Case Report

A Case Series Depicting PSMA Expression in Nonmalignant Lesions

Abstract

Prostate-specific membrane antigen (PSMA) is a widely accepted and used tracer in staging and biochemical recurrences of prostate cancer. PSMA is extensively expressed in normal prostatic epithelial cells and prostate cancer cells, with some amount of expression also in nonprostatic cells. False-positive PSMA uptake in nonmalignant lesions creates ambiguity in disease detection. In such cases, histopathological correlation and radiological follow-up assist in clinical decision-making. In this case series, we illustrate a few cases where PSMA uptake was incidentally found in some of the commonly occurring benign conditions.

Keywords: *Case series, nonmalignant, prostate-specific membrane antigen*

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Introduction

Prostate-specific membrane antigen (PSMA) is a type II transmembrane glycoprotein with apical membrane expression typically in normal prostatic epithelial cells and amplified expression in prostate cancer cells.[1] Physiological expression is also seen in renal tubules, lacrimal and salivary glands, and small intestine.[2] However, PSMA expression can also be seen in inflammation/infection, nonprostatic neoplastic cells, and nonprostatic tumor-associated neovasculature.[3] Endothelial and cytoplasmic PSMA expression is attributed to PSMA uptake in many nonprostatic tumor cells.[3] Nonspecific PSMA uptake in lesions unrelated to prostate cancer often mimics malignancy and gives rise to false positives. Here, we present a carefully curated series of cases where PSMA positron emission tomography (PET) is showing uptake in commonly seen incidentally detected benign lesions.

Case Reports

Skeletal lesions

Bone is the most common site of hematogenous metastases from prostate cancer. PSMA PET/computed tomography (PET/CT) is a very sensitive method for skeletal metastases detection. It outperforms bone scans in accuracy and sensitivity in detecting metastatic bone lesions.[4] Apart from PSMA uptake, other features of metastatic lesions include multiple sites, sclerosis, periosteal reaction, and soft-tissue mass. However, low-grade PSMA expression can also be present in benign bone lesions. Such lesions are generally solitary with well-demarcated margins and the absence of bone destruction or soft-tissue mass.

Case 1: Aneurysmal bone cyst

These are benign expansile osteoclastic giant cell-rich bony neoplasms composed of numerous blood-filled channels and cystic spaces.[5] On a CT scan, aneurysmal bone cysts are characterized as lucent bone lesions with a mean density higher than fat. It might also show cortical breach or soft-tissue extension [Figure 1].[6]

Case 2: Facetal arthropathy

Chronic low back pain (LBP) is the most common pain syndrome. Lumbar facet joints constitute a common source, accounting for 15%–45% of LBP. Facet joint degenerative osteoarthritis is the most frequent form of facet joint pain.[7] Degenerative arthritis in the vertebrae or peripheral joints might show mild-to-moderate PSMA uptake [Figure 2].[3]

Case 3: Nonspecific benign sclerotic lesion

Bone sclerosis is a very common finding on plain radiographs or CT scans and can often

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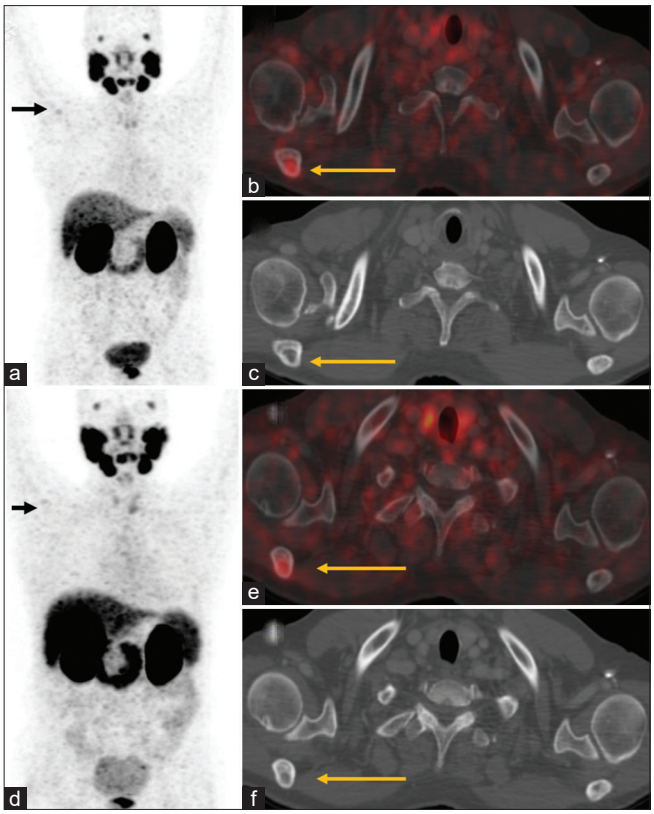

