Case Report

Tuberculosis in Posttransplant Recipients: Challenges in Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography Reporting in Countries with a High Prevalence of Tuberculosis

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Abstract

Tuberculosis (TB) is a common bacterial infection in developing countries. Solid-organ and hematopoietic stem cell transplant recipients are more prone to this infection. Reactivation from previously acquired infection is the most common mode. It has to be ruled out in cases of pyrexia of unknown origin (PUO) before ruling out the other possibilities. We present two cases of incidentally detected TB in the posttransplant patients referred for the evaluation of PUO.

Keywords: *Fluorodeoxyglucose positron emission tomography/computed tomography, myeloid sarcoma, posttransplant lymphoproliferative disorder, tuberculosis*

Introduction

India has one of the highest TB burden in the world with an incidence of 2.0–2.3 million tuberculosis (TB) cases and about 150 000–350 000 deaths per year.[1,2] Previous estimates states that TB was 20-74 times more frequent in solid organ transplant (SOT) and twice as frequent in hematopoietic stem cell transplant (HSCT) recipients and more often leads to fatal complications.[3] FDG PET/CT was proven useful in determining activity of lesions, to guide biopsy from active sites, assess disease extent, detect occult distant foci, and evaluate response to therapy.[4] We present two cases of incidentally detected TB in the post-transplant patients referred for the evaluation of PUO.

Case 1

A young male patient, who was a known case of chronic kidney disease (CKD), underwent renal transplantation for the same in 2009. He presented with a history of pyrexia of unknown origin in March 2020, 11 years after transplant. Relevant investigations showed anemia, normal C-reactive protein, and sterile blood culture. Procalcitonin level was elevated. Fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) done in April 2020 to rule out posttransplant lymphoproliferative disorder (<PTLD) showed [Figure 1] metabolically active multiple necrotic peripancreatic lymph nodes surrounding the head of the pancreas, conglomerated lymph nodal mass lesion with a central necrotic area in the anterior mediastinum encasing arch of the aorta and pulmonary artery. Diffuse pericardial thickening with increased metabolism suggestive of pericarditis was also noted. Based on PET-CT findings, posttransplant lymphoproliferative and granulomatous diseases were considered as the differentials. On further evaluation, sputum culture yielded mycobacteria with rifampicin sensitivity. Gene expert for *Mycobacterium tuberculosis* was positive.

Case 2

A middle-aged female, who was a known case of acute myeloid leukemia (AML), underwent bone marrow transplant in October 2019. She presented with a history of persistent fever in April 2020. Relevant investigation showed anemia with leukopenia. CT thorax showed miliary nodules in the lungs and mediastinal lymphadenopathy. FDG PET/ CT was done in May 2020 to rule out recurrent extramedullary AML. It showed [Figure

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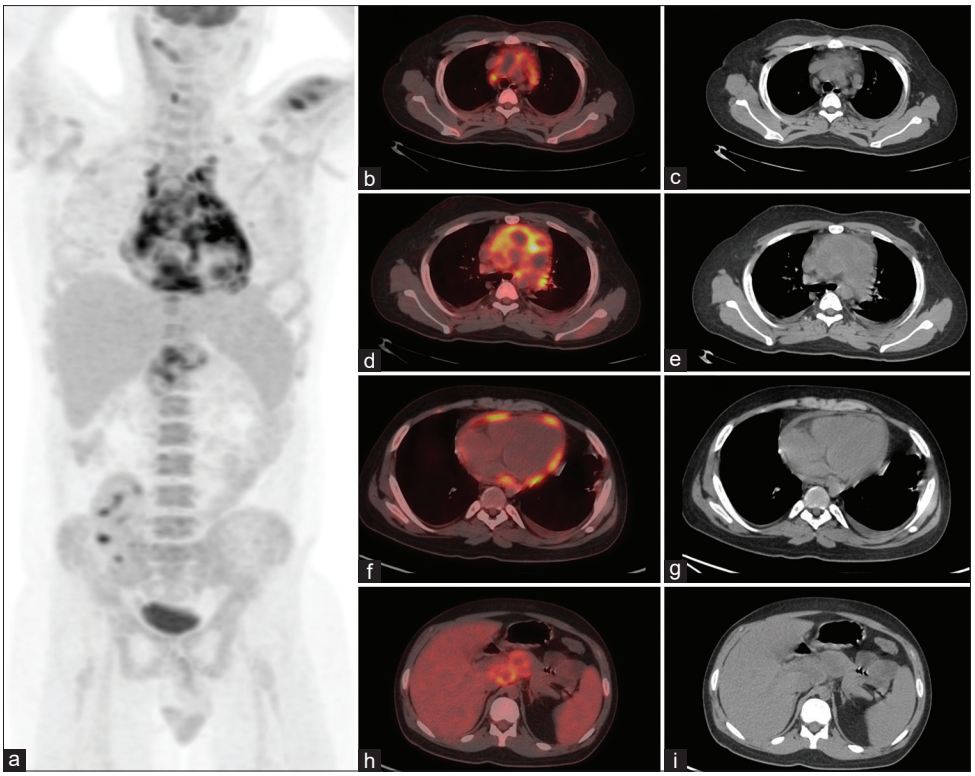

