Acta Radiologica Open
13(2) 1–4

DOI: 10.1177/20584601241240318
journals.sagepub.com/home/arr
Sage

Intense prostate-specific membrane antigen receptor expression in coronary artery pypass graft scar tissue: A potential molecular imaging pitfall

Akram Al-Ibraheem[1], Ahmed Saad Abdlkadir[1], Nabeela Al-Hajaj[1], Aysar Khalaf[2] and Samer Salah[3]

Abstract

^{68}Gallium-PSMA positron emission tomography/computer tomography has been utilized recently for the diagnosis and staging of prostate cancer. PSMA is a transmembrane protein that is expressed not only in the prostate gland but also in other tissues. While some pitfalls have been addressed, there are still uncertainties. Herein, we report a 79-year-old male with prostate cancer who underwent a PSMA scan after coronary artery bypass graft surgery, revealing disease progression and PSMA-avid foci at the surgical stitch sites. This report discusses the immunohistochemical and molecular imaging mechanisms underlying PSMA expression in surgical scar tissues, providing critical insights for optimizing radiologic reporting in such situations.

Keywords

^{68}GA-PSMA, pitfall, PSMA-avid scar, PSMA in CABG, unaddressed pitfalls, prostate cancer

Received 26 August 2023; accepted 4 March 2024

Introduction

Prostate cancer is the second most prevalent malignant neoplasm in men worldwide.[1] Currently, this challenging disease is experiencing a rise in its occurrence, emphasizing the growing necessity for personalized management.[2,3] To date, many developed and developing countries rely on ^{68}Gallium prostate-specific membrane antigen (^{68}Ga-PSMA) positron emission tomography/computed tomography (PET/CT) imaging to stage and monitor patients with prostate cancer.[4,5] This novel modality provides a comprehensive assessment of the entire body, offering valuable insights into the disease extent.[6] It has revolutionized the evaluation of the disease by enabling the detection of primary and recurrent lesions, as well as subtle metastatic sites.[7] It also showed superiority in evaluation of hybrid synchronous histopathologies as well as patients with multiple primary neoplasms.[8–10] The mechanism behind the uptake and localization of PSMA by cancer cells involves the overexpression of PSMA antigen on their surface, allowing for targeted binding and internalization of PSMA-targeted agents.[11] However, the specificity of PSMA is not absolute. PSMA expression has been observed in various non-prostatic malignancies, affecting its diagnostic accuracy.[10] It can also be expressed in benign conditions and can

[1]Department of Nuclear Medicine, King Hussein Cancer Center (KHCC), Amman, Jordan
[2]Warith International Cancer Institute, Karbala, Iraq
[3]Department of Medicine, King Hussein Cancer Center (KHCC), Amman, Jordan

Corresponding author:
Akram Al-Ibraheem, Department of Nuclear Medicine, King Hussein Cancer Center (KHCC), Queen Rania Street, Amman 11941, Jordan.
Email: akramalibrahim@gmail.com

occur in postsurgical and reactive scenarios, potentially compromising the reliability of PSMA-based imaging.[10] These factors highlight the importance of cautious interpretation when relying solely on PSMA-based imaging in clinical decision making. In this case report, we present a patient with prostate cancer who exhibited PSMA localization at the sites of coronary artery bypass graft (CABG) stitches, which is an unexpected location for PSMA expression. To our knowledge, this is the first reported instance of multifocal PSMA expression at the site of CABG surgery. This case also provides insights into the molecular and histopathological perspectives of this distinctive pattern of PSMA expression.

Case report

Clinical history

A 79-year-old male patient with a history of prostate cancer underwent multiple lines of therapy. These included bilateral surgical castration orchiectomy performed about 8 years ago, followed by salvage radiotherapy and 1 year of androgen deprivation therapy, resulting in complete remission up until a year ago. Recently, the patient experienced a myocardial infarction and subsequently underwent CABG surgery. Six months following the surgery, a ^{68}Ga-PSMA PET/CT scan was requested to assess disease status after a marginal rise in PSA (from 1 ng/mL to 3.2 ng/mL).

