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Case Report

^{18}F DCFPyL PSMA avid biopsy proven subcutaneous capillary haemangioma as a malignancy mimic in the setting of biochemical recurrent prostate carcinoma ☆

Manvinder Dhillon, MBBS, BMedSci, PGDAAD, MS[a], *Dalveer Singh, MBBS, FRANZCR, FAANMS*[a,b,*]

[a] *School of Medicine, University of Queensland, Herston, QLD 4006 Australia*
[b] *Qscan Radiology Clinics, Brisbane, QLD 7000 Australia*

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ABSTRACT

We present a case of a 65-year-old male with a biopsy proven subcutaneous capillary haemangioma identified on imaging for evaluation of further metastatic spread of prostatic carcinoma due to a rise in his prostate-specific antigen biochemistry. He was receiving salvage radiation therapy for his known isolated nodal disease, four years after prostatectomy. An intensely avid prostate-specific membrane antigen positron emission tomography-computed tomography lesion in the left paramedian back at the level of L1 was noted on his scan. A core biopsy revealed a dermal haemangioma with no evidence of metastatic prostatic carcinoma. To our knowledge, only one other incidental case of prostate-specific membrane antigen avid subcutaneous capillary haemangioma has been described in the literature. Whilst uncommon, incidental findings of prostate-specific membrane antigen PET avid dermal lesions are pathognomonic for haemangiomas and can be treated as "no touch" lesions with watchful observation.

Introduction

Prostate-specific membrane antigen (PSMA) targeted positron emission tomography (PET) has emerged as a new clinical standard for the imaging of metastatic prostate cancer. 2-(3-{1-carboxy-5-[(6-[^{18}F]fluoro-pyridine-3-carbonyl)-amino]-pentyl}-ureido)-pentanedioic acid (^{18}F DCFPyL) is a commonly used, novel second-generation low molecular weight radio-fluorinated PSMA PET radiotracer demonstrated to have a higher overall uptake in metastatic prostate cancer lesions [1].

Whilst the majority of PSMA protein expression is found in prostate cancer tissue, a variety of physiologic and other

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* Corresponding author.
E-mail address: dalveer.singh@qscan.com.au (D. Singh).

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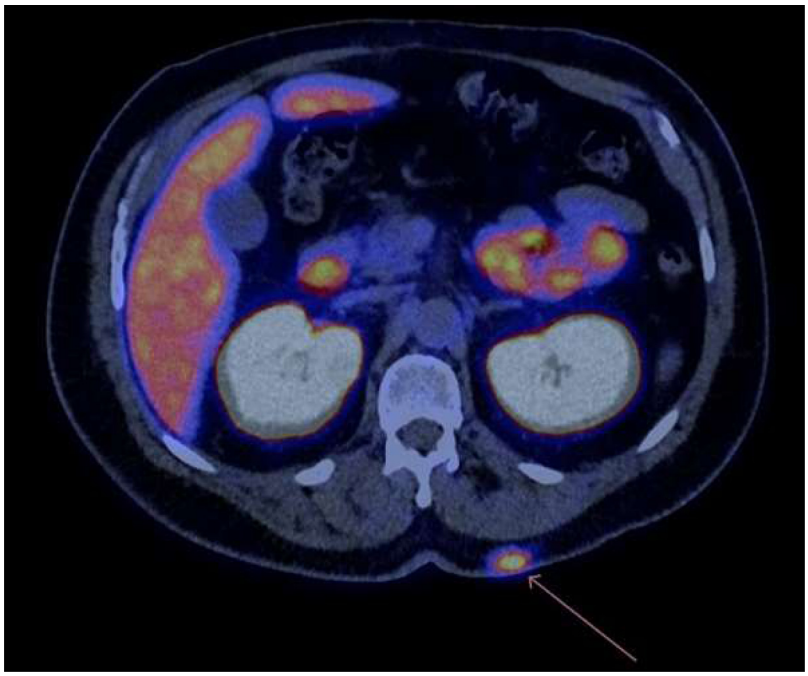

Fig. 1 – Key image above demonstrates an axial section of the abdomen at the L1 level on hybrid PSMA PET-CT examination of a 64-year-old male with biochemical recurrence of prostate carcinoma. In the subcutaneous tissues of the left paramedian back, there is a 16 x 24 mm nodular lesion of intense PSMA avidity demonstrated, as depicted by the red arrow.

pathologic tissue expression of PSMA may result in interpretative error. Increasing false positive findings from physiologic uptake in normal tissues, tissue neovasculature and ganglia, as well as uptake in tumours with PSMA expression, such as haemangiomas, meningiomas, and benign thyroid nodules with varying levels of PSMA PET-CT intensity have recently been documented [2]. We describe a rare, incidental case of a PSMA PET-CT avid dermal capillary haemangioma.

