AKADÉMIAI KIADÓ

Penile metastasis of prostate cancer imitating Peyronie's disease detected on [^{68}Ga]Ga-PSMA-11 PET/CT

IMAGING

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CASE REPORT

ABSTRACT

[^{68}Ga]Ga-PSMA-11 PET/CT (Gallium prostate-specific membrane antigen positron emission tomography/computed tomography) is an established molecular imaging technique for identifying the spread of prostate cancer in patients with biochemical recurrence (BCR) and for initial staging. Penile metastases from prostate cancer are very rare and can be easily misdiagnosed as noncancerous nodules as part of Peyronie's disease. Most cases of penile metastases occur in patients with disseminated disease and are typically diagnosed at advanced stages. In this case, a 74-year-old patient with prostate cancer underwent a successful prostatectomy, ADT, and radiation therapy to the prostate bed, achieving a PSAnadir of 0.01 ng mL^{-1}. Three and a half years after surgery, biochemical recurrence occurred, and the patient was referred to our clinic for a [^{68}Ga]Ga-PSMA-11 PET/CT scan. PET/CT revealed pathological PSMA expression in a proximal part of the penile root, later confirmed by pathohistological analysis as prostate cancer metastasis. Notably, our patient had a PSA value of only 0.53 ng mL^{-1}, one of the lowest serum PSA values reported in the literature for penile metastasis. This case underscores the critical role of [^{68}Ga]Ga-PSMA-11 PET/CT in differentiating benign conditions like Peyronie's disease from metastatic lesions and in detecting rare and unusual metastatic sites.

KEYWORDS

[^{68}Ga]Ga-PSMA-11 PET/CT, penile metastasis, PSMA, PET/CT, prostate cancer, Peyronie's disease

Introduction

According to World Cancer Research, prostate cancer ranks as the second most common cancer in men globally and the fourth most common overall [1]. The most common sites of metastases from prostate cancer are lymph nodes, bones, lungs, and liver [2]. Penile metastases of prostate cancer are extremely rare, and only a handful of case reports exist in the literature in patients with low PSA values [3–7]. Cancer usually spreads to the penis retrogradely via the venous or lymphatic route. Common indicators of penile metastasis include pain, detectable nodules, priapism, ulceration, and symptoms related to invasion of the urethra such as urinary retention, hematuria, and dysuria. Definitive diagnosis is set with needle core biopsy [6, 7].

Therapy options for metastatic prostate cancer depend on the stage of the disease. In cases of oligometastatic disease, a combination of systemic therapies (ADT) and metastasis-directed treatment, such as stereotactic body radiation therapy (SBRT), is usually used. In patients with hormone-sensitive metastatic prostate cancer (HSPC), the main therapeutic option is ADT, and depending on metastatic spread radiation therapy. For aggressive disease, ADT combined with chemotherapy (docetaxel) is recommended, while ADT + ART may also be considered. In patients with castration-resistant metastatic prostate cancer (CRPC),

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therapeutic options include ART, chemotherapy (docetaxel and cabazitaxel), PSMA-targeted radioligand therapy, Ra-223, and immunotherapy [4].

Peyronie's disease is a noncancerous, benign condition characterised by the development and spread of fibrous scar tissue in the form of plaques. Build-up over time can grow from palpable nodules to causing deformation to curvature of the penis, priapism, flaccidity, and pain during erection. The onset of this condition is gradual, and its symptoms can vary in severity [8]. Differentiating Peyronie's disease from penile metastasis can be challenging due to the overlapping clinical signs.

With the recent increased availability of [^{68}Ga]Ga-PSMA-11 PET/CT in both biochemical recurrence and initial staging, more attention should be given to rare metastatic manifestation sites of PC. Our case highlights a patient with a biochemical recurrence of PC, and to the best of our knowledge, one of the lowest serum PSA values associated with penile metastasis described in the literature.

Case presentation

A 74-year-old patient with biochemical recurrence of PC was referred to our clinic for [^{68}Ga]Ga-PSMA-11 PET/CT. In April 2019, transurethral resection of the prostate (TURP) was done because of prostate hyperplasia and urine retention. Initial PSA was 4.02 ng mL^{-1}. Subsequent pathological examination revealed the presence of prostate cancer in 24 out of 400 tissue samples, accounting for approximately 0.6% of available tissue. A radical prostatectomy performed three months after TURP indicated tumour tissue in both lobes with an aggressive Gleason score of 9 (4 + 5), ISUP/WHO group 5 and pTNM classification: pT3b, pN0, pMx. The PSA value after prostatectomy was 0.02 ng mL^{-1} (PSAnadir). In the following months, the value of PSA slowly increased. A year and a half after surgery (early 2021), at a PSA value of 0.27 ng mL^{-1} the oncologist decided to administer a short course of hormonal therapy (ADT) and conduct salvage radiotherapy of the prostate bed. Following both treatments, the patient recovered well, maintaining an ECOG performance status of 0 during follow-ups, with a PSA nadir of 0.01 ng mL^{-1}. Last year, the patient's PSA levels started to rise again, and at the PSA level of 0.53 ng mL^{-1}, he was referred to a [^{68}Ga]Ga-PSMA-11 PET/CT scan (Fig. 1 demonstrates the patient's progression up until PET/CT scan). Before the scan, the patient sought an evaluation from a urologist for a palpable lump under the skin of his penis, clinically consistent with an early stage of Peyronie's disease. At that time, his PSA level was 0.38 ng mL^{-1}.

