

## Case Report

# Uptake of prostate-specific membrane antigen-targeted $^{18}\text{F}$ -DCFPyL in avascular necrosis of the femoral head

## ABSTRACT

In recent years, the emergence of prostate-specific membrane antigen (PSMA)-targeted positron-emission tomography (PET) imaging has brought about a paradigm shift in the way that prostate cancer (PCa) is imaged in many parts of the world. Although PSMA-targeted PET imaging has been demonstrated to be a highly sensitive and specific imaging modality for the identification of sites of PCa, its clinical utility hinges on the ability of imaging specialists and their clinical colleagues to recognize potential false-positive sources of uptake and to tailor therapy based on that recognition. In this manuscript, we report the case of a 74-year-old male with a history of recurrent PCa who was referred for a restaging PSMA-targeted  $^{18}\text{F}$ -DCFPyL PET/computed tomography (PET/CT). PET images demonstrated low level but focal and definitive uptake in the left femoral head. This uptake corresponded to sclerotic changes on CT whose morphology was most compatible with avascular necrosis without femoral head collapse. In the presented case, the integrated assessment of the CT imaging together with the PET findings was fundamental to avoid misinterpretation of the left femur finding as metastatic disease, which would have ultimately altered the clinical management of the patient.

**Keywords:**  $^{18}\text{F}$ -DCFPyL, avascular necrosis, positron-emission tomography/computed tomography, prostate cancer, prostate-specific membrane antigen

## INTRODUCTION

Prostate cancer (PCa) is the most common noncutaneous malignancy in men. Over the past more than three decades, computed tomography (CT) and  $^{99\text{m}}\text{Tc}$ -methylene diphosphonate bone scan have remained the mainstays for imaging PCa. These imaging modalities, however, offer only limited sensitivity and specificity for detecting sites of disease.<sup>[1]</sup> In recent years, molecular imaging with small-molecule radiotracers has gained traction as a means to more reliably image men with PCa. Perhaps, the most promising target for PCa molecular imaging is the transmembrane Type II glycoprotein prostate-specific membrane antigen (PSMA), which is highly expressed on the vast majority of PCa tumors.<sup>[2]</sup> Indeed, a number of clinical studies have shown promising results for PSMA-targeted, small-molecule, positron-emission tomography (PET) agents in the initial staging, and follow-up of men with PCa.<sup>[3,4]</sup>

Despite the high sensitivity and specificity of PSMA-targeted agents for imaging PCa, a number of interpretive pitfalls

have been described which have the potential to confuse radiologists and treating physicians alike.<sup>[5]</sup> For instance, a number of benign bone lesions have previously been

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**Submission:** 29-11-2018 **Accepted:** 24-01-2019 **Published:** 18-12-2019

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**How to cite this article:** Torga G, Yin Y, Pomper MG, Pienta KJ, Gorin MA, Rowe SP. Uptake of prostate-specific membrane antigen-targeted  $^{18}\text{F}$ -DCFPyL in avascular necrosis of the femoral head. *World J Nucl Med* 2019;18:416-9.

Access this article online	
<b>Website:</b> www.wjnm.org	<b>Quick Response Code</b> 
<b>DOI:</b> 10.4103/wjnm.WJNM_106_18	

described that might mistakenly be interpreted as evidence of M1b disease.<sup>[5]</sup>

In this manuscript, we describe the case of a patient with recurrent PCa who underwent a restaging PET/CT examination with the PSMA-targeted small molecule <sup>18</sup>F-DCFPyL and was found to have uptake in an area of avascular necrosis (AVN) of the femoral head. This case adds to the growing body of the literature on interpretive pitfalls with PSMA-targeted imaging.