Case report

A 65-year-old male underwent an ^{18}F DCFPyL PSMA PET-CT examination to evaluate for further metastatic spread of prostate adenocarcinoma due to a rising serum prostate-specific antigen while receiving salvage radiotherapy to isolated nodal disease, four years after prostatectomy. Imaging revealed a 16 × 24 mm subcutaneous nodule in the left paramedian back, at the level of L1, which demonstrated intense PSMA avidity and was not seen on previous imaging (Fig. 1). The rest of the PSMA PET-CT study revealed a known cluster of PSMA avid para-aortic nodal disease, but no further metastases.

Although the new dermal lesion was thought unlikely to be a prostate metastasis, biopsy confirmation was thought prudent given the potential for altering therapy and core biopsy of this PSMA avid lesion was performed. Histology demonstrated a lobulated vascular lesion composed of varying sized capillaries with a positive staining pattern for CD34, CD31, and ERG (ETS-related gene) (Fig. 2). The diagnosis was a haemangioendothelioma/vascular malformation, and no evidence of metastatic prostatic carcinoma was detected. The patient then resumed salvage radiotherapy under the care of the radiation oncologist. Three years on, the capillary haemangioma remains unchanged on follow up PSMA PET-CT (Fig. 3).

Discussion

Prostate cancer is the most common solid organ malignancy in men, with 1.3 million new cases diagnosed worldwide in 2018 [3]. As part of treatment planning, staging of disease extent is a prerequisite to management, and most importantly, determining the presence of distant metastases is vital to planning the treatment pathway that is most appropriate for the patient.

PSMA is a transmembrane glycoprotein which is ubiquitously expressed in various tissues under normal physiological conditions, however, it has been found to be overexpressed in the neoplastic cells of prostate adenocarcinoma [4]. Through the development of radiotracer labelled molecules which selectively bind to the PSMA molecule, hybrid imaging PET-CT techniques have shown immense utility for the staging of prostate carcinoma as well as determining adequacy of surgical clearance and evaluating recurrence of disease [2].

In fact, a large series comparing routine cross-sectional imaging to PSMA PET for staging of prostate cancer, with pelvic node dissection as the standard of reference, demonstrated that PSMA PET was significantly superior in both sensitivity (66% vs 44%) and specificity (99% vs 85%) for evalu-

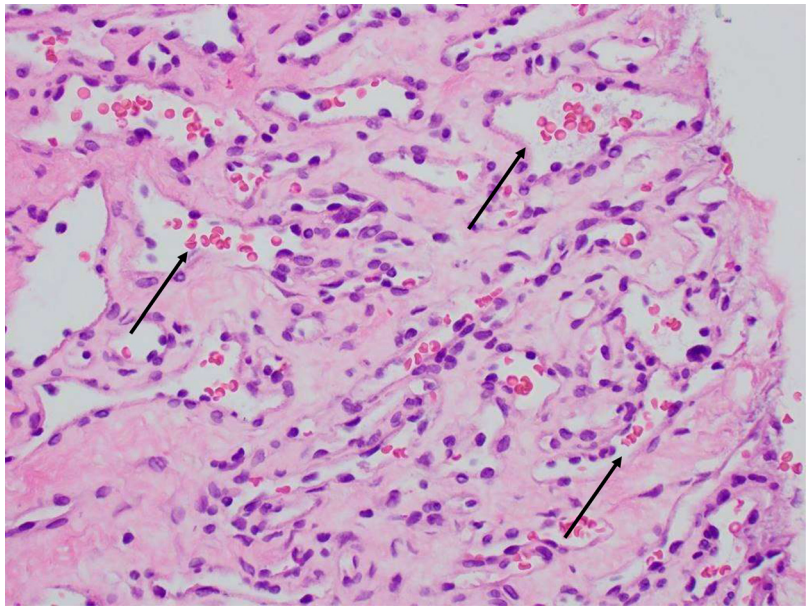

Fig. 2 – Histology demonstrates various sized capillaries (arrows) with normal appearing endothelial cells and connective tissue, with positive staining for CD31, CD34 and ERG consistent with a diagnosis of capillary haemangioma.