Figure 1: This is a case of a 70-year-old male patient with adenocarcinoma prostate (Gleason score 3+3=6) with a baseline serum PSA- 15.5 ng/ml. A 68Ga PSMA PET/CT scan reported increased tracer uptake in prostate and a well-defined lytic lesion in right scapula with low grade tracer uptake (SUVmax 4.37) (MIP (a), fused (b) & CT (c), respectively; arrows). Patient was kept on active surveillance. After 8 months, he presented with rising serum PSA (32.33 ng/ml) for which he underwent a repeat 68Ga PSMA PET/CT scan. The disease in prostate had no significant changes in size and PSMA uptake; nor, the right scapular lesion showed any increase in PSMA uptake (SUVmax 4.80) or lysis (MIP (d), fused (e) & CT (f), respectively; arrows). The patient also complained of vague pain in right shoulder region which remain unchanged. Biopsy from the scapular lesion suggested aneurysmal bone cyst

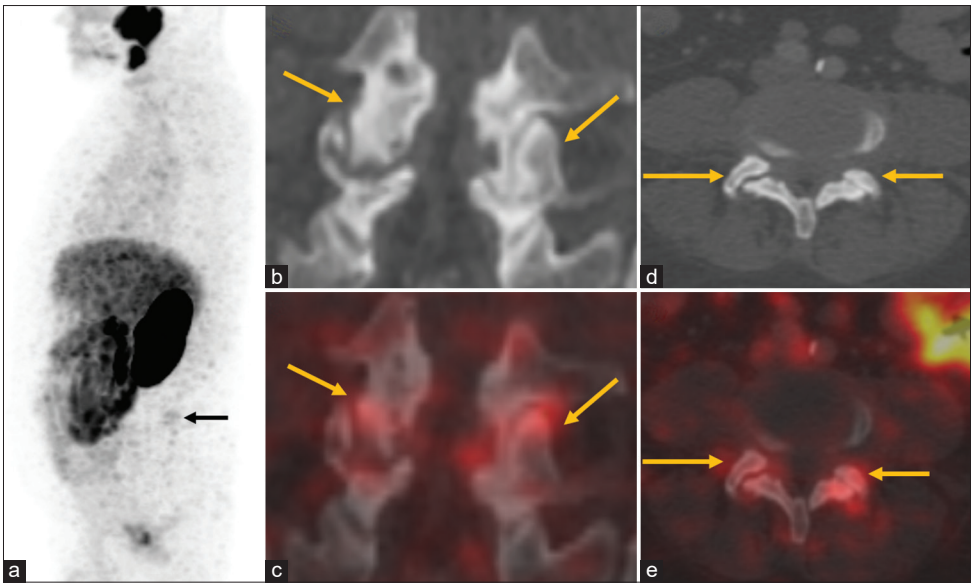

Figure 2: This is a case of a 70-year-old male with newly diagnosed adenocarcinoma prostate with Gleason score of 4+4=8 and a serum PSA of 6.5ng/ml. Baseline 68Ga PSMA PET/CT scan shows low grade tracer uptake (SUVmax 2.3) in bilateral facetal arthropathy involving L4-L5 and L5-S1 intervertebral facets displayed in the MIP (image a, black arrow), coronal and axial planes of CT (b & d; arrows) and fused (c & e; arrows) images, respectively

be challenging to diagnose. It can range from nonspecific findings to metastasis and represent various disease entities. Bentestuen M *et al.*, in their case report, showed how some benign bone lesions express low-grade PSMA uptake where a bone biopsy ruled out metastases [Figure 3].[8]

