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 at a public sector hospital in South India.. 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**: Tuberculosis remains a significant concern in renal transplant recipients, requiring prompt diagnosis and careful management with vigilant monitoring of immunosuppressive levels to prevent complications. |

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

1. INTRODUCTION

Tuberculosis (TB) is a significant opportunistic infection in kidney transplant recipients, with a higher incidence and prevalence compared to the general population, resulting in substantial morbidity and mortality. The global prevalence of active TB in transplant recipients varies widely, ranging from 0.3% to 15.2% (Sorohan et al., 2021), with regional disparities: 3.1% to 15% in Asia, 1.7% to 5% in Europe, and approximately 1.5% in the USA (Anand et al., 2017).

Notably, transplant recipients are 37 to 50 times more likely to develop TB than the general population. In India, the incidence of TB among renal transplant recipients is particularly high, ranging from 11.8% to 12.3% (Parameswaran et al., 2010).

Diagnosing and treating TB in this population poses challenges due to nonspecific symptoms, potential drug interactions, and side effects, often resulting in delayed diagnosis and treatment. Reactivation of latent TB is the most common cause, further complicating management. Here we report a case of post transplant disseminated TB at a public sector hospital in South India.

**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(Table 1). 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, as per the institutional protocol. Subsequently, standard Antituberculoustherapy (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( Table 1). 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. There were no surgical complications.

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 followup, with better appetite, stable renal function and on dual immunosuppression and ATT.

**Table 1:- Laboratory profile of the case**

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| Laboratory parameters | Initial presentation | After Two months | Normal values |
| Hemoglobin(g/dl)  Perpheral smear | 7  Microcytic hypochromic | 9.5 | 10-12 |
| Total white cell count (cells/mm3)  Neutrophils(%) | 5500  65% | 35000  90% | 4000-11000  60-70% |
| Serum creatinine(mg/dl) | 2 | 1.1 | 0.6-1.1 |
| Serum sodium(meq/l) | 133 | 134 | 135-145 |
| Serum potassium (meq/l) | 4 | 3.7 | 3.5-5 |
| Serum magnesium (meq/l) | 1.7 | 1.6 | 1.5-2.4 |
| Liver function tests |  |  |  |
| Bilirubin- total(mg/dl) | 0.9 | 1.3 | 0.1-1.2 |
| Aspartate aminotransferase/alanine aminotransferase(u/l) | 12/14 | 16/18 | 8-33/7-55 |
| Albumin(g/dl) | 3.2 | 3.3 | 3.5-5 |
| C reactive protein(mg/l) | 5 | 180 | <3 |
| Erythrocyte sedimentation rate(mm/hr) | 110 |  | 0-20 |
| Tacrolimus level(ng/ml) | 7 |  | 4-8 |
| Viral serology  (infection profile screening) | Hepatits C ELISA- positive  HCV RNA load- 300,000 IU/L |  |  |
| Urine analysis and culture | No growth | No growth |  |
| Blood culture | No growth | No growth |  |
| Sputum | Gram stain and culture – No pathogenic organsim isolated.  Fungal and acid fast bacilli negative  Repeat- after 2 months- postive for acid fast bacilli, Rifampicin sensitive. | | |
| Bronchoalveolar lavage | Acid fast bacilli in Gene Xpert |  |  |
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FIGURES:1-5-Radiology, Intra-operative and Histo-pathology images.



3. discussion

Post-transplant tuberculosis (TB) manifests in various organ systems, with respiratory involvement in 50% of cases, disseminated TB in 30%, and other forms affecting lymph nodes(5%), skin(4%), genitourinary system(4%), intestines(3%), CNS(2%), and bones(1%). The clinical features of TB can be unusual and masked due to the blunted response to infection. Disseminated TB accounts for 30% of transplant cases, often presenting as fever of unknown origin (Sasi et al., 2020, Fiske et al., 2010).

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). The major risk factors of disseminated TB are chronic liver disease, other coexisting infections like deep mycoses, pneumocystis pneumonia, nocardia and cytomegalovirus and Antithymocyte globulin. Allograft biopsies done for unexplained graft dysfunction may show granulomas on rare occasions in disseminated TB (Sundaram et al., 2008).

The choice of immunosuppressive regimen can significantly impact the risk and presentation of TB. For instance, calcineurin inhibitors increase the risk of TB by 2.5 fold and predispose to more disseminated disease (John et al., 2001). Specific donor and recipient characteristics, such as preexisting infections or immunosuppressed states, also influence the timing and manifestation of infections. HLA68(28)/A69(28) locus has predisposition towards post-transplantation TB in the Indian population (Sakhuja et al., 2015).

Samples from unusual sites of involvement and even sputum may not have a positive acid-fast bacilli stain, and there may be a delay in the confirmation of diagnosis. Therefore, quick diagnostic techniques like adenosine deaminase and rapid molecular diagnostic tests ( Gene Xpert/ RIF or TB polymerase chain reaction-PCR) should be performed for an early and prompt diagnosis (Bansal et al., 2023). Those with significant loss of weight, pyrexia, and have little sputum should be aggressively evaluated with bronchoalveolar lavage and computed tomography of the chest should be performed (Prasad et al., 2024).  
  
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).

The emergence of drug-resistant TB strains in transplant recipients is a growing concern, with studies suggesting that poor compliance and drug toxicities contribute to resistance (Shu et al., 2020). Recent studies have highlighted the need for vigilant monitoring and tailored treatment approaches to manage drug-resistant TB in transplant recipients. Bedaquiline-based regimens have shown promise in treating drug-resistant TB in transplant recipients (Babar et al., 2021). Other studies have explored the use of pretomanid and linezolid in treating multidrug resistant TB (Rashid et al., 2021).

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, pretransplantationTB and post transplant TB(after two years),chronic liver disease, Diabetes, posttransplant Diabetes and presence of coexisting infections( John et al., 2001).

The clinical significance of this case lies in the importance of early recognition and prompt treatment of tuberculosis in immunocompromised patients, particularly in transplant recipients. Delayed diagnosis can lead to severe consequences, including graft dysfunction and increased mortality. Minimization of immunosuppression, along with administration of ATT, is needed in the treatment of disseminated TB after transplantation, as observed in this case. This case highlights the need for clinicians to maintain a high index of suspicion for TB in transplant patients, especially in high-risk populations, and to consider alternative diagnostic tools and treatment approaches in complex cases. This also enlighten the importance of being vigilant in monitoring drug interactions, treatment efficacy, and patient outcomes in immunosuppressed patients with TB.

By sharing our experience and insights, we aim to contribute to the growing body of literature on TB in transplant patients. The importance of this manuscript lies in its potential to inform clinical practice and stimulate further research on TB in immunosuppressed patients. Given the complexities of managing TB in transplant patients, it is crucial to carefully consider immunosuppressive regimens and potential resistance patterns. Enhancing discussions on these topics can help optimize care and improve outcomes for immunocompromised patients with TB.

**4.CONCLUSION**

Tuberculosis in allograft recipients is a common problem in developing countries. A high index of suspicion is needed for diagnosis. The interaction of antituberculous drugs with immunosuppressive agents requires careful monitoring. Our case differs from previously reported cases in that it highlights the importance of considering Tuberculosis in the differential diagnosis of transplant patients with nonspecific symptoms.

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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