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Diagnosing small bowel carcinoid tumor in a patient with oligometastatic prostate cancer imaged with PSMA-Targeted [^{18}F] DCFPyL PET/CT: Value of the PSMA-RADS-3D Designation

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ABSTRACT

Radiotracers targeting prostate-specific membrane antigen (PSMA), including [^{18}F]DCFPyL, have been extensively investigated as a means to image prostate cancer more accurately. We present the case of a man with oligometastatic prostate cancer who was also diagnosed with a metastatic small bowel carcinoid tumor following the detection of indeterminate findings on a [^{18}F]DCFPyL PET and discuss how this case highlights the utility of a newly proposed reporting system for PSMA-targeted PET (PSMA-RADS version 1.0).

Introduction

Prostate-specific membrane antigen (PSMA) is a cell surface protein that is highly expressed on prostate cancer epithelial cells; as such, it has been extensively studied as a target for the molecular imaging of prostate cancer.[1] As PSMA-targeted imaging with small molecule radiotracers appropriately labeled for positron emission tomography (PET) has become widespread throughout much of the world, the interpretive pitfalls of this new imaging modality have begun to come to light.[2] Among these pitfalls are findings that have radiotracer uptake but represent a process other than prostate cancer, including non-prostate malignancies,[3] and important findings that lack radiotracer uptake but demonstrate abnormalities on accompanying anatomic imaging.[4] The proper management of patients being imaged with PSMA-targeted PET will often rely on the correct interpretation of these pitfalls, and for this purpose our group has recently proposed a systematic method (PSMA-RADS Version 1.0) to categorize findings on PSMA-targeted PET including recommendations for appropriate follow-up.[5]

In the following report, we present the case of a patient with high-risk prostate cancer who presented for a systemic staging examination with the PSMA-targeted radiotracer [^{18}F]DCFPyL and was found to harbor a second malignancy that was not radiotracer avid. The importance of recognizing suspicious findings on anatomic imaging that lack radiotracer uptake and the utility of PSMA-RADS in this context are highlighted.

Case presentation

A 65 year old man presented with a prostate specific antigen (PSA) level of 5.7 ng/mL. Prostate biopsy showed Gleason 4 + 4 = 8 adenocarcinoma, and a digital rectal examination was consistent with stage T1c disease. Consistent with NCCN guidelines for high risk patients (Gleason ≥8) a staging computed tomography (CT) scan was obtained and showed an enlarged 2.0 cm short axis lymph node between the common iliac vasculature just below the aortic

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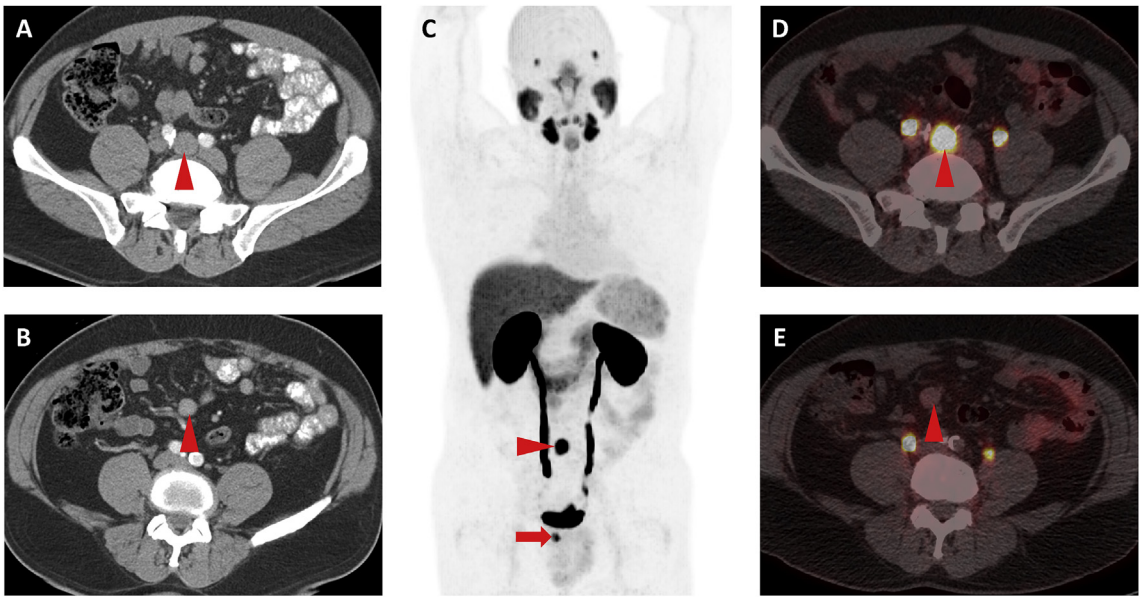

