Case report

Disseminated Tuberculosis in a Kidney Transplant Recipient: A Case Report

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ABSTRACT

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| **Aim:** To know about various presentations of Tuberculosis in post renal transplant recipient**.**  **Presentation of the Case**: A 32 year old female renal transplant recipient, presented with fever, cough and weight loss, 7 years post transplant. Pulmonary tuberculosis was diagnosed through bronchoscopy and treated with standard antituberculous therapy and immunosuppression was modified. However, she developed intestinal obstruction requiring emergency surgery and had ileal perforation with histopathology report of granulomatous inflammation and subsequently found to have disseminated infection on detailed evaluation.  **Discussion**: The case highlights the challenges in diagnosing and managing Tuberculosis in transplanted patients. It also underscores the importance of surveillance for drug interactions and adverse effects.  **Conclusion**: TB remains a significant concern in renal transplant recipients, requiring prompt diagnosis and careful management to prevent complications. |

*Keywords: Kidney transplant, Infections, Tuberculosis, Disseminated*

1. INTRODUCTION

Tuberculosis is a common opportunistic infection in renal allograft recipient worldwide. The prevalence varies from, 3.1% to 15% in Asia,1.7% to 5% in Europe, and approximately 1.5% in the USA (Anand et al., 2017).

The incidence of TB among transplant recipients is 37 to 50 fold higher than the general population. India has a reported incidence of Tuberculosis(TB) in 11.8%–12.3% among renal transplant recipients. The diagnosis and treatment, however remain challenging (Parameswaran et al., 2010).

The most common cause is due to reactivation of latent TB. Symptoms are often nonspecific and hence diagnosis are delayed and treatment is difficult due to drug interactions and side effects.

Here we report a case of post transplant disseminated TB.

**2.CASE REPORT**

A 32 yr old lady, presented to our transplant clinic, with complaints of low grade fever and minimally productive cough of mucoid expectoration, of 2 weeks duration. She noticed loss of appetite and a weight loss of 6 kg over the previous 3 months.

The patient is a known chronic kidney disease with native kidney disease of cystic kidney disease, diagnosed in 2010 and underwent deceased donor transplant in 2017, after a dialysis vintage of 7 years. She received induction with Basiliximab and was started on triple immunosuppression with Prednisolone, Tacrolimus and Mycophenolate and had a stable graft function. She developed post transplant Diabetes one month later, controlled with single oral hypoglycemic drug. She was also given antimicrobial prophylaxis of Valgancyclovir and Cotrimoxazole for a year. She maintained strict compliance with medications as well as with followup.

She had no previous history of Tuberculosis(TB) or history of contact with a tuberculous patient. The tuberculin skin test and chest X ray of patient were normal prior to transplant. No chemoprophylaxis for TB was given in the post transplant period. No history of exposure to pets or long distance travel.

On physical examination, patient looked pale, emaciated and malnourished, with stable vitals and body mass index of 15kg/m2. Systemic examination was normal. Laboratory investigations revealed Hemoglobin of 7 g/dl, microcytic picture in smear, Erythrocyte sedimentation rate of 110mm/hour, creatinine of 2 mg/dl and viral serology was positive for Hepatitis C. Blood and urine culture showed no growth. Chest X ray was suggestive of right upper lobe consolidation with cavity.

Sputum studies were negative for any bacterial, tuberculous or fungal infection. Computed Tomography(CT) chest showed thin walled cavitatory lesion of 21mm\* 18mm with consolidation and fibrotic bands and opacities and patchy fibrocavitatory and traction bronchiectatic changes in right lower lobe and multiple centrilobular nodules with tree in bud appearance in bilateral lung fields (Figure 1). Hence Bronchoscopy was done, bronchoalveolar washings was positive for acid fast bacilli by Gene Xpert.

Initially after admission, she was given, broad spectrum antibiotics, adequate hydration, correction of anemia and improvement of nutrition. Immunosuppression modified, by holding Mycophenolate. Subsequently, standard Antituberculous therapy(ATT) of daily Rifampicin (10 mg/kg/day) and Isoniazid (5 mg/kg/day) and thrice weekly dose of Ethambutol (25 mg/kg/day) and Pyrazinamide (15 mg/kg/day) and Pyridoxine (10 mg/day) was initiated along with Sofosbuvir 400mg/day and Velpatasvir 100mg/day.

After initiation of ATT, fever subsided and her general condition improved in 2 weeks, with Hemoglobin of 9.5 g/dl, creatinine of 1.2mg/dl and normal liver functions and Pyrazinamide and Ethambutol changed to daily dose. Blood Tacrolimus level was at 7ng/ml.

Two months later, she presented to Emergency department with severe abdominal pain and multiple episodes of vomiting. Blood pressure was 80 systolic with thready pulse, and had rigid, tender abdomen. Laboratory profile showed leucocytosis (35000 cells/mm3, 90% neutrophils), creatinine of 1.1mg/dl, normal electrolytes. Abdominal imaging showed dilated small bowel loops with bowel fecal sign suggestive of intestinal obstruction. She underwent Emergency laparotomy and had distal ileal perforation of 2\*2 cm noted in ileum, with dense adhesions between ileum and bladder (Figure 2). Adhesiolysis and end ileostomy was done. Postoperatively, though initially patient was dependent on organ supports, she got improved over the next 3 days, with stable renal function and normalising blood counts.