Benign thyroid nodule

A thyroid nodule is a discrete lesion within the thyroid gland that is radiologically distinct from the surrounding parenchyma. Nonpalpable nodules discovered on any anatomic imaging are termed as incidentally detected nodules.[9] Ultrasound is the modality of choice for thyroid lesion evaluation due to its superior spatial resolution compared to CT examinations.[10] Kanthan *et al.*, in their case report, presented PSMA-avid left thyroid nodule (maximum standardized uptake value [SUVmax]: 25.3 in comparison to 1.6 in normal right thyroid lobe) in a known case of prostate cancer. Biopsy from the thyroid nodule was follicular adenoma, emphasizing the importance of evaluating such lesions on PSMA PET to rule out co-existing thyroid neoplasm [Figure 4].[11]

Benign tumors

Case 1: Neurofibromatosis

It is a rare autosomal dominant disorder with neurological and cutaneous manifestations. It is of 2 types: Type I occurs in childhood and causes neurofibromas, cafe-au-lait macules, freckling, and optic gliomas. Type II typically occurs in adolescence or early adulthood and causes bilateral vestibular schwannomas and meningiomas.[12] Gulhane *et al.* presented a case of neurofibromatosis type 1 with variable PSMA uptake in multiple cutaneous neurofibromas [Figure 5].[13]

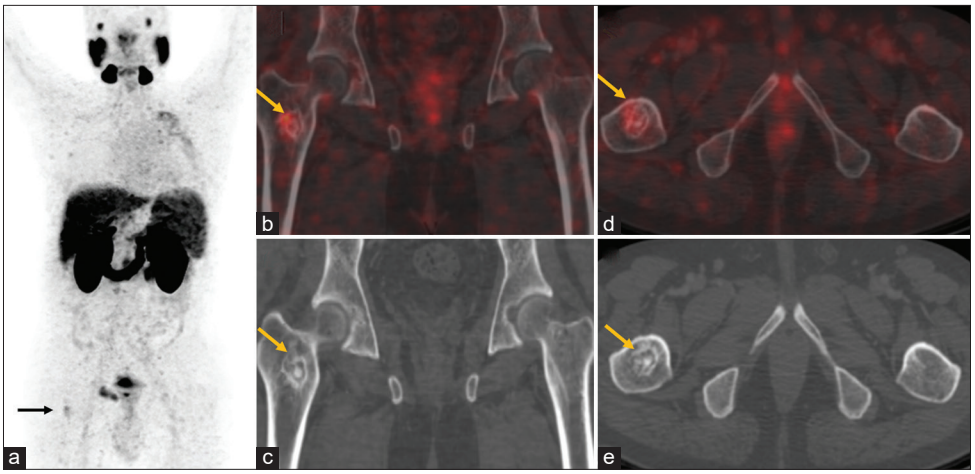

Figure 3: This is a case of a 56-year-old patient with adenocarcinoma prostate (Gleason score 4+5=9), post bilateral orchidectomy and TURP. 68Ga PSMA PET/CT scan was done for staging and MIP image (maximum intensity projection; a) shows focal low grade tracer uptake (SUVmax 2.67) in right femur (black arrow). The fused and CT images in coronal and axial planes show low grade uptake in a sclerotic focus surrounded by a well-defined sclerotic rim with intermittent osteolytic features. Radiologically, this lesion appears to be a benign skeletal lesion not otherwise specified (b-e; yellow arrows).

