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Hereditary spherocytosis presenting as diffuse bone marrow activation and splenomegaly on PSMA-targeted ^{18}F -DCFPyL PET/CT

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Abstract

We present the case of a 71-year-old man with Gleason 3+3=6 pT2N0MxR0 adenocarcinoma of the prostate who presented with rising PSA level sixteen years following radical prostatectomy. PSMA-targeted ^{18}F -DCFPyL PET/CT was performed, which demonstrated recurrent disease in the prostatectomy bed as well as splenomegaly and mild-diffuse bone marrow activation, consistent with the patient's history of hereditary spherocytosis. We briefly review the clinical characteristics of hereditary spherocytosis, its appearance on molecular imaging studies, the normal biodistribution of ^{18}F -DCFPyL, and the PSMA-RADS scoring system for characterizing findings on PSMA-targeted PET imaging.

Keywords

Prostate cancer; PSMA-targeted PET; hereditary spherocytosis; PSMA-RADS; ^{18}F -DCFPyL

Hereditary spherocytosis is a form of hemolytic anemia that is characterized by increased RBC fragility due to a number of known genetic mutations in RBC plasma membrane proteins [1]. Clinical presentation is variable, ranging from a lack of symptoms to jaundice, severe anemia requiring transfusion and/or splenectomy, gallstones, and aplastic crises in the setting of viral infections [2]. Hematologic and bone marrow disorders are often detected on molecular imaging, particularly ^{18}F -FDG PET [3]. The normal biodistribution of ^{18}F -FDG often includes low-level marrow and reticuloendothelial system uptake, with increased marrow activity in the setting of anemia, hematologic malignancy, or administration of granulocyte colony stimulating factor [4].

Prostate-specific membrane antigen (PSMA) is a type II transmembrane glycoprotein that is overexpressed by prostate cancer epithelial cells. PET imaging with PSMA-targeted radiotracers has emerged as a highly sensitive and specific means of detecting sites of minimal residual and recurrent disease [5]. The normal biodistribution of the PSMA-targeted PET radiotracer ^{18}F -DCFPyL includes uptake in the salivary glands, liver, spleen, small bowel, kidneys and urinary tract [6]. Bone marrow uptake on ^{18}F -DCFPyL PET/CT is never considered normal and a number of benign pathologies may demonstrate osseous or marrow cavity uptake, including Paget's disease, fibrous dysplasia, and fractures [7].

In 2017, the PSMA-RADS structured reporting system for PSMA-targeted PET imaging was proposed [8]. Similar to BI-RADS scoring for breast lesions, PSMA-RADS categorizes lesions based on the likelihood of prostate cancer involvement, ranging from 1 (benign) to 5 (prostate cancer almost certainly present). PSMA-RADS can be applied to individual lesions and/or the imaging study as a whole and has been validated with a high level of interobserver agreement for detection of metastases and overall scan impression [9]. One study confirmed the indeterminate nature of PSMA-3A and 3B lesions, with an increased likelihood of 3A lesions to represent true malignancy on follow-up imaging [10]. Given the appearance of the marrow activity for this patient, these findings were scored PSMA-RADS-3C (intense uptake in site highly atypical of all but advanced stages of prostate cancer; high likelihood of non-prostatic malignancy or other benign tumor.)

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Conflicts of Interest and Sources of Funding:

M.G.P. is a coinventor on a US 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 for Progenics Pharmaceuticals, Inc, the licensee of ^{18}F -DCFPyL. K.J.P., M.G.P., M.A.G., and S.P.R. have received research funding from Progenics Pharmaceuticals, Inc. Funding was received from the Prostate Cancer Foundation Young Investigator Award and National Institutes of Health grants CA134675, CA184228, EB024495, and CA183031.

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Figure 1:

A 71-year old man with a history of pT2N0MxR0, Gleason 3+3 prostate adenocarcinoma status post radical prostatectomy on 4/30/2001 presented for follow-up imaging given recent rise in PSA to 10.06 ng/ml on 12/14/2017. As part of his evaluation, ^{18}F -DCFPyL PET/CT was performed which revealed a 1.4 cm soft tissue lesion with intense radiotracer uptake in the prostatectomy bed (PSMA-RADS-5). Additionally, the scan - (a) sagittal bone window CT; (b) sagittal attenuation corrected PET; (c) sagittal PET/CT fusion, and (d) maximum intensity projection (MIP) images demonstrated marked splenomegaly and mild diffusely increased radiotracer uptake within the bone marrow (PSMA-RADS-3C). A complete blood count demonstrated anemia, increased red blood cell (RBC) distribution width, and increased mean corpuscular hemoglobin concentration, consistent with the patient's known history of hereditary spherocytosis.

Figure 2:
Comparison ^{18}F -DCFPyL PET images of a patient without a history of hematologic or bone marrow pathology demonstrate no evidence of radiotracer uptake (PSMA-RADS-1A).