Her Histopathology report of resected ileum and omentum, was suggestive of chronic granulomatous inflammation (Figure 3). Thorough evaluation for resistant TB was done, due to persistent pulmonary cavitatory lesion, despite after intensive phase of 2 months. Subsequently subjected to whole body Positron emission tomography(PET) imaging and showed metabolically active lesions in mesentery, distal ileal loops, abdominal wall, and right lung upper and lower lobe ,indicative of multifocal tuberculosis (Figure 4,5).

However repeat CBNAAT was done with induced sputum and Rifampicin sensitivity was confirmed, thus ruling out drug resistance. Hence continued her ATT regimen in same dose. Patient is on regular follow up, with better appetite, stable renal function and on dual immunosuppression and ATT.

3. discussion

Post transplant Tuberculosis(TB) manifest in different organ systems like respiratory involvement in 50% of cases, disseminated TB in 30%, lymph nodes in 5%, skin and soft tissues in 4%, genitourinary system in 4%, intestines in 3%, CNS in 2%, and bones in 1%. It presents as Fever of Unknown Origin too, in about 16% of cases (Fiske et al, 2010).

Chest radiograph is abnormal in the majority, showing focal infiltrates, nodules, military pattern, pleural effusion, and/or diffuse interstitial infiltrates. The clinical features of TB can be unusual and may be masked because of the blunted response to infection (Klote et al., 2004). In addition, extra pulmonary lesions are more frequent in patients following transplantation compared to patients without immunosuppression (Hussam et al., 2002).

Disseminated TB account for 30% of transplant cases, in contrast to the 0.6–1.4% incidence in general population and commonly presents as fever of unknown origin (Hussam et al., 2004). The high rate of miliary spread in transplant recipients can be attributed to their continuing use of immunosuppressive drugs that weaken T cell immunity, which is the body’s main defense against TB (Khattab et al., 2007). Allograft biopsies done for unexplained graft dysfunction may show granulomas on rare occasion in disseminated TB (Sundaram et al., 2008).

Sundaram et al (2008), stated that major risk factors of disseminated TB are chronic liver disease, other coexisting infections like deep mycoses, pneumocystis pneumonia, nocardia and cytomegalovirus and Antithymocyte globulin. In addition, John et al.(2001) found that compared to Prednisolone and Azathioprine based immunosuppression, Calcineurin inhibitors increase the risk of TB 2.5 fold, and causes the infection to occur earlier and also predisposes to more disseminated disease. Specific donor and recipient characteristics such as a preexisting infection or immunosuppressed state, use of antimicrobial prophylaxis, and the net level of immunosuppression influence the timing of infections.HLA68(28)/A69(28) locus has predisposition towards post transplantation TB in Indian population (Sakhuja et al.,2015). There are case reports where TB manifested immediately after substitution of Azathioprine with Mycophenolate (Mercadel et al., 2005).

The overall mortality among renal allograft recipients with TB is 29%. The factors associated with death are recipient age, HLA less than 1 antigen match, Prednisolone- Azathioprine immunosuppression, pretransplantation TB and post transplant TB (after two years),chronic liver disease, Diabetes, post transplant Diabetes and presence of coexisting infections( John et al., 2001).

Treatment of TB in renal transplant patients is not different from the normal population. However, the use of Rifampicin must be cautious because of its frequent drug interaction, and blood levels of immunosuppressive drugs should be monitored (Sasi et al., 2020). Routine chemoprophylaxis against TB often remained controversial, however studies suggest Isoniazid prophylaxis for high risk patients(Shu et al., 2020).Often multidrug resistant TB develops in transplant patients, which is predominantly due to poor compliance to lengthy treatment and drug toxicities. Studies based on newer regimen with Bedaquiline, Pretomanid, Linezolid and Moxifloxacin are limited, with evidence of side effects and drug interaction (Babar et al, 2021).

Disseminated nature of TB in transplant recipients may lead to delay in diagnosis due to atypical presentation hence aggressive evaluation including whole body PET imaging to be utilised. Minimization of immunosuppression, along with administration of ATT is needed in treatment of disseminated TB after transplantation, as observed in this case.

**4. CONCLUSION**

Tuberculosis in allograft recipient is a common problem in developing countries, where the incidence in general population is high. The presentation of the disease differs in transplant patients, and high index of suspicion is needed in diagnosing. The interaction of antituberculous drugs with immunosuppressive agents has to be looked into and surveillance for adverse effects and the duration of treatment has to be prolonged. Drug resistance and atypical mycobacterial infections also needs to be suspected in non responding cases.

Consent

All authors declare that ‘written informed consent was obtained for publication of this case report and accompanying images, as per international standards or university standards, and preserved by the authors.

Ethical approval

As per international standards or university standards written ethical approval has been collected and preserved by the authors.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Authors hereby declare that no generative AI technologies have been used during writing or editing of this manuscript.

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**FIGURES:** 1-5-Radiology, Intra-operative and Histo-pathology images**.**