Figure 1: Fluorodeoxyglucose positron emission tomography/computed tomography image (a) showing increased fluorodeoxyglucose uptake in multiple mediastinal lymph nodes (b-e); Thickened pericardium (f-g); Peripancreatic lymph nodes (h-i)

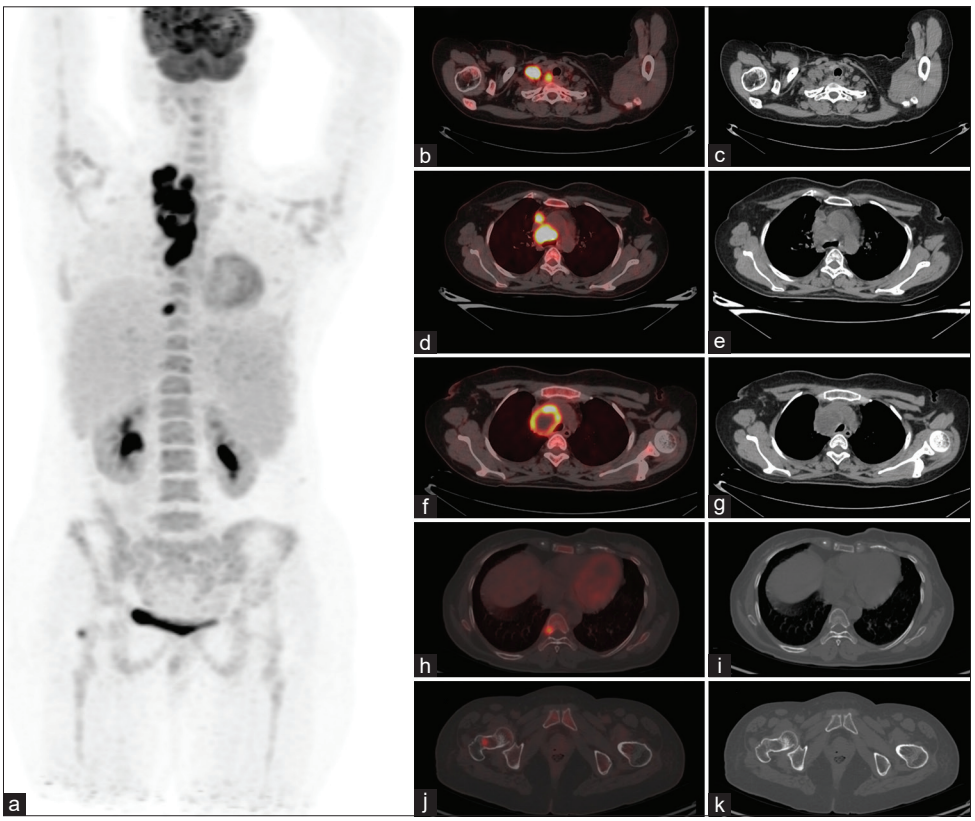

Figure 2: Fluorodeoxyglucose positron emission tomography/computed tomography image (a) showing increased fluorodeoxyglucose uptake in right supraclavicular lymph nodes (b and c); prevascular and right upper paratracheal lymph nodes (d and e); necrotic right lower paratracheal lymph node mass (f and g); lytic lesion in T8 vertebra (h and i) and lytic lesion in the neck of the right femur (j and k)