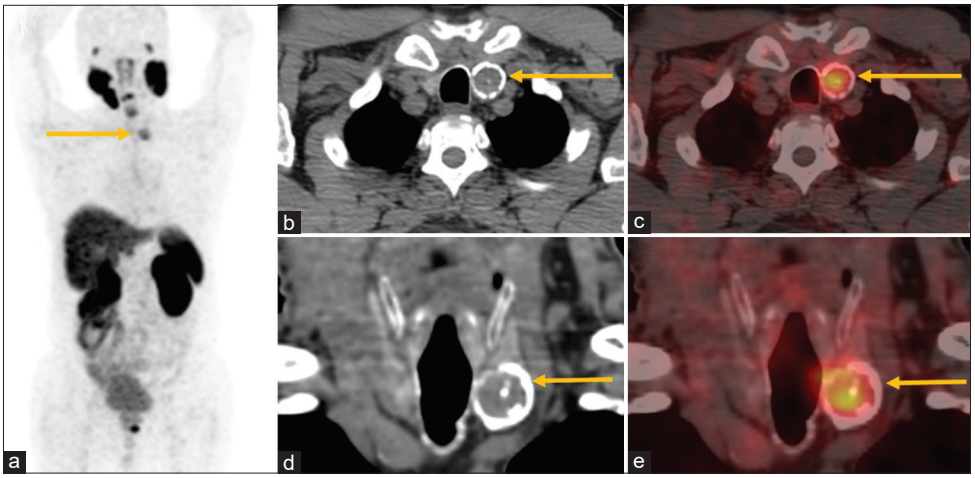

Figure 4: This is a case of a 73-year-old male, adenocarcinoma prostate with a Gleason score of 4+4= 8 and a baseline serum PSA level of 38.95 ng/ml. (a) of 68Ga PSMA PET/CECT scan done for staging shows increased tracer uptake in prostatic lesion (black arrow) and in the neck region (yellow arrow). CT and fused images in axial and coronal planes show increased tracer uptake in the hypodense nodular lesion with peripheral calcification involving left lobe of thyroid (SUVmax 8.17) (b-e; respectively). USG neck reported the lesion as benign and FNAC suggested Bethesda category II (benign).

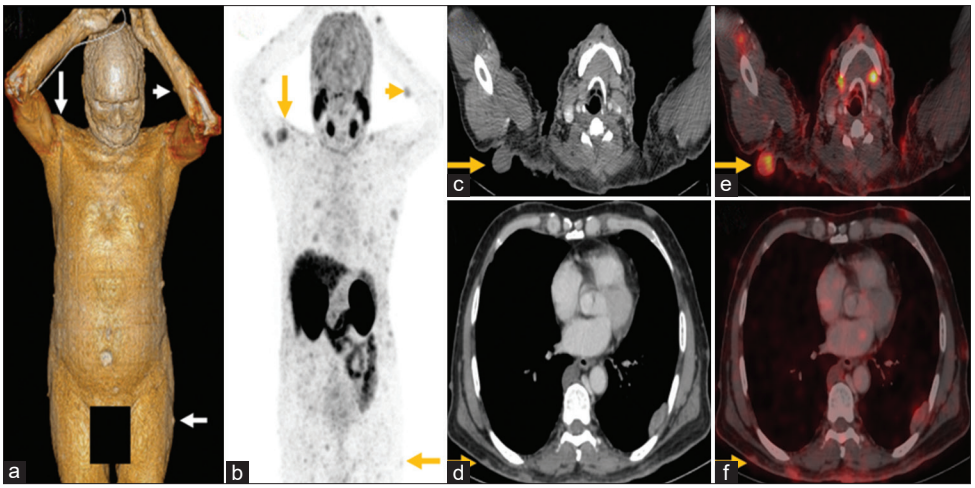

Figure 5: This is a 65-year-old male, known case of neurofibromatosis (NF type II), presented with urinary hesitancy, frequency for 1 month with one acute episode of urinary retention. Serum PSA- 14.98ng/ml. 68Ga PSMA PET/CT scan was advised and done. 3D volumetric reconstruction was performed on the CT scan for finer visualization of the cutaneous neurofibromas (a). MIP (Maximum Intensity Projection) image shows low grade PSMA expression in multiple neurofibromas (b; arrows); CT and fused images of cervical and thoracic regions in axial plane (c-f, respectively; arrows) show multiple PSMA expressing cutaneous, subcutaneous, thoracic and abdominal neurofibromas (SUVmax 7.39)