Imaging findings

The ^{68}Ga-PSMA PET/CT study revealed evidence of a few enlarged abdominopelvic lymphadenopathy (LAP) indicating disease recurrence. These PSMA-avid metastatic LAP were found involving right external iliac, para-aortic, and aortocaval regions (Figure 1). In addition, sagittal PET and sagittal PET/CT images of the chest revealed recent ancillary evidence of multifocal PSMA lesions localized within CABG surgical stitches (Figure 1). The maximum standardized uptake value (SUVmax) was high (up to 11.2). The patient's clinical scenario was discussed in a multidisciplinary clinic in order to establish a course of action. Due to the patient's clinical condition and low level of prostate-specific antigen (PSA), obtaining histopathologic confirmation from the CABG site was deemed burdensome and invasive. Instead, it was preferred to rely on biochemical correlation by measuring alkaline phosphatase levels and regularly monitoring PSA. With the exception of a minor elevation in PSA, all other laboratory tests yielded normal results. When correlated with the patient's past surgical history, it was confirmed that this expression is attributable to non-neoplastic surgical scar PSMA tissue uptake. The patient is currently scheduled to receive hormonal therapy and maintain regular follow-up until adequate disease control is achieved.

Discussion

After a thorough analysis of the patient's ^{68}Ga-PSMA PET/CT images, an initial suspicion of metastatic involvement might arise. While rare, cutaneous metastases typically present with a more superficial localization and irregular demarcations.[12] When they occur, these cutaneous manifestations often appear as numerous dispersed lesions, distributed in a non-uniform manner.[12] Common sites include the lower abdomen, thighs, and scrotum, with occasional extension to the chest, back, and face.[13] In most cases, cutaneous lesions present as multiple rubbery nodules or plaques, occasionally as solitary nodules, and rarely as edematous areas or non-specific rashes.[13,14] However, in this particular case, the observed pattern differs from these characteristic attributes as the PSMA-avid foci exhibit a consecutive and deeper distribution. Additionally, in this instance, the possibility of bone metastases can be dismissed from consideration. It is important to highlight that the patient did not encounter specific localized bone discomfort, and the CT scans did not reveal any radiologic signs to indicate bone metastasis. Equally important is the lack of a significant increase in PSA levels and the absence of an elevation beyond normal levels in alkaline phosphatase levels, effectively ruling out these two potential causes.

In certain clinical situations, the adoption of an alternative radiotracer in molecular imaging can prove advantageous in mitigating the occurrence of false-positive findings in instances of diagnostic uncertainty. For such contexts, the utilization of ^{11}C-choline PET/CT represents a viable approach. ^{11}C-choline PET/CT can detect recurrent prostate cancer sites based on phosphatidylcholine synthesis, a constituent of the cell membrane in prostate cancer.[15] Conversely, surgical scars, primarily comprising collagen, exhibit dissimilar cellular characteristics in comparison to neoplastic tissue. Therefore, it is improbable that ^{11}C-choline PET/CT would manifest substantial radiotracer uptake within surgical scar tissue.

^{68}Ga-PSMA PET/CT is an effective imaging modality that offers comprehensive evaluation of the prostate, lymph nodes, soft tissues, and bones.[4] Compared to traditional imaging methods, ^{68}Ga-PSMA PET/CT demonstrates higher levels of sensitivity and specificity, making it a valuable tool in the staging of high-risk prostate cancer and the detection of oligometastatic disease during biochemical recurrence.[16] This is not applicable in all scenarios; for example, the specificity of ^{68}Ga-PSMA PET/CT tends to be underwhelmed by various pitfalls that become increasingly unraveled with time. Inflammatory and infective conditions can mimic PSMA-avid lesions, but these can often be distinguished based on morphologic criteria seen on CT images.[16] For instance, subcutaneous multifocal PSMA-avid lesions have been reported in patients with prostate cancer, which were later identified as angiolipomas through