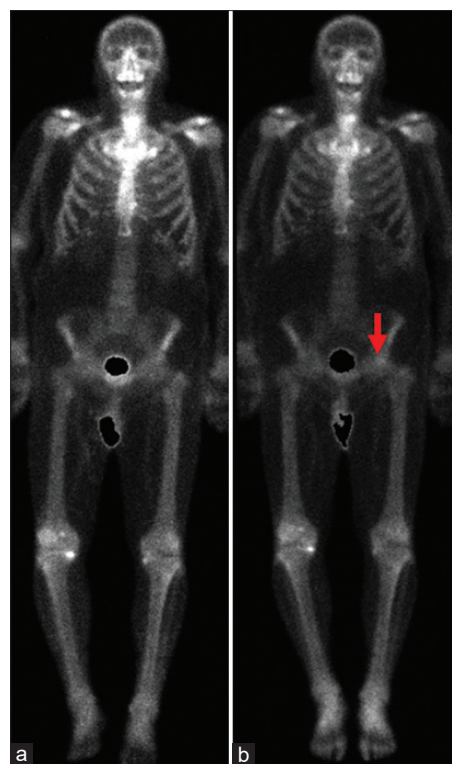
## CASE REPORT

A 74-year-old man with a history of Gleason 3 + 3 = 6 PCa treated with external beam radiation therapy subsequently developed biochemical failure with a most recent serum prostate-specific antigen (PSA) level of 40.9 ng/mL. Rebiopsy of the treated gland demonstrated recurrent PCa (Gleason score 4 + 4 = 8). Given the high PSA and associated suspicion for metastatic disease, the patient underwent restaging with conventional imaging as well as with PSMA-targeted <sup>18</sup>F-DCFPyL-PET/CT.

The conventional imaging staging evaluation was reported to be unremarkable except for the appearance of increased uptake of <sup>99m</sup>Tc-methylene diphosphonate in the region of the left femoral head, a new finding that had not been present on a bone scan performed 6 months previously [Figure 1]. Although this would be a typical site for degenerative change and would normally be viewed with low suspicion, the new appearance of this lesion in a patient with known active PCa raised concern that this may be a metastatic lesion.

Particular attention was paid to the left femoral head during interpretation of the <sup>18</sup>F-DCFPyL-PET/CT. This area was noted to have mild, but definitive and focal, radiotracer uptake (lean body mass corrected standardized uptake value 1.3) in an area corresponding to the new bone scan finding [Figure 2]. However, the CT morphology of the bone lesion fusing to the <sup>18</sup>F-DCFPyL uptake was not consistent with metastatic PCa. This location, as well as the dense peripheral sclerosis with less sclerosis centrally, was most compatible with AVN of the left femoral head. Although the degree of uptake in this case is subtle, it is important for any interpreter of PSMA-targeted PET scans to be aware of such pitfalls, as this patient could have been misclassified as having M1b disease instead of M0, leading to very different therapeutic options.

In the parlance of the recently-introduced PSMA reporting and data system (PSMA-RADS) version 1.0, uptake in AVN would be considered a PSMA-RADS-1B lesion, i.e., radiotracer uptake lesion that is definitively benign on anatomic imaging.<sup>[6,7]</sup>

