Pancreatic Transplant Associated Tuberculosis Diagnosed and Followed up on Whole-Body 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography

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Abstract

Infection attributable to impaired host immunity is the most commonly reported cause of morbidity and mortality among pancreatic transplant recipients. Among these, tuberculosis (TB) has been reported sporadically. Herein, we present a case illustrating the role of whole-body 18F-fluorodeoxyglucose positron emission tomography/computed tomography in diagnosis and follow-up of peripancreatic abdominal TB in a pancreas-only transplant recipient who presented with unexplained fever.

Keywords: Infection-imaging, pancreatic transplant, posttransplant lymphoproliferative disorder, tuberculosis, whole-body F-fluorodeoxyglucose positron emission tomography/computed tomography

Introduction

18F FDG PET/CT is being increasingly employed in clinical practice for infection and inflammation imaging. Its role in imaging and management of tuberculosis has been reported, often extensively. However, its role in management of post transplantation associated tuberculosis is sporadically reported. Herein, we illustrate a case demonstrating its utility in diagnosis and follow-up of peripancreatic abdominal TB in a pancreas only transplant recipient who presented with unexplained fever.

Case Report

A 23-year-old male patient, a known case of type 1 diabetes mellitus (DM) postpancreatic transplant was referred to the Department of Molecular Imaging and positron emission tomography/computed tomography (PET-CT) for a whole-body 18F-fluorodeoxyglucose (18F-FDG) PET-CT for suspected graft assessment. On history and review of clinical records, patient gave a history of a single episode of acute pancreatitis in 2006 followed by progressively worsening glycemic control and renal function on follow-up. Subsequently, a renal biopsy was performed which revealed early diabetic nephropathic changes. The patient was then selected for and underwent a deceased donor pancreas-only transplant at a leading transplant center for progressive type 1 DM post-acute pancreatitis. Pancreatic transplant alone was chosen over simultaneous pancreas-kidney transplant and pancreas after kidney transplant owing to the presence of macroalbuminuria, limited renal dysfunction, possibility of worsening of renal function by the immunosuppressive (IS) regimen, and experience of referring surgeon with the pancreatic transplant. The IS regimen used consisted of induction with alemtuzumab and solumedrol following which patient was maintained on tacrolimus, mycophenolate mofetil (MMF), and prednisone.

Post-transplant sequential ultrasonography Doppler and CT abdomen performed 3–5 days posttransplant documenting a patent arterial and venous anastomosis. Posttransplant, patient had a complicated clinical course with poor inspiratory effort, developed pleural effusion with high-pleural fluid amylase levels and peritonitis eventually transforming into a chronic

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febrile illness within 3 months. The patient had no history of active tuberculosis (TB) or antitubercular therapy (ATT) intake. Tuberculin skin tests (Montaux) performed both pretransplantation and on readmission came out as negative. The pleural fluid analysis did not reveal any acid-fast bacilli positive cells or atypical cells to suggest tubercular or lymphomatous involvement. Subsequently, the patient was referred for a whole-body 18F-FDG PET/CT [Figure 1] to evaluate the cause of febrile illness.

Anterior and lateral PET maximum intensity projection (MIP) images [Figure 1a] demonstrated an intensely hypermetabolic soft-tissue mass lesion with a maximum standardized uptake value (SUVmax) of 15.1 involving the right lumbar region with extension into the right iliac fossa and pelvis (green-arrow). Corresponding axial sections at two different vertebral levels [Figure 1b], sagittal [Figure 1c], and coronal Figure 1d] of CT and fused 18F-FDG PET/CT images revealed large well defined homogenous conglomerated mesenteric soft-tissue density mass lesion measuring 13.5 (craniocaudal) cm × 6.0 (anteroposterior) cm × 6.6 (transverse dimensions) cm abutting and partly encasing a vertically oriented apparently normal transplanted pancreas along its inferomedial aspect (white-arrowhead). The mass was also seen to encase the bowel loops, abutting the right psoas major muscle posteriorly, and right lateral wall of the rectum inferiorly. In addition, a FDG avid (SUVmax of 4.5) enlarged mesenteric lymph node measuring 1.4 cm × 0.7 cm was also observed [Figure 2c]. Considering the imaging characteristics, a diagnosis of possible infection/inflammation was considered with a competing differential diagnosis of early posttransplant lymphoproliferative disorder (PTLD). Subsequently performed CT-guided needle cytology suggested a granulomatous inflammation and polymerase chain reaction (PCR) was positive for TB. Consequently, a final diagnosis of TB of the transplanted pancreas was made and ATT initiated. Isoniazid, rifampicin, ethambutol, and pyrazinamide were included as part of ATT initially for at least 2 months followed by isoniazid, rifampicin, ethambutol for the subsequent 4 months. IS was modified with discontinuation of MMF and patient was maintained on tacrolimus and prednisone. Post-ATT initiation, the patient was planned for weekly follow-up for the next 1 month followed by a monthly follow-up. During this period, imaging follow-up was also planned as part of an interim analysis to monitor therapy effectiveness and at the end of treatment.

