsy demonstrated adenocarcinoma. The adenocarcinoma cells showed positive staining for PSA and NKX3.1 by immunohistochemistry; these markers are, highly specific for prostatic origin, thus the diagnosis of metastatic prostatic adenocarcinoma to the penis was made.

Broad spectrum antibiotics was administered and an elective radical penectomy was urgently arranged on the admission for penile biopsy

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related sepsis. A radical penectomy was performed without complications. Histopathology confirmed innumerable deposits of metastatic prostate adenocarcinoma throughout the shaft of the penis, with involvement of the proximal margins of the specimen. Macroscopically, tumour invasion into the corpus cavernosum was seen throughout the entire length (Fig. 2a and b).

Post-penectomy, the patient recovered well and was discharged with continued ADT. He has been followed up for 2 years. He demonstrated biochemical remission with PSA decreasing from 10 (4 months post penectomy) to 0.05 (1 year post penectomy). The patient currently remains asymptomatic on ADT, with 6-monthly reviews in the Urology outpatient setting.

3. Discussion

Metastatic spread from prostate cancer occurs via local invasion, lymphatic or haematogenous spread.[2] Common sites of prostate cancer metastasis include bladder, bone, distant lymph nodes, liver and the thorax. Penile metastases remain an extremely rare presentation and is usually seen with diffuse metastatic disease throughout the body. Penile metastases have shown an aggressive disease pattern and is associated with significant comorbidity with a poor prognosis. Patients present with palpable nodules, penile pain, dysuria, priapism, urinary voiding issues and ulcerations. Average survival rates for penile metastases from the prostate is 9 months with the longest documented being 5 years, described by Fujita et al.[3] Patients with penile metastasis from urological source, presenting with priapism have been known to demonstrate worse survival rates when compared to those without priapism.

Needle core biopsy remains the most reliable diagnostic tool. Quality of life and palliation are the treatment goals in penile metastasis. Radiation therapy, surgical excision, partial or radical amputation, systemic treatment with chemotherapy and hormonal therapy, or a combination of the aforementioned. In this particular case, given the isolated prostatic metastasis without involvement of other organs, radical amputation with ongoing hormonal therapy was selected as the therapy of choice, which induced disease control.

PSMA-PET scans in general have shown to have higher sensitivity for metastatic prostate cancer when compared to conventional staging techniques such as CT. Jansen et al. also demonstrated that PSMA-PET in metastatic castration resistant prostate cancer (mCRPC) possessed an higher sensitivity for metastases when compared to conventional imaging modalities.[4] Chen et al. found the additional benefit of 18F-FDG PET/CT staging in patients with biochemical recurrence (especially in those with a negative 68Ga-PSMA PET), with a strong association between PSA levels and 18F-FDG findings. Higher PSA levels (PSA $\geq$2.3) resulted in higher 18F-FDG detection rates in 68Ga-PSMA-negative patients. Furthermore, higher Gleason scores (Gleason $\geq$8) were an independent predictor of positive 18F-FDG findings in 68Ga-PSMA-negative patients. Chen et al. suggested that in patients with high Gleason scores and PSA levels with 68Ga-PSMA-negative scans, the use of 18F-FDG PET aided in identification of an additional 16.7% of metastatic disease.[5] This was reflected with our patient, who had a Gleason 9 disease and a PSA level of 354, where the penile metastasis was not identified on 68Ga-PSMA PET, but apparent on 18F-FDG PET.

4. Conclusion

The authors present, to their knowledge, the first case of metastatic prostate adenocarcinoma, with an isolated metastasis to penis, identified using an 18F-FDG PET. Penile metastases from prostate adenocarcinoma remains a rare presentation. Careful clinical examination and biochemical surveillance allows for early detection of recurrence or metastasis. While PSMA PET has a high sensitivity for prostatic metastasis over conventional imaging, in patients with biochemical recurrence who are PSMA-PET-negative, FDG-PET can provide additional value if they possess high PSA (>2.3) and Gleason scores (Gleason >8). Due to the poor prognosis of penile metastases, palliative intent treatment should be pursued, especially in cases of widespread metastases.

