Myelofibrosis on ^{18}F-FDG-PET/CT in a case suspicious for post-transplant lymphoproliferative disorder

Vineet Khanna[1] BSc,
Sharanya Nama[2] BSc,
Rajiv Tailor[3] BSc,
Ashok Muthukrishnan[1] MD, MSc

1. *Division of Nuclear Medicine, Department of Radiology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, U.S.A., 15213*
2. *Temple University School of Medicine, Philadelphia, Pennsylvania, U.S.A., 19140*
3. *Ross University School of Medicine, North Brunswick, New Jersey, U.S.A., 08902*

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Correspondence address:
Ashok Muthukrishnan, MD, MSc,
Division of Nuclear Medicine
University of Pittsburgh
Medical Center PUH E-177
200 Lothrop Street
Pittsburgh, PA 15213
Phone: 412-647-0104
Fax: 412-647-2601
Email: muthukrishnana@upmc.edu

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Abstract

Recent studies have advocated the utility of fluorine-18 fluorodeoxyglucose-positron emission tomography ^{18}F-FDG-PET imaging in evaluation of various hematological disorders. We report a case of a 61-year-old man with clinical suspicion of post-transplant lymphoproliferative disorder (PTLD) where ^{18}F-FDG-PET/CT (computerized tomography) was helpful in identifying myelofibrosis. This paper aims to reveal the potential diagnostic value of PET/CT as an imaging modality in the evaluation of myelofibrosis.

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Introduction

Myelofibrosis is a chronic myeloproliferative disease of clonal stem cells that leads to ineffective erythropoiesis, dysplastic megakaryocyte hyperplasia, and an increase in immature granulocytes. It is typically accompanied by reactive bone marrow fibrosis, extramedullary hematopoiesis in the spleen or other organs, and substantial constitutional symptoms [1, 2]. Post-transplant lymphoproliferative disorder (PTLD), however, is characterized by abnormal lymphoid proliferation secondary to pharmacologic immunosuppression after organ transplantation. In these patients, infection with Epstein-Barr virus coupled with immunosuppression results in a loss of control over B cell proliferation and thus PTLD [3, 4]**.** Myelofibrosis and post-transplant lymphoproliferative disorder can both present with pancytopenia, confounding the problem of accurate clinical diagnosis. In this case, we present a 61 years-old patient where PTLD was suspected because of a history of heart transplant. Fluorine-18 fluorodesoxyglucose-positron emission tomography/computerized tomography (^{18}F-FDG PET/CT), however, led to an eventual diagnosis of myelofibrosis.

Description of the case

A 61 years old man with history of idiopathic cardiomyopathy, who had undergone a heart transplant six years ago, presented to us with fatigue, night sweats, and pancytopenia. This patient's presentation was highly suspicious for PTLD, one of the most common diseases complicating solid organ transplantation [5]. PET/CT imaging was performed to diagnose and localize PTLD. PTLD is a well-known indication where PET-CT imaging is widely used in the United States to diagnose and localize the disease process. Imaging revealed massive splenomegaly with increased ^{18}F-FDG avidity. There were also diffuse skeletal sclerotic changes with increased ^{18}F-FDG uptake. There was no evidence of ^{18}F-FDG avid lymph nodes or extranodal masses to support the diagnosis of PTLD.

The axial PET and CT images at the level of the pelvis showed diffuse ^{18}F-FDG activity throughout the bone marrow and on the CT sclerotic changes, with small scattered lytic areas within the pelvic bones. These findings coupled with splenomegaly, the latter due to extramedullary hematopoiesis, were clearly suggestive of myelofibrosis [6]. The imaging findings in this patient led to a bone marrow biopsy. The DNA analysis from the marrow tested positive for JAK2 V617F point mutation. This DNA genetic analysis test is routinely performed in the United States in patients with suspected myeloproliferative diseases. Leukocytes from the majority of polycythemia vera patients and up to half of essential thrombocythemia patients and idiopathic myelofibrosis patients carry this activating point mutation in the auto-inhibitory domain of the JAK2 tyrosine kinase [7].