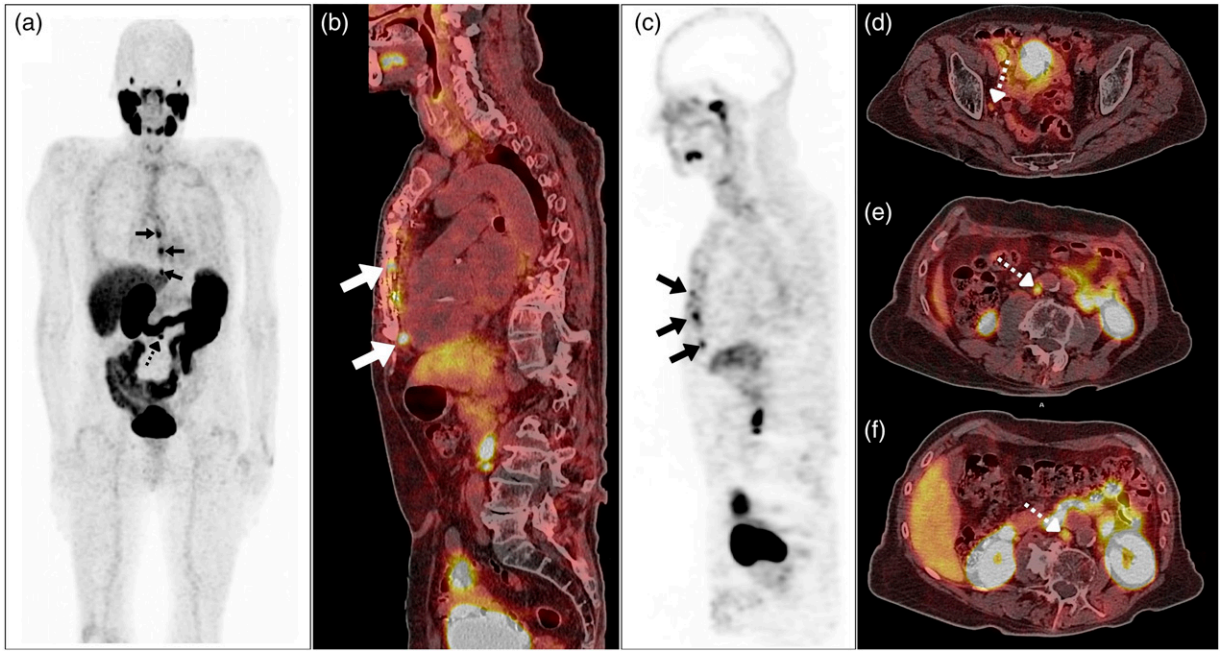

Figure 1. A gallium-68 prostate-specific membrane antigen (^{68}Ga-PSMA PET/CT) scan was performed for a 79-year-old man 6 months after coronary artery bypass graft (CABG) surgery. (a) Maximum intensity projection; (b) sagittal PET/CT; and (c), sagittal PET images showed multiple PSMA avid foci at the site of CABG surgical stitches with the maximum standardized uptake value (SUVmax: 11.2) (arrows). Increased PSMA expression in abdominal lymph nodes was also observed (dotted arrow). (d)-(f) Axial PET/CT images of abdominopelvic regions revealed evidence of a few PSMA-avid enlarged abdominopelvic lymphadenopathy (LAP), indicating nodal disease recurrence. These PSMA-avid metastatic LAP were found involving the right external iliac, para-aortic, and aortocaval regions, with SUVmax values of 3.6, 10.1, and 7.3, respectively (dotted arrows).

histopathological examination.[17] Non-specific PSMA uptake at sites of recent surgical interventions, such as hernia repair with mesh grafting, has also been reported.[18] Clinical history correlation can be helpful in identifying and understanding these pitfalls. Immunohistochemistry (IHC) studies have shown that PSMA expression is associated with angiogenesis and vasculogenesis, which contributes to the discriminative power of PSMA PET/CT compared to contrast-enhanced magnetic imaging resonance (CEMRI). PSMA PET/CT has been successful in detecting local prostatic recurrence 5 years after prostatectomy that was initially misinterpreted as postsurgical scar on CEMRI.[19] Same evidence was also endorsed by patient with non-prostatic Juvenile Nasopharyngeal Angiofibroma.[20] Post-operative PSMA PET/CT was helpful in accurately and sharply depicting tumor contour for LRT planning while MRI failed to do so due to post-inflammatory scarring.[20]

This advantage was not seen ultimately in all previous reports as evidence by IHC suggested that PSMA expression could be found in non-neoplastic reparative and regenerative scar tissues.[21] Focal PSMA expression was observed in non-neoplastic scar tissues, with varying degrees of intensity.[21] The pattern of expression denoted was focal and nearly half of the positive cases had weak expression, and the other half had strong expression. Recent observations have shown mild PSMA expression at the site of surgical scars using ^{68}Ga-PSMA PET/CT.[22] In our reported case, multifocal PSMA-avid foci were observed following CABG surgery, showing intense PSMA expression (SUVmax up to 11.2).

In conclusion, the presence of focal PSMA uptake at sites of surgical intervention should not be automatically attributed to prostate cancer. Careful clinical and biochemical correlation is necessary to make accurate interpretations. Such approach can help reach definitive diagnosis in uncertain cases and when biopsy seems impractical.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Akram Al-Ibraheem https://orcid.org/0000-0002-0978-4716
Ahmed Saad Abdlkadir https://orcid.org/0000-0002-2009-5110