Postcompletion of 3 months of ATT, patient reported with resolution of fever and significant improvement of general condition. Consequently, a follow-up whole-body PET/CT was performed for imaging response assessment [Figure 2]. Anterior and lateral MIP images (a) demonstrated significant partial regression of the soft-tissue mass in terms of size and metabolic activity surrounding the transplanted pancreas. Comparative axial CT and fused PET/CT images performed before and after 3 months ATT (b) demonstrated the organization of the previously seen mesenteric soft-tissue mass into a well-defined peripherally enhancing collection (green arrow) which now measured 7.1 (CC) cm × 3.7 (AP) cm × 3.8 (TR) cm. There was a new development of peripheral curvilinear wall calcifications.

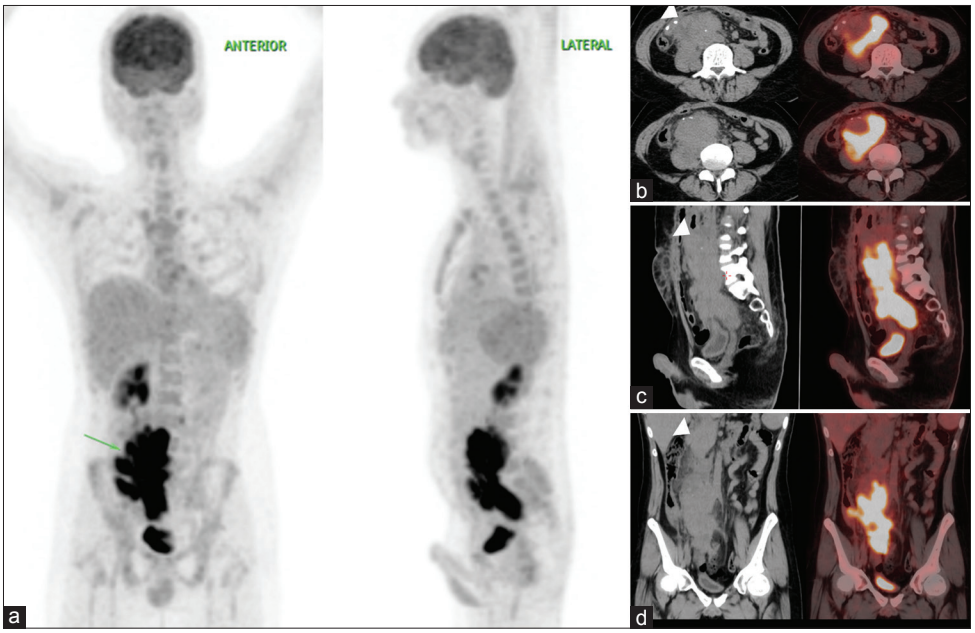

Figure 1: Whole-body 18F-fluorodeoxyglucose positron emission tomography/computed tomography anterior and lateral maximum intensity projection images (a) Demonstrating an intensely hypermetabolic soft-tissue mass lesion (maximum standardized uptake value: 15.1) involving the right lumbar region extending into the right iliac fossa and pelvis (green-arrow). Corresponding axial sections at two vertebral levels (b), sagittal (c), coronal (d) computed tomography and fused 18F-fluorodeoxyglucose positron emission tomography/computed tomography images revealed large well-defined homogenous conglomerate mesenteric soft-tissue density mass measuring 13.5 (CC) cm × 6.0 (AP) cm × 6.6 (TR) cm abutting a vertically oriented apparently normal transplanted pancreas inferomedially (white-arrowhead)

