Case Report

Decoding positron emission tomography–computed tomography avidity in prostate cancer: Why metastases light up brighter than the primary tumor: A case-based insight

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ABSTRACT

Prostate cancer is one of the most common malignancies affecting men worldwide, with a substantial proportion presenting with or eventually developing metastatic disease. Molecular imaging using positron emission tomography–computed tomography, particularly with prostate-specific membrane antigen (PSMA)–based tracers, has significantly improved the detection and characterization of metastatic prostate cancer. We report the case of a 67-year-old male with high-risk prostate adenocarcinoma in whom metastatic lesions demonstrated markedly higher PSMA avidity than the primary tumor. This case highlights the biological heterogeneity between primary and metastatic disease, discusses the implications of differential tracer uptake on staging and treatment planning, and reviews relevant literature to explain this phenomenon.

Key words: Fluorodeoxyglucose positron emission tomography–computed tomography, Metastatic disease, Prostate cancer, Prostate-specific membrane antigen positron emission tomography–computed tomography, Tumor heterogeneity

Prostate cancer is the second most frequently diagnosed cancer and the fifth leading cause of cancer-related mortality among men globally [1]. The incidence increases with age, and although many cases follow an indolent course, a significant subset presents with aggressive features and metastatic spread at diagnosis. Bone and lymph nodes are the most common sites of metastases, and their early detection is crucial for accurate staging, prognostication, and therapeutic decision-making. Conventional imaging modalities, such as computed tomography (CT) and bone scintigraphy have limited sensitivity in detecting early or small-volume metastatic disease. The advent of molecular imaging, particularly prostate-specific membrane antigen (PSMA)-based positron emission tomography–CT (PET-CT), has revolutionized prostate cancer imaging by enabling visualization of disease based on tumor biology rather than anatomy alone [2,3]. Interestingly, several studies and case reports have noted that metastatic lesions often demonstrate higher tracer uptake than the primary prostate tumor.

The rationale for reporting this case is to illustrate this imaging phenomenon, explore the underlying biological mechanisms, and emphasize its clinical relevance in guiding personalized treatment strategies.

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CASE REPORT

A 67-year-old male presented with complaints of progressive lower back pain and increased urinary frequency for 6 months. There was no history of hematuria, weight loss, or neurological deficits. He had no significant past medical or surgical history and no known family history of malignancy.

Abdominal and respiratory system examinations were unremarkable. Digital rectal examination revealed an enlarged, hard, irregular, and nodular prostate with obliteration of the median sulcus, suggestive of malignancy.

Serum prostate-specific antigen (PSA) level was markedly elevated at 112 ng/mL. Multiparametric magnetic resonance imaging of the prostate demonstrated a 4.2 cm lesion involving the peripheral zone with extracapsular extension, corresponding to a PI-RADS 5 lesion. Transrectal ultrasound-guided prostate biopsy confirmed adenocarcinoma of the prostate with a Gleason score of 4 + 5 = 9 (Grade Group 5), consistent with high-risk disease. Given the high PSA level and

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aggressive histology, staging with 68Ga-PSMA PET-CT was performed. Imaging (Fig. 1) revealed mild PSMA uptake in the primary prostate lesion (SUVmax 8.2), while multiple metastatic sites demonstrated intense tracer avidity. These included enlarged pelvic and para-aortic lymph nodes (SUVmax 12.6) and multiple skeletal metastases involving the vertebrae and pelvic bones (SUVmax 17.4).

The patient was initiated on androgen deprivation therapy (ADT) using a luteinizing hormone-releasing hormone analogue along with a second-generation androgen receptor pathway inhibitor (abiraterone acetate). Considering the high PSMA expression in metastatic lesions, he was evaluated for eligibility for 177Lu-PSMA radioligand therapy as a potential future option. At the 6-month follow-up, the patient showed significant clinical improvement with a reduction in back pain and urinary symptoms. Serum PSA levels declined to 8.4 ng/mL. Follow-up PSMA PET-CT demonstrated a partial metabolic response, with reduced tracer uptake in bone metastases and stable nodal disease.

DISCUSSION

This case demonstrates a striking disparity in PSMA tracer uptake between the primary prostate tumor and metastatic lesions, a finding that has been increasingly recognized in the era of molecular imaging [2,4]. The disparity in tracer avidity between the primary tumor and metastases raises important diagnostic and biological considerations. PSMA overexpression in metastases is a key factor, as metastatic lesions often exhibit higher PSMA expression compared to the primary tumor due to tumor dedifferentiation, hypoxia-induced PSMA upregulation, and alterations in the tumor microenvironment. In addition, increased neovascularity at metastatic sites facilitates greater delivery and retention of PSMA radiotracers, resulting in higher SUV values [1,2,4].