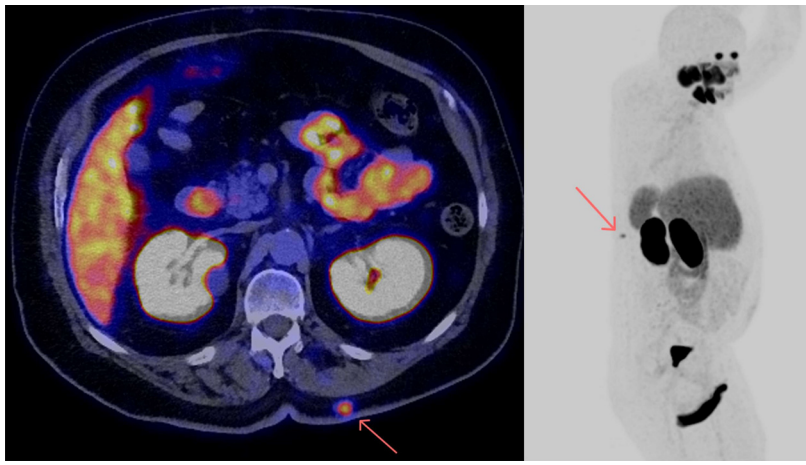

Fig. 3 – 3-year follow-up PSMA PET-CT showing stable lesion (red arrow) at the L1 level with similar PSMA intense avidity to Figure 1 with the axial hybrid PSMA PET-CT (left) and whole-body PET maximum intensity projection image on right anterior oblique projection (right) (Color version of figure is available online).

ation of pelvic nodal involvement by carcinoma [5]. Similarly, a recent meta-analysis by Pereira et al. demonstrated that in patients with biochemical recurrent prostate cancer, pooled detection rate in restaging prostate cancer was 72% [6].

Although PSMA PET-CT has improved management of patients, as our experience grows with this modality, we are learning of various case reports of incidental PSMA avid findings, with varying degrees of clinical significance. Low-to-moderate PSMA expression due to osteoblastic activity is observed in fibrous dysplasia, degenerative changes, fractures and Paget's disease and moderate activity can be seen in haemangiomas [2,7,8]. A retrospective review conducted by McEwan et al. further analysed these findings, and based on the data from their centre, found that 5.7% of 68Ga-PSMA PET-CT examinations demonstrated significant findings which were unrelated to prostate cancer, with 3.2% of findings being incidental neoplasms [9]. There is also growing evidence of possible contemporaneous malignancy, such as a sarcomatous malignancy, as haemangiosarcoma cells have been found to overexpress PSMA in canine tumour samples [10].

Due to increasing case reports, it seems very likely that PSMA is physiologically expressed in various endothelial and non-neoplastic tissues, which may help us further understand the physiological distribution of PSMA [11]. Whilst other PSMA PET avid haemangioma cases have been reported in the literature, namely in the spleen, liver, vertebrae and ribs, the dermal capillary subtype is much more uncommon and more discrete [12–16].

In this article, we present an interesting case report of an unusual, yet clinically significant, intensely PSMA avid lesion which was discovered on ^{18}F DCFPyL PSMA PET-CT imaging in a male with biochemically recurrent prostate cancer receiving salvage radiotherapy for isolated nodal recurrence of prostate carcinoma. To our knowledge, this is the second case report of a subcutaneous capillary haemangioma presenting as an incidental finding on a PSMA PET examination [17].

It is also a good illustration of a potential pitfall of PSMA PET examinations in the evaluation of prostate cancer and highlights the need to exercise caution and apply clinical judgment when unusual PSMA avid lesions are encountered in such clinical contexts, as dermal and visceral haemangiomatous lesions can cause false positive results on PSMA-PET studies and even mimic metastatic lesions. Furthermore, these defined dermal/subcutaneous PSMA PET avid haemangiomas are pathognomonic and can be regarded as a "no touch" lesions if encountered as an incidental finding.

Conclusion

The advent of PSMA PET technology has significantly improved the management of prostate cancer, especially in the setting of biochemical recurrence, however, as our experience with this modality grows, we are learning of various incidental findings with a range of clinical implications. As demonstrated in this case report, benign dermal haemangiomatous lesions can be PSMA avid and may mimic contemporaneous or metastatic malignancy. As such, when subcutaneous lesions are encountered on PSMA PET-CT examinations, a differential diagnosis of a haemangioma should be strongly considered.

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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