Case Report

Oligometastasis to testis in prostate cancer: Role of gallium-68 prostate-specific membrane antigen positron-emission tomography computed tomography

ABSTRACT

Accurate staging and restaging with early detection of recurrent site is the key for planning treatment in patients of prostate cancer. Recently, gallium-68 prostate-specific membrane antigen positron-emission tomography computed tomography (^{68}Ga-PSMA PET/CT) has emerged as a better tool for this. Few uncommon sites of early metastasis can also be identified in addition to the other common sites. Herein, we present three cases of early metastasis to testis in prostate cancer identified on ^{68}Ga-PSMA PET/CT scan.

Keywords: Gallium-68 prostate-specific membrane antigen positron-emission tomography computed tomography, oligometastasis, prostate cancer, testicular metastasis

INTRODUCTION

Prostate cancer is the second common cancer and the third leading cause of cancer-related deaths in men. Accurate staging and restaging with early detection of recurrence is the key for planning treatment. With the availability of gallium-68 prostate-specific membrane antigen positron-emission tomography computed tomography (^{68}Ga-PSMA PET/CT) and better lymph node staging, early identification of metastatic or recurrent sites has been documented in recent time in the literature. With this prostate cancer-specific molecular imaging, we are not only able to identify metastatic sites early, but also can detect few uncommon sites. Here, we present three cases of metastatic disease involving testis in prostate cancer.

METHOD

On analysis of 1860 ^{68}Ga-PSMA PET/CT scans which were done for various clinical indications from July 2014 to February 2020, we identified three patients with oligometastasis to the testis [Table 1]. In-house synthesis of ^{68}Ga-PSMA-11 was done as per company-specific protocol in IQS-Fluidic labeling module (iTG) using PSMA peptide GMP kits from advanced biochemical compounds (ABx, GmbH, Germany). 2 MBq/kg body weight of ^{68}Ga-PSMA was injected intravenously, and the patients were rested for 1 h in an isolation room. Plain water was allowed during the uptake period. A whole-body scan was performed on a dedicated full-ring hybrid PET-CT system (Biograph TruePoint40 with LSO crystal from Siemens Healthcare, USA) with 4 min/bed position starting from the base of the skull to the midthigh. A noncontrast-enhanced CT scan (100 mAs and 120 kVp) was used for attenuation correction and anatomical interpretation.

Manoj Gupta, Partha Sarathi Choudhury, Sudhir Rawal[1], Amitabh Singh[1]

Departments of Nuclear Medicine and [1]Uro-Gynae Surgical Oncology, Rajiv Gandhi Cancer Institute and Research Centre, New Delhi, India

Address for correspondence: Dr. Manoj Gupta, Department of Nuclear Medicine, Rajiv Gandhi Cancer Institute and Research Centre, Sector 5, Rohini, New Delhi - 110 085, India.
E-mail: docmanojgupta@yahoo.com

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Table 1: Clinical characteristics of the patients

Case	Gleason score	PSA (ng/ml) at the time of testicular lesion detected	Local symptoms related to testis	Time interval (Months) between testicular lesion detected on ^{68}Ga-PSMA PET/CT and the first diagnosis of prostate cance
1	9 (4+5)	13.2	No	43
2	9 (5+4)	79.3	No	<1
3	7 (4+3)	3.0	No	88

PSA: Prostate specific antigen, ^{68}Ga-PSMA PET/CT: Gallium-68 prostate specific membrane antigen positron emission tomography computed tomography

CASE REPORTS

Case 1

A 62-year-old male was diagnosed with prostate cancer in July 2013. His initial prostate-specific antigen (PSA) was 11.5 ng/ml, and bone scan was normal. He underwent high-intensity focused ultrasound and channel transurethral resection of prostate (TURP). Microscopic examination of channel TURP chips showed prostatic acinar adenocarcinoma and Gleason score of 9 (4 + 5). He was started on hormone therapy (goserelin acetate). His PSA reduced up to 0.102 ng/ml. On follow-up, he presented with hematuria and difficulty in passing urine in February 2017. His PSA level was 13.2 ng/ml. A ^{68}Ga-PSMA PET/CT was performed which revealed PSMA-avid lesion in the prostate with infiltration in the bilateral seminal vesicles, posterior urinary bladder wall, and anterior rectal wall (maximum standardized uptake value [SUV_{max}] 8.9). Focal PSMA uptake was also noticed in the right testis (SUV_{max} 10.4) and fifth lumbar vertebra [Figure 1]. Ultrasound of the scrotum showed a hypoechoic lesion in the right testis with internal vascularity [Figure 1]. The patient underwent bilateral orchiectomy, and the final histopathology confirmed right testicular metastasis. The left testis and epididymis were free of tumor. He was further treated with antiandrogen (bicalutamide) and developed disease progression within 12 months.