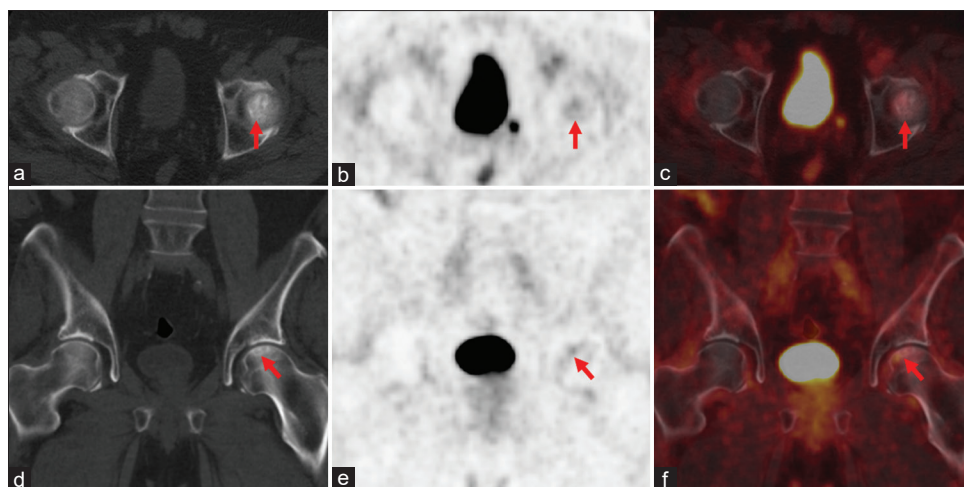


**Figure 1:** (a) Planar, whole-body <sup>99m</sup>Tc-methylene diphosphonate bone scan image from 6 months before <sup>18</sup>F-DCFPyL-positron-emission tomography/computed tomography imaging demonstrates multifocal degenerative changes, but no suspicious uptake that would suggest osseous metastatic disease. (b) Planar, whole-body <sup>99m</sup>Tc-methylene diphosphonate bone scan image obtained contemporaneously with the <sup>18</sup>F-DCFPyL-positron-emission tomography/computed tomography demonstrates new uptake in the left hip (red arrow), raising the possibility of a new metastatic bone lesion at this site

## DISCUSSION

PSMA-targeted radiotracers have generally demonstrated better diagnostic performance than other molecular imaging agents in detecting sites of PCa, even at low PSA levels.<sup>[6]</sup> However, as a consequence of the growing clinical experience with PSMA-targeted radiotracers, a number of potential interpretive pitfalls have been described in the literature.<sup>[8]</sup> Findings from multiple groups suggest increased PSMA-targeted radiotracer uptake can occur in a variety of malignant and benign entities.<sup>[5,9]</sup> Moreover, careful comparison to conventional imaging such as CT and bone scintigraphy, and the occasional use of other advanced modalities such as magnetic resonance imaging, may be necessary to arrive at a correct diagnosis.

AVN of the femoral head may lead to progressive destruction of the hip joint. Incidence in the United States is estimated at 20,000–30,000 new AVN cases/year and most frequently affects patients in the third-to-fifth decades of life. Risk factors include alcohol consumption, trauma, corticosteroid therapy,



**Figure 2:** (a) Axial computed tomography. (b) Axial  $^{18}\text{F}$ -DCFPyL-positron-emission tomography. (c) Axial  $^{18}\text{F}$ -DCFPyL-positron-emission tomography/computed tomography images through the pelvis shows a focus of uptake in the left femoral head fusing to sclerotic bone changes (red arrows). Excreted radiotracer in the left ureter and bladder is present; the patient's biopsy-proven locally recurrent disease is not visible on these images but was intensely radiotracer-avid. (d) Coronal computed tomography. (e) coronal  $^{18}\text{F}$ -DCFPyL positron-emission tomography. (f) Coronal  $^{18}\text{F}$ -DCFPyL positron-emission tomography/computed tomography recapitulates the findings on the axial images, with more clear delineation that the sclerotic changes are along the articular surface of the left femoral head. These findings confirmed that the newly appearing uptake on the bone scan shown in Figure 1b was most consistent with left femoral head avascular necrosis

coagulation abnormalities, and radiation therapy (a possible cause in this patient's case); however, its pathobiology has not been completely elucidated.<sup>[8,10]</sup> Given that patients with PCa may be exposed to multiple risk factors for femoral head AVN, cross-sectional imaging in these patients should be carefully scrutinized for findings compatible with AVN and abnormal radiotracer uptake with either bone-seeking or tumor-targeted agents should not be erroneously interpreted.

While it is a limitation of this report that a pathologic diagnosis of the left femoral head lesion is not available, the findings on anatomic cross-sectional imaging are essentially pathognomonic for AVN. In the future, we plan to assess the frequency with which these findings are present on PSMA-targeted PET scans and determine the range of uptake levels that can be seen.

## CONCLUSION

Uptake of PSMA-targeted radiotracers can be observed in the femoral head AVN and interpreting imaging specialists and referring clinicians should be aware of this imaging pitfall.

## 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.

## Acknowledgments

We gratefully acknowledge funding from the PCa Foundation Young Investigator Award, Progenics Pharmaceuticals, Inc., and the United States National Institutes of Health (CA134675, CA183031, CA184228, and EB024495).

## Financial support and sponsorship

Nil.

## Conflicts of interest

M.G.P. is a coinventor on a US patent covering  $^{18}\text{F}$ -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  $^{18}\text{F}$ -DCFPyL. M.A.G., K.J.P., M.G.P., and S.P.R. have received research support from the Progenics Pharmaceuticals.

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