References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71: 209–249.
2. Withrow D, Pilleron S, Nikita N, et al. Current and projected number of years of life lost due to prostate cancer: a global study. Prostate 2022; 82: 1088–1097.
3. Al-Ibraheem A, Scott AM. 161Tb-PSMA unleashed: a promising new player in the theranostics of prostate cancer. Nucl Med Mol Imaging 2010; 2023: 1–4.
4. Cerci JJ, Fanti S, Lobato EE, et al. Diagnostic performance and clinical impact of 68Ga-PSMA-11 PET/CT imaging in early relapsed prostate cancer after radical therapy: a prospective multicenter study (IAEA-PSMA Study). J Nucl Med 2022; 63: 240–247.
5. Al-Ibraheem A. Theranostics in developing countries: addressing challenges and potentials from training to practice. World J Nucl Med 2023; 22(3): 171–173.
6. Al-Ibraheem A, Abuhijla F, Salah S, et al. The influence of 68Ga-prostate-specific membrane antigen PET/computed tomography on prostate cancer staging and planning of definitive radiation therapy. Nucl Med Commun 2021; 42: 811–817. DOI: 10.1097/MNM.0000000000001394.
7. Zhou J, Wu R, Wang W, et al. 68Ga-PSMA PET/CT for the evaluation of metastasis in patients with prostate cancer: a systematic review and meta-analysis. Hell J Nucl Med 2022; 25: 297–311.
8. Al-Ibraheem A, Al-Adhami DA, Abdlkadir AS, et al. Molecular imaging in recurrent prostate cancer presented as a mixed small neuroendocrine tumor/acinar adenocarcinoma. Nucl Med Mol Imaging 2010; 2023: 1–3.
9. Al-Ibraheem A, Hammoudeh R, Kasasbeh N, et al. Synchronous colorectal and prostate cancer: dual PET/CT approach for detecting and distinguishing metastatic patterns. Nucl Med Mol Imaging 2010; 2023: 1–4.
10. Ozcan PP, Serdengectı M, Koc ZP, et al. Cancers and benign processes on 68Ga PSMA PET-CT imaging other than prostate cancer. World J Nucl Med 2022; 21: 106–111.
11. Wang F, Li Z, Feng X, et al. Advances in PSMA-targeted therapy for prostate cancer. Prostate Cancer Prostatic Dis 2022; 25: 11–26.
12. Dills A, Obi O, Bustos K, et al. Cutaneous metastasis of prostate adenocarcinoma: a rare presentation of a common disease. J Investig Med High Impact Case Rep 2021; 9: 2324709621990769.
13. Wang SQ, Mecca PS, Myskowski PL, et al. Scrotal and penile papules and plaques as the initial manifestation of a cutaneous metastasis of adenocarcinoma of the prostate: case report and review of the literature. J Cutan Pathol 2008; 35: 681–684.
14. Habermehl G, Ko J. Cutaneous metastases: a review and diagnostic approach to tumors of unknown origin. Arch Pathol Lab Med 2019; 143: 943–957.
15. Schuster DM, Nanni C, Fanti S. PET tracers beyond FDG in prostate cancer. Semin Nucl Med. Amsterdam, Netherlands: Elsevier, 2016, pp. 507–521.
16. Malan N, Vangu M-d-T. Normal variants, pitfalls, and artifacts in Ga-68 prostate specific membrane antigen (PSMA) PET/CT imaging. Front Nucl Med 2022; 2: 2.
17. Wang L, Tang Y, Yin H, et al. 18F-PSMA-1007 PET/CT uptake in multiple angiolipomas caused by PSMA expression in capillaries: a case report. Transl Androl Urol 2021; 10: 991.
18. de Galiza Barbosa F, Queiroz MA, Nunes RF, et al. Non-prostatic diseases on PSMA PET imaging: a spectrum of benign and malignant findings. Cancer Imag 2020; 20: 23. DOI: 10.1186/s40644-020-00300-7.
19. Harris N, Tan MY, Ng M, et al. PSMA-PET detection of unusual metastases in castrate-sensitive prostate carcinoma. Clin Nucl Med 2023; 48: 85–89. DOI: 10.1097/RLU.0000000000004469.
20. Sakthivel P, Thakar A, Prashanth A, et al. Clinical applications of 68 Ga-PSMA PET/CT on residual disease assessment of juvenile nasopharyngeal angiofibroma (JNA). Nucl Med Mol Imaging (2010) 2020; 54: 63–64.
21. Gordon IO, Tretiakova MS, Noffsinger AE, et al. Prostate-specific membrane antigen expression in regeneration and repair. Mod Pathol 2008; 21: 1421–1427. DOI: 10.1038/modpathol.2008.143.
22. Keidar Z, Gill R, Goshen E, et al. 68Ga-PSMA PET/CT in prostate cancer patients–patterns of disease, benign findings and pitfalls. Cancer Imag 2018; 18: 1–8.