[^{68}Ga]Ga-PSMA-11 PET/CT scan revealed pathological PSMA expression in one non-enlarged lymph node in the external iliac lymph node group. Pathological [^{68}Ga]Ga-PSMA-11 uptake was also seen in the proximal part of the penis, correlating with a palpable lump (Fig. 2), with SUVmax value of 7.9. For a definitive diagnosis, the patient was referred for a biopsy. Histology revealed pseudoglandular formations lined with atypical epithelial cells that are immunohistochemically positive for PSA, PSAP, and NKX3.1. The finding corresponded to metastasis of prostate cancer. Following consultation with an oncology multidisciplinary team, it was decided to initiate treatment with a long-lasting LHRH agonist.

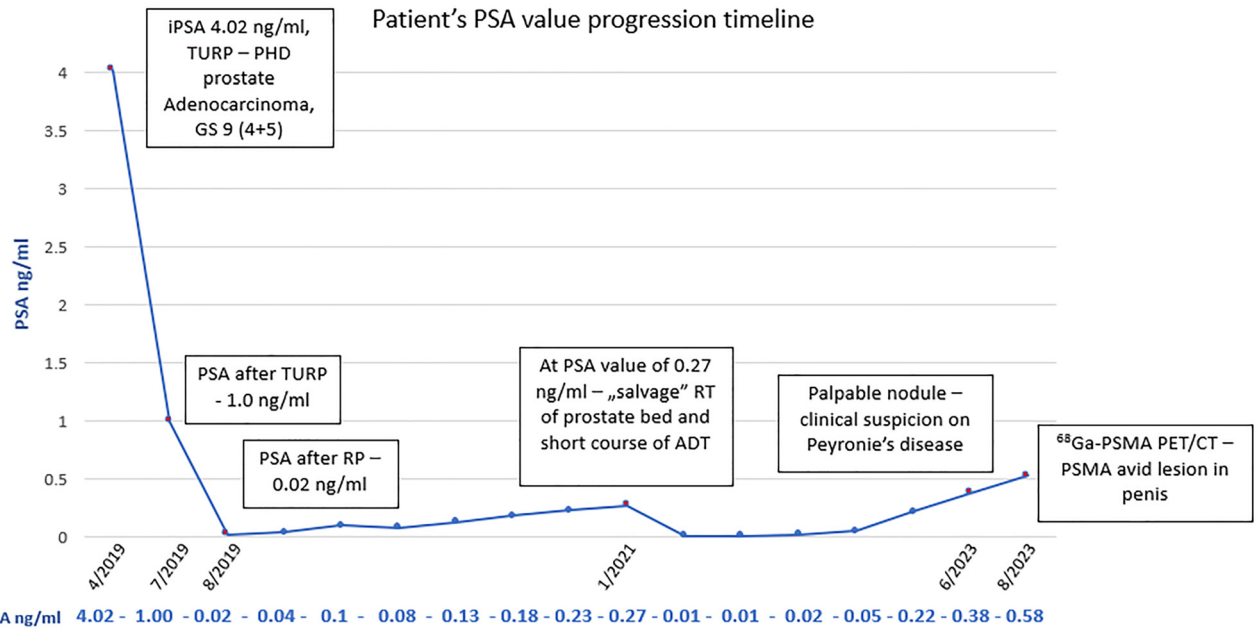

Fig. 1. Patient's progression and PSA levels from diagnosis up until [^{68}Ga]Ga-PSMA-11 PET/CT (iPSA – initial value of PSA; TURP – transurethral resection of the prostate; RP – radical prostatectomy)