Fig. 1. (A) Axial contrast-enhanced CT image through the upper pelvis, inferior to the aortic bifurcation, demonstrating an enlarged (2.0 cm short axis) lymph node between the common iliac vasculature (arrowhead). (B) More superiorly, an axial contrast-enhanced CT image demonstrates mesenteric adenopathy with lymph nodes measuring up to 1.6 cm in short axis (arrowhead). (C) Maximum intensity projection image from a [^{18}F]DCFPyL PSMA-targeted PET study in which the lymph node inferior to the aortic bifurcation shows intense radiotracer uptake (arrowhead) and the patient's primary prostate cancer is also visible (arrow). Although there is overlapping small bowel with normal radiotracer uptake, there is no focal central abdominal uptake to suggest that the mesenteric adenopathy is radiotracer-avid. (D) Axial PET/CT fused image from the [^{18}F]DCFPyL study again showing the intense uptake in the lymph node inferior to the aortic bifurcation (arrowhead). (E) Axial PET/CT image from the [^{18}F]DCFPyL study at the level of the mesenteric adenopathy demonstrates no radiotracer uptake above background (arrowhead).

bifurcation (Fig. 1A), resulting in a diagnosis of oligometastatic disease. Additionally, the same imaging study revealed an enlarged and hyperenhancing mesenteric lymph node measuring 1.6 cm in short axis (Fig. 1B). A technetium-99 m methylene diphosphonate bone scan was negative for osseous disease. A PSMA-targeted PET study as part of clinical trial NCT02151760 in advanced prostate cancer patients, employing the investigational agent [^{18}F]DCFPyL, was ordered and demonstrated intense radiotracer uptake fusing to the iliac lymph node (Fig. 1D), but no uptake above background at the level of the mesenteric node (Fig. 1E).

The patient's prostatectomy was postponed due to his oligometastatic disease (T1c, N1, M1; stage IV), and the patient began chemohormonal therapy with docetaxel, leuprolide, and abiraterone with a plan to undergo subsequent cytoreductive prostatectomy. After chemotherapy, IV contrast-enhanced CT revealed a notable decrease in size of the PSMA-positive inferior iliac node from 2.0 cm to 0.8 cm in short axis (Fig. 2A), but unchanged size of the mesenteric node (Fig. 2B). As the PSMA scan described above was a research study and not clinically approved to guide treatment, the mesenteric node was treated as still being likely prostate carcinoma based on best available clinical data. The patient underwent radical prostatectomy with bilateral pelvic lymph node dissection and excisional biopsy of the mesenteric lymph node. Pathology from the prostatectomy specimen confirmed adenocarcinoma positive for NKX3.1 and PSMA with extensive treatment effect, negative surgical margins, and ypT2 disease with negative pelvic lymph nodes (0/11). The mesenteric lymph node was found to be sclerotic and negative for all prostate lineage markers: PSMA, NKX3.1, PSA, and p501s. This then prompted concern for a secondary gastrointestinal malignancy and the patient underwent upper endoscopy and colonoscopy; however both were negative. He then underwent adjuvant stereotactic radiotherapy to the previously noted PSMA positive inferior iliac node. Restaging contrast-enhanced CT imaging revealed an enhancing 2 cm polypoid mass in