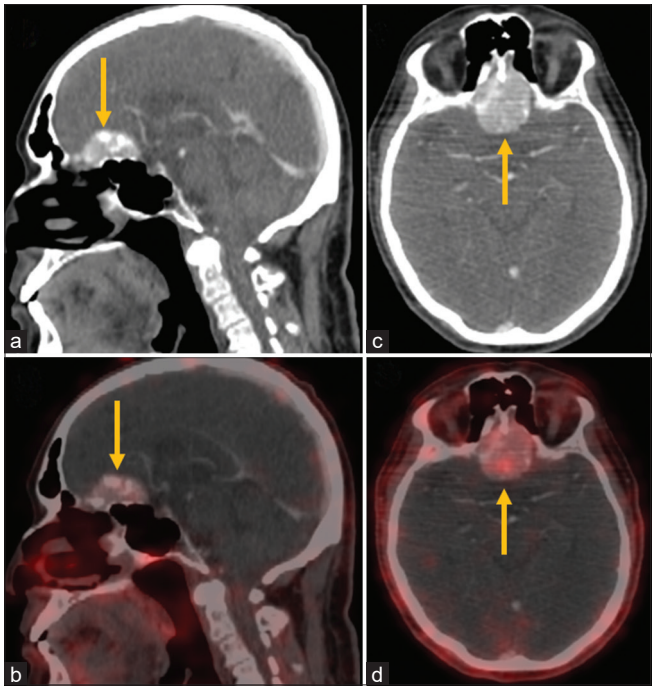

Figure 6: A 65-year-old male patient with adenocarcinoma prostate (Gleason score 4+4=8), serum PSA – 40 ng/ml, post TURP on androgen deprivation therapy was advised a 68Ga PSMA PET/CT scan which incidentally detected a well-defined enhancing dural based frontal lobe lesion with low grade tracer uptake (SUVmax 2.03) favouring meningioma (a-d; arrows)

Case 2: Meningioma

It is the most common type of primary central nervous system tumor.[14] These are extra-axial tumors arising from the meningothelial cells of the arachnoid membrane. Routine imaging modalities used for diagnosis include CT scan and magnetic resonance imaging; however, they also express high-density Somatostatin receptors (SSTR) receptors.[15] It has been studied that meningioma

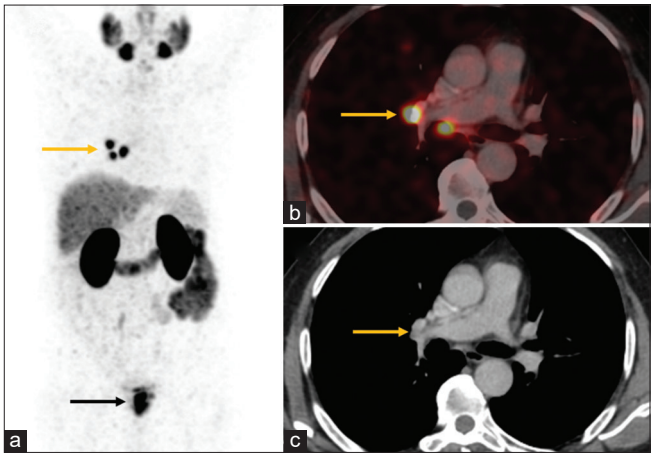

Figure 7: This is a case of a 61-year-old patient with adenocarcinoma prostate with Gleason score 4+5=9 and serum PSA of 51ng/ml. MIP image (a) of 68Ga PSMA PET/CECT scan done for baseline staging shows increased tracer uptake in the prostate (black arrow) and mediastinal nodes (SUVmax 14.23) (yellow arrow). No pelvic or retroperitoneal nodes were identified. Axial fused and CT images (b & c) shows elongated tiny sub cm sized mediastinal nodes. On the basis of location and morphology of these nodes and in the absence of any regional nodes, the mediastinal nodes were reckoned benign/infective. Patient received radiation therapy to the primary site following which he had falling PSA trend and is doing clinically well

specimens express PSMA within their endothelial cells.[16] This is a case where low-grade PSMA expression has been noted in a meningioma [Figure 6].