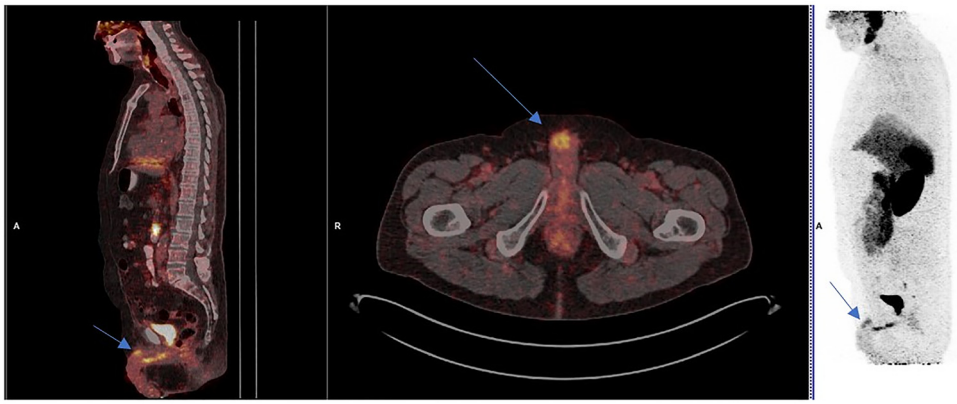

Fig. 2. [^{68}Ga]Ga-PSMA-11 PET/CT sagittal, transversal fused images and maximum intensity projection (MIP) image showing pathological [^{68}Ga]Ga-PSMA-11 uptake in the root of the penis (SUVmax 7,9). The physiological urethral activity of [^{68}Ga]Ga-PSMA-11 is seen caudal of metastasis, usually occurring in patients with a history of TURP and can mask or mimic disease recurrence. (PET Hot body colour scale; threshold 0 – 10 SUV-bw)

Discussion

Penile tissue metastases are exceedingly rare, despite the rich and intricate vascularization of the corpus cavernosum [3]. The earliest case of penile metastasis was reported by Eberth in 1870 [5]. A Japanese scientific review in 1997 described only 110 cases, with prostate cancer metastases accounting for 25 (23%) of them [6]. A comprehensive review conducted by Zhang et al. compiled 480 cases of penile metastases, with 143 cases of prostate cancer metastases (29.8%) [7].

In a retrospective study done by Tatkovic et al. out of 4,860 [^{68}Ga]Ga-PSMA-11 PET/CT studies reported, that the incidence of PC penile metastases was 0.1% [9]. This was the first case of PSMA-avid lesion detected in the penis at our clinic with more than 300 [^{68}Ga]Ga-PSMA-11 PET/CT scans done. Most literature describes these cases in patients with late-stage disseminated PC and being linked to poor prognosis. The survival time for patients with penile metastases varies widely from one to twenty-four months [6], averaging no longer than 1 year [7].

Both Peyronie's disease and prostate cancer metastases can have similar symptoms, including penile pain, palpable nodules, painful erections, and erectile dysfunction [6–11]. This underscores the need for clinicians to consider the possibility of penile metastases in older patients, particularly those with a history of biochemical recurrence in prostate cancer where serum PSA levels remain measurable.

Our case is exceptionally uncommon since penile metastasis developed over three and a half years after radical prostatectomy as part of an oligometastatic presentation of the disease. At the time of [^{68}Ga]Ga-PSMA-11 PET/CT scan, the PSA level was 0.58 ng mL^{-1} and even lower when the palpable nodule first appeared – 0.38 ng mL^{-1}.

Patients diagnosed with prostate cancer and penile metastases are categorized as stage M1c, representing an advanced stage associated with reduced survival rates. In this instance, the patient presented with oligometastatic disease characterized by a single PSMA-positive pelvic lymph node and penile metastasis, without indication of further disease spread. However, as penile metastasis is considered visceral, the patient was classified as M1c stage, and systemic therapy with long-lasting ADT was started.

Landen et al. [11] conducted a systematic review that revealed the lack of consensus on treatment approaches for patients with penile metastases. According to European Association of Urology guidelines, systemic therapy accompanied by long-lasting androgen deprivation therapy is the most commonly used treatment for these patients [4]. In the literature there are described cases of local excision, partial or complete penectomy, external beam radiotherapy, brachytherapy, and penile denervation, all depending on disease progression and clinical symptoms [11]. [^{177}Lu]Lu-PSMA therapy should also be very useful in the future, as most of the patients with penile metastasis have disseminated metastatic PC.

Conclusion

Our case affirms the importance of [^{68}Ga]Ga-PSMA-11 PET/CT in evaluating patients with prostate cancer, as it enables the detection of rare and unusual metastases. In patients with biochemical recurrence irrespective of PSA levels, or in those with a risk of undiagnosed cancer when clinical suspicion arises for Peyronie's disease, it is crucial to consider the differential diagnosis of penile metastasis.

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Ethical statement: The study protocol and content adhered to the guidelines outlined in the Declaration of Helsinki.

ABBREVIATIONS

ADT	androgen deprivation therapy
ART	adjuvant radiation therapy
BCR	biochemical recurrence
ECOG	Eastern Cooperative Oncology Group performance score
iPSA	initial value of PSA
ISUP/WHO	International Society of Urological Pathology/World health organisation
LHRH	luteinizing hormone-releasing hormone
MIP	maximum intensity projection
NKx3.1	homeobox protein/prostatic tumour suppressor gene
PSA	prostate-specific antigen
PSMA	prostate-specific membrane antigen
PSAP	prostatic specific acid phosphatase
pTNM	Pathological tumour-node-metastasis
RP	radical prostatectomy
SUVmax	maximum standardized uptake value
TURP	transurethral resection of the prostate
[^{68}Ga]Ga-PSMA-11 PET/CT	Gallium prostate-specific membrane antigen – 11 positron emission tomography/computed tomography

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