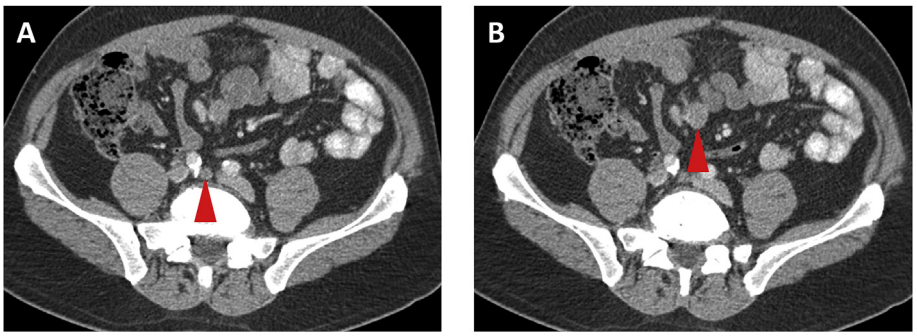

Fig. 2. (A) Follow-up, post-chemotherapy axial contrast-enhanced CT image showing treatment response in the lymph node inferior to the aortic bifurcation, with short axis measurement now 0.8 cm (arrowhead). (B) However, the mesenteric adenopathy remained unchanged after chemotherapy on the follow-up contrast-enhanced CT (arrowhead).