Case 2

A 77-year-old male was recently diagnosed with prostate cancer with a Gleason score of 9 (5 + 4) and PSA level of 79.38 ng/ml. A pelvic contrast magnetic resonance imaging revealed prostate lesion with the involvement of the bilateral seminal vesicles and bladder neck. Bone scan was normal. In view of high PSA level, he was referred for^{68}Ga-PSMA PET/CT to look for any site of metastasis. PET/CT scan revealed PSMA-avid prostate lesion involving

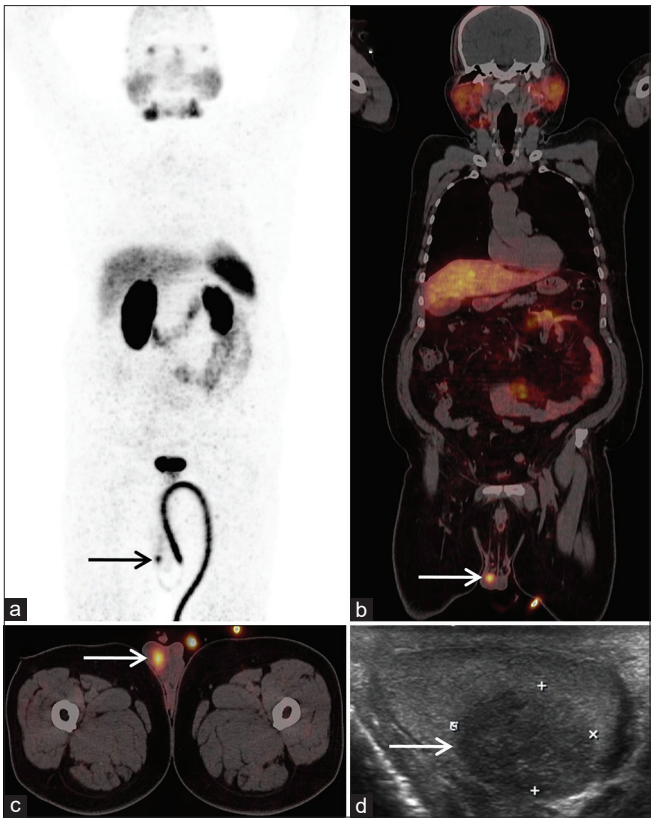

Figure 1: Gallium-68 prostate-specific membrane antigen positron-emission tomography computed tomography maximum intensity projection (a), fused coronal (b) and fused axial (c) images. Images showed prostate-specific membrane antigen-avid lesions in the prostate and right testis. A correlative ultrasonography of the scrotum showing a hypoechoic lesion in the right testis (d)

bilateral seminal vesicles (SUV_{max} 57.0), a right external iliac lymph node (size 1.0 cm × 0.9 cm, SUV_{max} 14.4), and focal PSMA uptake in the right testis (SUV_{max} 12.8) [Figure 2]. A mild focal PSMA uptake was also seen in the right iliac bone (SUV_{max} 3.2). In view of oligometastasis with locally advanced disease, the patient was started on hormone treatment.

Case 3

A 69-year-old male, diagnosed with prostate cancer, underwent open radical prostatectomy in October 2012. Histopathology was prostatic acinar adenocarcinoma Gleason score of 7 (4 + 3) with pelvic lymph node metastasis (pT3bN1). Subsequently, he was treated with hormone (goserelin acetate). On follow-up, his PSA started rising and reached to 0.456 ng/ml in September 2017. ^{68}Ga-PSMA PET/CT scan showed mild PSMA-avid thickening in the prostatic bed and a subcentimeter left external iliac lymph node (SUV_{max} 2.5). In view of biochemical recurrence, he was further treated with image-guided radiotherapy, and post therapy, his PSA reduced to 0.076 ng/ml. On follow-up, he again presented with raised PSA 3.0 ng/ml in February 2020. ^{68}Ga-PSMA