Infection/inflammation

Case 1: Mediastinal nodes

Malignancies that commonly metastasize to mediastinal nodes include carcinoma of the lung, esophagus, stomach, pancreas, testes, breast, and colon. Prostate cancer very rarely spreads to mediastinal nodes and occurs with advanced disease.[17] The most common causes of

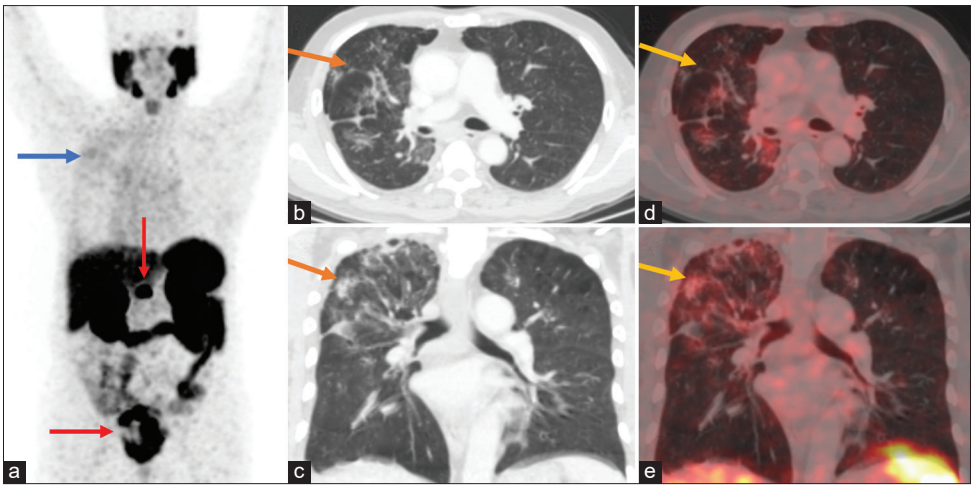

Figure 8: This is a case of a 72-year-old patient with adenocarcinoma prostate with Gleason score 4+4=8 and serum PSA of 208 ng/ml presented with back pain. 68Ga PSMA PET/CECT scan was done for staging. MIP image (a) shows increased tracer uptake in prostatic mass and lumbar vertebral lesion (red arrows), low grade tracer uptake (SUVmax 4.63) is seen in upper lobe of right lung (blue arrow). Fused and CT images in axial and coronal planes show low grade tracer uptake in a few patches of consolidation and ground-glass opacities with intermittent reticular thickening in right lung (b-e; respectively)

mediastinal adenopathy in India include tuberculosis, sarcoidosis, histoplasmosis, and lymphoma, and these should be ruled out before making the diagnosis of metastasis from prostate cancer.[18] PSMA uptake in inflammation can be explained by increased vascularity at such sites [Figure 7].[3]

Case 2: Infective lung changes

PSMA uptake is upregulated in inflammatory and infectious conditions due to neovascularization and increased vascular permeability.[3] Low-grade PSMA expression has been seen in lung infections such as pneumonia, inflamed pleural plaques, and atelectasis [Figure 8].[19]

Discussion

Nonprostatic diseases with PSMA uptake might pose a challenge in specific conditions mimicking malignancy. There are a few case series, case reports, and pictorial reviews available in the literature exhibiting PSMA uptake in nonmalignant conditions. In literature, the SUVmax ranges from 2.5 to 7 for benign findings which is close to the SUVmax values in this case series, i.e., 2–8 with one outlier having SUVmax of 14.23.[20] Clinicians must use a combination of morphological, molecular, and clinical aspects to answer such dilemmas. Awareness about normal physiological PSMA uptake patterns, variations in physiological biodistribution, and confounding uptake in nonprostatic malignancies or benign pathologies is essential. Knowledge of patterns of disease spread also needs to be considered, for example, skeletal metastases from high-risk prostate cancer cases generally are sclerotic and affect the pelvis and vertebral column.

Conclusion

PSMA is a routinely used tracer for imaging in prostate cancer, and careful consideration must be made to rule out nonspecific tracer uptake in benign lesions. Utilizing imaging features such as the intensity of uptake, CT characteristics, and clinical history is crucial in arriving at an accurate diagnosis. By incorporating these factors, clinicians can ensure that patients receive the best possible care and treatment.

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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