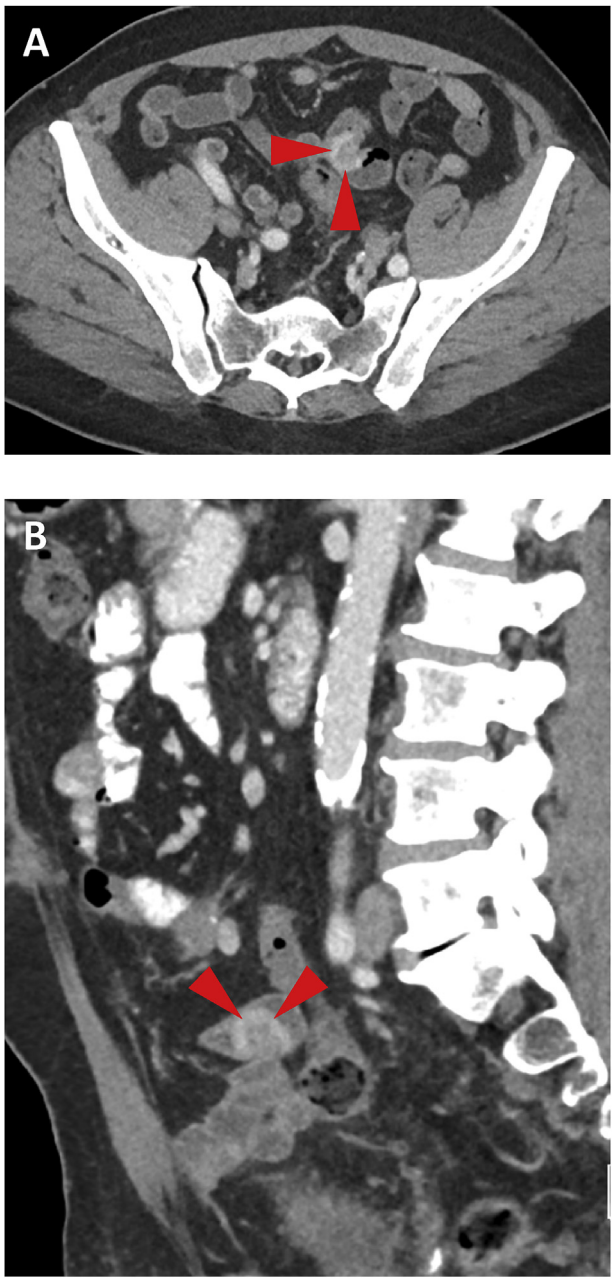

Fig. 3. (A) Axial and (B) sagittal contrast-enhanced CT images from an additional follow-up study performed after the patient's excisional mesenteric lymph node biopsy suggested that the mesenteric adenopathy was not related to his prostate cancer. The arrowheads point to an enhancing polypoid mass in the small bowel that was determined to be a carcinoid tumor after resection. In retrospect, this appears to have been obscured by overlying oral contrast on the previous CT and was only distinctly visible on this study because the administered oral contrast had not reached as distal as the mass at the time the images were acquired.

the small bowel with luminal narrowing and small adjacent enhancing mesenteric nodes that had not previously been visible (Fig. 3A and B), with the interpretation that these findings were consistent with a second primary cancer and unlikely to reflect metastatic prostate cancer. The polypoid mass was surgically resected to prevent future small bowel obstruction, and pathology revealed a well-differentiated neuroendocrine tumor of the small bowel (carcinoid).

Follow up has revealed no evidence of recurrent carcinoid or prostate carcinoma, with negative CT scans and undetectable PSA four months from resection.

Discussion

As demonstrated in this case, suspicious findings on the CT portion of [^{18}F]DCFPyL PSMA-targeted PET/CT scans that are not radiotracer-avid need to be noted during interpretation and receive appropriate follow-up. [^{18}F]DCFPyL has been investigated as a novel imaging method to detect lesions in patients with prostate cancer; this technique has been noted to have interpretive pitfalls that necessitate supplementation with other imaging modalities and biochemical markers.[2] The lack of uptake by a small bowel carcinoid tumor demonstrated in this cases supports the accuracy of [^{18}F]DCFPyL as a diagnostic tool for identifying metastatic disease from prostate cancer.

We have recently proposed a systematic approach to the interpretation of PSMA-targeted PET scans, PSMA-RADS version 1.0[5]. Now that PSMA-targeted PET scans are becoming a more accepted part of clinical care worldwide, and are increasingly used as a more integral part of patient care at our institution, the PSMA-RADS version 1.0 framework has been deployed in our clinic to help account for the possibility of second malignancies and also to provide the interpreter's relative confidence in the finding. One of the most important aspects of this approach is the inclusion of management recommendations to ensure that indeterminate findings receive appropriate work-up. According to the PSMA-RADS version 1.0 algorithm, the mesenteric lymph node in this patient would be classified as PSMA-RADS-3D (i.e. a finding that is suspicious for cancer on the basis of anatomic imaging but lacks radiotracer uptake). A non-prostate malignancy would be the most likely PSMA-RADS-3D entity to fall into this category, but non-PSMA-expressing prostate adenocarcinoma and neuroendocrine differentiated prostate cancer may also be non-PSMA-radiotracer avid. Finally, this case underscores the importance of imaging specialists' understanding patterns of metastatic disease to avoid misdiagnosis and mismanagement of patients with two primary malignancies.

Conclusions

PSMA-targeted PET radiotracers are proving to be powerful tools for the imaging of prostate cancer. However, important findings that lack radiotracer uptake but are visible on accompanying anatomic imaging must be recognized and appropriately worked-up in order to optimize patient management. The recently proposed PSMA-RADS Version 1.0 may be useful for the categorization and work-up decision making for such findings.

Conflicts of interest

M.G.P. is a co-inventor on a U.S. patent covering [^{18}F]DCFPyL and as such is entitled to a portion of any licensing fees and royalties generated by this technology. This arrangement has been reviewed and approved by the Johns Hopkins University in accordance with its conflict-of-interest policies. M.A.G. has served as a consultant to Progenics Pharmaceuticals, the licensee of [^{18}F]DCFPyL. S.P.R., M.A.G., K.J.P., and M.G.P. have all received research funding from Progenics Pharmaceuticals. No other authors have declared any relevant conflicts of interest.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eucr.2017.12.011.

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