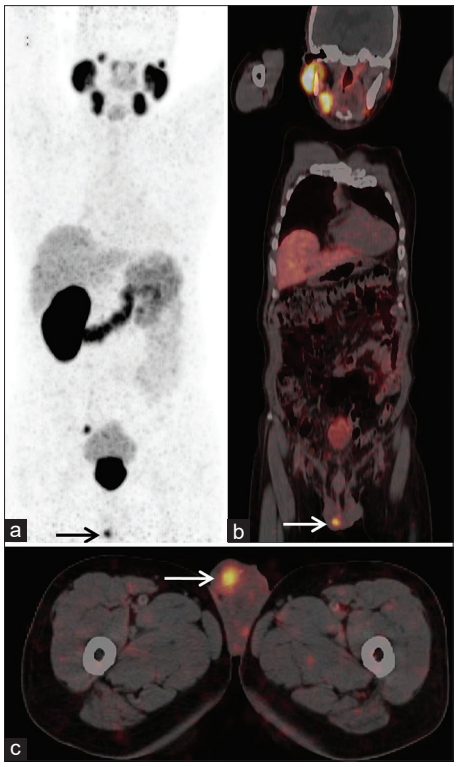

Figure 2: Gallium-68 prostate-specific membrane antigen positron-emission tomography computed tomography maximum intensity projection (a), fused coronal (b) and fused axial (c) images. Images showing prostate-specific membrane antigen-avid lesions in the prostate, right pelvic lymph node, and right testis

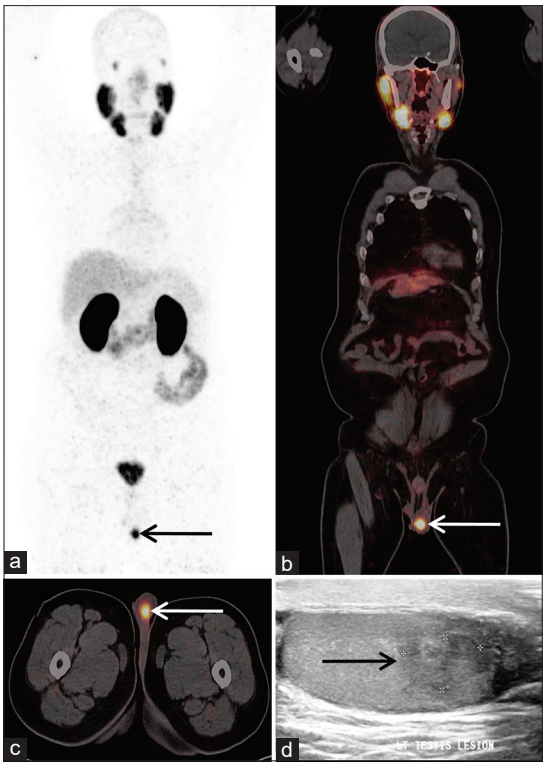

Figure 3: Gallium-68 prostate-specific membrane antigen positron-emission tomography computed tomography maximum intensity projection (a), fused coronal (b) and fused axial (c) images. Images showing a prostate-specific membrane antigen-avid lesion in the left testis. A correlative ultrasonography of the scrotum showing a hypoechoic lesion in the left testis (d)

PET/CT revealed focal PSMA-avid (SUV_{max} 24.2) lesion in the left testis [Figure 3]. Ultrasound of the scrotum showed a hypoechoic lesion in the left testis [Figure 3]. He was advised for bilateral orchiectomy, however the patient refused to undergo surgery. He was started on hormone treatment.

DISCUSSION

Testicular metastasis is an uncommon event and constitutes 0.02%–2.5% of all testicular malignancies. It is most commonly associated with prostate cancer (35.4%), followed by lung (19.7%), melanoma (9.4%), and colon (8.7%) cancers.[1] In general, it is associated with multiple sites of metastases and asymptomatic at presentation. Testicular metastasis has been diagnosed in 2%–4% of bilateral orchiectomy specimens in prostate cancer patients done for hormone control.[2] Various routes of testicular metastasis from prostate cancer have been considered, which include retrograde vein spreading or embolization, arterial embolization, and lymphatic or endocanalicular spread. Unilateral testicular involvement with laterality toward the left side has been reported in a recent autopsy study on 738 adult males with solid malignant neoplasm.[3] Even in prostate cancer, a preference toward left testicular metastasis has been reported in literature.[4] This favoritism may be attributed to the location of the primary tumor in the prostate or may be just by chance or attributed to an unidentified reason. In paradox to that, in our three cases, two were involving the right testis. We are not able to identify any cause of this favoritism as in our cases both lobes of the prostate were involved by the tumor. A high Gleason score (≥7) has been attributed to testicular metastasis, which is in line with our case series as well. This may indicate the aggressiveness of the primary tumor for metastasis as such. On literature search, we identified four cases of testicular oligometastasis reported on ^{68}Ga-PSMA PET/CT scan.[4-7] All these cases identified testicular metastasis following biochemical relapse. In one of our cases, testicular metastasis was also diagnosed at staging workup. However, histopathology was not available in two of our cases due to nonsurgical treatment plan.

CONCLUSIONS

We believe that the novel imaging ^{68}Ga-PSMA PET/CT will further improve staging and restaging of prostate cancer. Recognizing testis as noncustomary site of metastasis will

impact treatment planning and may also impact patient outcome.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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