2] metabolically active disease in level VI cervical lymph node;right medial supraclavicular lymph node with a central necrotic area;multiple mediastinal lymph nodes involving right paratracheal prevascular, and subcarinal regions; T8 vertebra, and neck of the right femur. Non-FDG-avid multiple miliary nodules are noted in bilateral lung fields. Based on PET-CT findings, differentials were recurrent extramedullary AML and granulomatous disease. Blood culture and sensitivity was sterile. Serum beta-D-glucan test was negative. Fine-needle aspiration cytology from the right cervical lymph node was consistent with granulomatous lymphadenitis due to tuberculosis (TB). Sputum culture yielded mycobacteria.

Discussion

India has the highest TB burden in the world, with an incidence of 2.0–2.3 million TB cases and about 150,000–350,000 deaths per year.[1,2] Previous estimates state that TB was 20–74 times more frequent in solid-organ transplant (SOT) and twice as frequent in hematopoietic stem cell transplant (HSCT) recipients and more often leads to fatal complications.[3] FDG PET/CT was proven useful in determining the activity of lesions, to guide biopsy from active sites, assess disease extent, detect occult distant foci, and evaluate response to therapy.[4]

Posttransplant lymphoproliferative disease (PTLD) consists of lymphoproliferative conditions which include lymphoid hyperplasia and lymphoid neoplasia post-SOT and HSCT. The median onset of PTLD after transplantation was approximately 6 months in SOT patients and 2–3 months in HSCT recipients.[5] PTLD can be a clonal proliferation of the B-cells or tumors arising from T-cells, natural killer cells, or tumors resembling or indistinguishable from Hodgkin's lymphoma in the posttransplantation setting. PTLD will manifest with lymphadenopathy or mass lesion along with fever, weight loss, and transplant dysfunction. Involvement of the lymph nodes, lung, liver, spleen, kidneys, and bones had been reported. Involved lymph nodes can be discrete or conglomeration of enlarged nodes. Sometimes, it can present as a mass lesion with central necrosis.[6] The National Comprehensive Cancer Network recommends FDG PET-CT as a first-line investigation for evaluating PTLD. The American Society of Transplantation stated that FDG PET-CT may provide additional information during staging and response assessment. FDG PET-CT showed a diagnostic accuracy of 89% in assessing PTLD.[5,7,8]

Extramedullary AML (E-AML) can occur as a primary lesion or concurrent with a medullary disease or in a relapsed setting. In the relapsed setting, it is more common among patients with HSCT. The most common site of involvement was skin, followed by bone and lymph nodes.[9,10] Marrow involvement was the most common skeletal manifestation. Skeletal involvement without marrow disease can arise due to hematogenous seeding and can be seen as lytic lesions in CT scan. Mediastinal lymph node involvement was the common manifestation of thoracic AML.[11,12] FDG PET-CT can help in early detection of occult E-AML. It can guide biopsy from the active site.[9,13]

In view of transplant history, lymph node mass with a necrotic center, PTLD was considered in Case 1. However, because of pericarditis and conglomerated necrotic nature of lymph nodes, TB was considered as the close differential. In Case 2, bone marrow examination following HSCT showed features of remission. The presence of lytic bone lesions, discrete multiple mediastinal, right supraclavicular lymph nodes, and history of remission following transplantation favored the diagnosis of E-AML. Considering the rarity of thoracic involvement in myeloid disease and the presence of few necrotic lymph nodes, TB was considered as the close differential. Interestingly, both the cases turned out to be TB.

Conclusion

Although AML recurrence in post-HSCT and PLTD post-SOT can occur, India being the country with a high incidence of TB, the chance of TB infection is higher. FDG PET-CT lacks specificity in differentiating TB from PTLD and E-AML. The diagnosis had to be made after considering the clinical context, examination findings, and imaging features. However, it can help in assessing the disease extent, guiding biopsy, detecting occult disease foci, and evaluating response to therapy in PTLD and E-AML.

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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