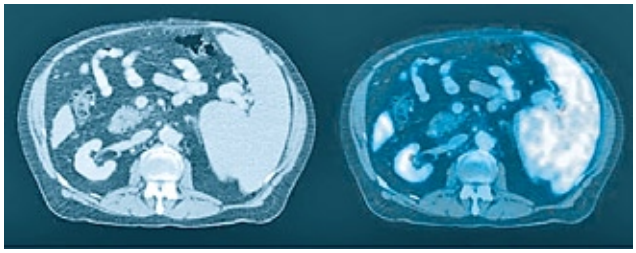

Figure 1. Axial PET/CT images demonstrate marked splenomegaly (23cm in the craniocaudal dimension) with diffuse ^{18}F-FDG uptake.

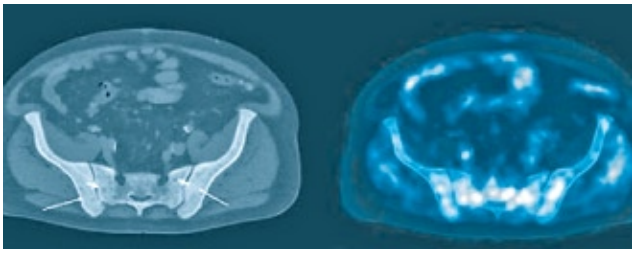

Figure 3. Additional axial PET and CT images at the level of the pelvis show diffuse ^{18}F-FDG activity throughout the bone marrow with sclerotic changes (long arrows) and small scattered lytic lesions (short arrows) of the pelvic bones on the CT portion of the examination suggestive of myelofibrosis.

Discussion

Patients undergoing immunosuppressive therapy presenting with constitutional symptoms and anemia must be evaluated for PTLD. Many studies have demonstrated the potential for PET/CT imaging to efficiently diagnose, stage, and follow PTLD after various types of organ transplantations. Most patients in one case series demonstrated extranodal lesions that were visualized early by PET/CT [8]. Studies have also demonstrated that combined PET/CT is more accurate than PET or CT alone in detecting extranodal disease [9]. A previous case study showed that myelofibrosis may present with increased ^{18}F-FDG uptake in the liver and spleen, accompanying hepatosplenomegaly, and increased ^{18}F-FDG uptake in the bone marrow [10].

In this case, the absence of extranodal masses or suspicious lymph nodes, excludes the diagnosis of PTLD. Careful review of the axial skeleton however, revealed small scattered lytic areas with diffuse sclerotic changes and ^{18}F-FDG avidity. This strongly suggested the diagnosis of myelofibrosis. The importance of careful examination of the skeleton in post-transplant patients is crucial when extranodal masses or suspicious lymph nodes cannot explain the patient's symptomatology. These findings also underline the significance of meticulous examination of the CT portion of the PET/CT, which often tends to be overlooked by the PET reader. Also increased ^{18}F-FDG uptake was found in the patient's enlarged spleen. This could be explained by the increased metabolism seen in the expansion of peripheral bone marrow and in extramedullary hematopoiesis typically located in the spleen and/or liver. Osteosclerosis, a common finding in myelofibrosis, was also seen in our case, and studies show that it is associated with an increased ^{18}F-FDG uptake [9].

In conclusion, this case illustrates the potential role of ^{18}F-FDG PET/CT in diagnosing myelofibrosis that could serve as the preferred imaging tool. More clinical studies in this area will be needed as the data currently available is scarce.

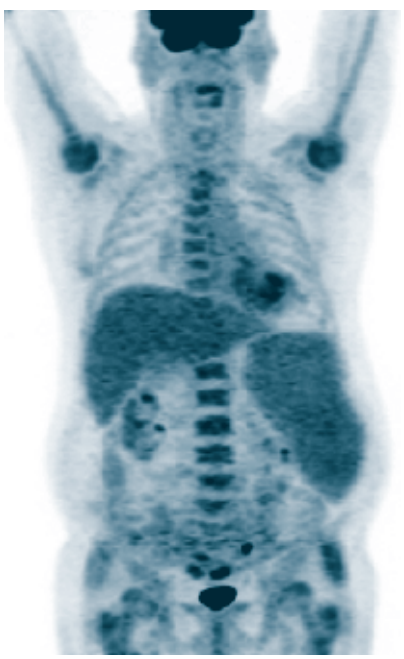

Figure 2. A maximum intensity projection (MIP) whole body image demonstrates massive splenomegaly with diffuse ^{18}F-FDG activity throughout the axial skeleton.

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