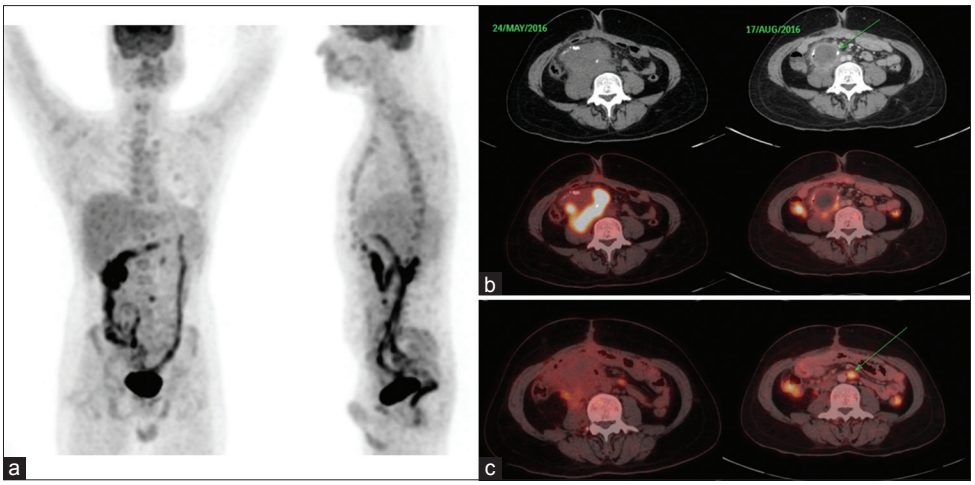

Figure 2: Follow up Wholebody 18F-FDG PET/CT 3 months post completion of ATT; anterior and lateral MIP images (a) demonstrated regression of the soft tissue mass in terms of size and metabolic activity surrounding the transplanted pancreas. Comparative axial CT and fused PET/CT images performed before and after 3 months ATT (b) demonstrated the organization of the soft tissue mass into a well defined peripherally enhancing collection (green arrow) measuring 7.1 × (CC) 3.7 (AP) × 3.8 (TR) cms showing peripheral curvilinear wall calcification and pockets of air [SUVmax: 8.5, previously 15.1]. (c) Multiple enlarged mesenteric nodes with largest one showing FDG uptake (SUV max 5.7, previously 4.5) measured 1.6 × 0.6 cm (green arrow). Imaging feature suggested partial response to treatment (ATT)

Significant reduction of metabolic activity with a SUVmax of 8.5 was also observed and was now seen limited to the peripheral enhancing wall of the collection compared to a previous SUV value of 15.1. Multiple enlarged mesenteric nodes were noted (likely due to disintegration from the previous mass lesion) with the largest one showing FDG uptake (SUVmax 5.7, previously 4.5) and measured 1.6 cm × 0.6 cm (green arrow). Overall imaging feature suggested partial response to treatment with active residual disease. Subsequently, the patient was continued on ATT amounting to a total duration of 9 months. Last follow-up done at 12 months posttransplant using a CT abdomen (not shown) revealed complete resolution of preexisting disease and asymptomatic status. The patient was deemed cured of TB.

The increasing success of pancreas only and simultaneous pancreas-kidney transplantation (SPKT) has been a result of improved organ preservation surgical techniques, availability and use of novel antirejection therapies and antibiotics for infection prevention/treatment. Infection is the most common cause for high morbidity and mortality[1,2] among both pancreatic and SPKT patients primarily due to impaired host immunity associated with IS treatment.[3] Reported infection-associated mortality ranges from 5.54% to 24.5% in the limited available literature.[2,4]

The occurrence of PTLD post pancreatic transplantation is a risk factor in all organ allograft recipients, especially after Epstein–Barr virus infection. Reported incidence in a large series of 1000 patients has been as low as <2%, including only 0.6% in pancreas only recipients.[5,6] Although the possibility of early PTLD was considered as a competing differential in this patient on initial scan, the presence of cytological and PCR evidence in favor of TB effectively ruled out PTLD. This was further confirmed with clinical and imaging validated response to treatment with ATT as documented on the interim scan.

Both local and systemic infections have been reported after pancreatic transplantation. Most commonly reported systemic infection is due to cytomegalovirus or Epstein–Barr virus. TB has been reported to be more common in solid organ transplants and also in pancreatic recipients sporadically. A large study of 4634 solid organ transplant recipients reported an overall incidence of 1.1% of TB.[7] TB in transplant recipients may be associated with mortality rates ranging up to 25%–40% with allograft loss in up to 33% of the patients.[8]

Management of TB in post-transplant setting is challenging owing to the side effects of ATT agents, and their potential interactions with IS drugs.

The use of PET/CT has been only recently explored for the detection of both infection and malignancy in transplant recipients.[9] Features of pancreatic TB on FDG PET/CT have also been described. However, this is probably the first report exploring the use of 18F-FDG PET for diagnosis and response monitoring of TB in the pancreas only transplant.

The decision to perform FDG PET-CT over CECT alone was made owing to known superior sensitivity of FDG PET for the diagnosis of both PTLD and infectious complications, greater whole-body coverage than offered by CT abdomen alone and most importantly the ability of FDG PET to provide early response assessment than conventional anatomical modalities.

A recent exploratory randomized controlled trial exploring the use of isoniazid prophylaxis based on interferon-γ-releasing assay in the kidney and pancreas transplant recipients demonstrated a trend toward reducing TB development.[10]

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.

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Conflicts of interest

There are no conflicts of interest.

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