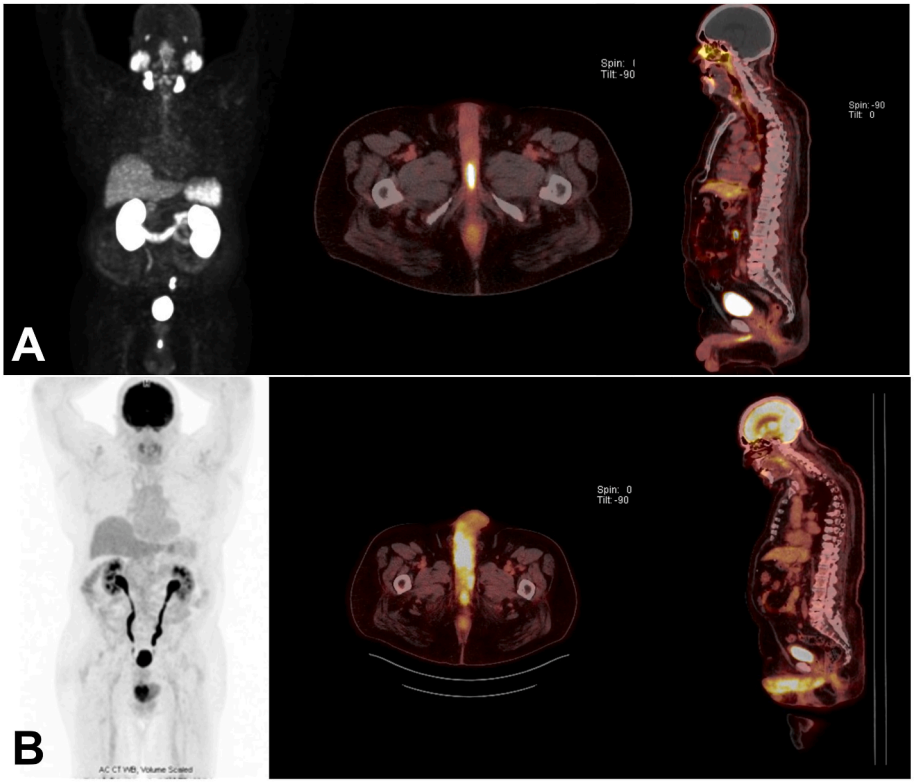

Fig. 1. (A) 68Ga-PSMA PET coronal, axial and sagittal views demonstrating no abnormal heterogenous and (B) 16F-FDG-PET coronal, axial and sagittal views demonstrating abnormal heterogenous uptake throughout the penis, without other avid areas.

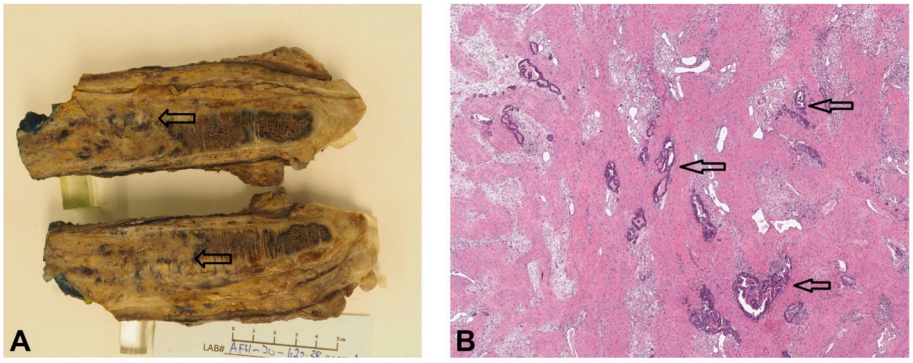

Fig. 2. (A) Macroscopic dissection of penile specimen showing tumour invasion within the corpus cavernosum, indicated by the moth-eaten appearance due to the massive infiltration by carcinoma and (B) H&E, x20 magnification. The corpus cavernosum is heavily infiltrated by malignant cells arranged in glands, situated within the stroma and in vascular spaces (arrows).

Author statement

Matthew Chau: Conceptualization; Data curation; Writing - original draft; Writing - review & editing, Nicole Swarbrick: Data curation; Validation; Writing - review & editing, Sunny Lee: Writing - review & editing; Supervision.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

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Nil.

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