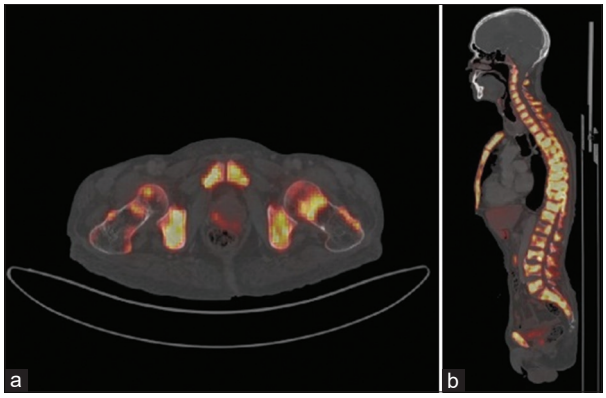

Figure 1: (a) Axial fused positron emission tomography–computed tomography (PET/CT) image at the level of the pelvis showing intense Fluorodeoxyglucose uptake in multiple sites, such as bilateral proximal femora and acetabula and primary tumor site prostate with SUVmax 8.2. (b) Sagittal fused PET/CT image showing multiple hypermetabolic foci throughout the axial skeleton, including the vertebral column and pelvic bones, indicative of widespread skeletal involvement with SUVmax 17.4, likely metastatic disease

Fluorodeoxyglucose (FDG) PET-CT considerations are also relevant, particularly in poorly differentiated or castration-resistant prostate cancer. Such tumors rely increasingly on glycolytic metabolism (the Warburg effect), making FDG PET-CT more informative in advanced disease states [5,6]. In contrast, the primary tumor may retain partial glandular differentiation and androgen sensitivity, leading to relatively lower glucose metabolism and reduced FDG uptake compared with metastatic deposits.

Clinical implications for treatment planning are significant. Higher tracer uptake in metastatic lesions generally reflects aggressive tumor biology and a higher disease burden, thereby influencing therapeutic decisions, such as early initiation of intensified ADT, addition of chemotherapy or androgen receptor pathway inhibitors, and selection of patients for PSMA-targeted radioligand therapy [4,5,7]. Furthermore, higher SUVmax values in metastatic sites have been associated with poorer prognosis and potential resistance to conventional therapies, emphasizing the prognostic value of molecular imaging parameters in advanced prostate cancer. Metastatic lesions, particularly in bone, may have increased neovascularization and altered stromal interactions, facilitating higher radiotracer delivery and retention. In contrast, the primary tumor may retain partial glandular differentiation, resulting in comparatively lower PSMA expression and tracer uptake.

Several previous case reports and series have documented similar findings, where metastatic lesions demonstrated higher PSMA or FDG avidity than the primary tumor [3,8,9]. This phenomenon has important clinical implications, as it underscores the role of PSMA PET-CT in detecting occult metastatic disease and in selecting patients for targeted therapies, such as radioligand treatment. High SUVmax values in metastatic sites have also been associated with poorer prognosis and higher tumor burden.

Differential diagnoses for intense PSMA-avid lesions include benign conditions, such as fractures, degenerative bone disease, Paget's disease, and inflammatory lymphadenopathy, as well as other malignancies that may show PSMA expression, including renal cell carcinoma and hepatocellular carcinoma [2,10,11]. Correlation with clinical findings, anatomical imaging, and PSA levels is therefore essential to avoid misinterpretation.

Finally, this case highlights the importance of integrating molecular imaging findings with clinical and pathological data to guide management. The demonstration of high PSMA expression in metastases supported the use of intensified systemic therapy and consideration of PSMA-targeted radioligand therapy, reflecting a move toward precision oncology in advanced prostate cancer [4,5].

CONCLUSION

Metastatic prostate cancer may demonstrate significantly higher PSMA avidity than the primary tumor due to biological heterogeneity, tumor dedifferentiation, and microenvironmental factors. PSMA PET-CT plays a pivotal role in accurately staging disease, assessing tumor burden, and guiding individualized treatment strategies. Awareness of this imaging pattern and its differential diagnoses is essential for optimal interpretation and clinical decision-making.

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