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Case Report of Intestinal Tuberculosis 6 Years After Simultaneous Pancreas and Kidney Transplant

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ABSTRACT

Tuberculosis (TB) is often difficult to diagnose in immunocompromised patients and occurs 20 to 74 times more frequently in recipients of solid organ transplants than in the general population. We present the case of a 40-year-old female immigrant from Mexico previously treated for latent TB who underwent a simultaneous pancreas and kidney transplant. She experienced 3 episodes of rejection and then presented with 4 months of nonspecific abdominal pain. She was ultimately diagnosed with disseminated TB presenting with intestinal perforation and pulmonary involvement. This case illustrates the need for clinicians to maintain a high index of suspicion for TB in transplant recipients, especially those previously treated for TB or rejection.

TUBERCULOSIS (TB) remains a significant global health burden, accounting for 1.4 million deaths in 2011 [1], with 95% of deaths occurring in the developing world. Astoundingly, up to one third of the world's population is estimated to be latently infected with TB. The greatest risk of reactivation in this population occurs during episodes of significant immune suppression. In fact, TB occurs 20 to 74 times more frequently in solid organ transplant recipients than in the general population [2]. Although transplant recipients are at increased risk of TB, intestinal TB is very rare in any patient population.

We report the case of a patient who underwent a deceased donor simultaneous pancreas and kidney (SPK) transplant in 2007 complicated by 3 episodes of rejection; she was ultimately diagnosed with intestinal TB leading to perforation and pulmonary TB.

CASE REPORT

A 40-year-old female immigrant from Mexico with type 1 diabetes mellitus complicated by end-stage renal disease underwent a deceased donor SPK transplant in June 2007 at the University of California San Francisco. She was previously treated with 9 months of isoniazid for a positive Mantoux skin test result in 2003. At the time of transplant, the patient was given thymoglobulin 6 mg/kg for induction and transitioned to an outpatient regimen of mycophenolate mofetil, prednisone, and tacrolimus. Her immediate postoperative course was unremarkable, but she later experienced 3 episodes of rejection. The first episode was an acute cellular rejection of the pancreas graft (confirmed by biopsy) treated with steroid pulse 3 months after SPK transplant. The second episode of rejection was an antibody-mediated rejection of the pancreas graft (confirmed by biopsy) 2 years after transplant that was treated with thymoglobulin and intravenous immunoglobulin. The final episode was a combined acute cellular and C4D-positive antibody-mediated rejection of the pancreas graft 5 years after the SPK transplant, again requiring thymoglobulin and intravenous immunoglobulin. She subsequently had good function of both allografts until she presented to the emergency department 6 years after the SPK transplant describing vague abdominal pain of 4 months' duration, with intermittent nausea and diarrhea. The pain was characterized as diffuse but often localized to the right lower quadrant. The patient denied any associated symptoms such as cough, hemoptysis, fever, night sweats, or shortness of breath, and also denied any incarceration, travel outside of the United States since transplant, or contact with people known to be infected with TB.

The initial laboratory evaluation revealed a serum creatinine level of 1.92 mg/dL, white blood cell count of 8.0×10^{-9}/L, serum amylase level of 68 U/L, and serum tacrolimus level of 22.1 μg/L. The patient's abdomen was not distended but was mildly tender to palpation in the right lower quadrant. Plain chest radiography demonstrated no abnormalities. Sonograms of the pancreas and kidney grafts were unremarkable. A computed tomography (CT) scan of her abdomen and pelvis with intravenous contrast demonstrated a heterogeneous enhancing fluid collection anteromedial to the pancreas graft adjacent to a short segment of thickened ileum

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(Fig 1). There was no safe route for percutaneous drainage of the collection, and intravenous antibiotics for an intra-abdominal abscess were started. The abdominal pain in her right lower quadrant worsened over 48 hours, and she was taken to the operating room for an exploratory laparotomy. The abscess cavity within the mesentery of the distal ileum was identified adjacent to the segment of significantly thickened ileum seen on the CT scan. Assuming the abscess was caused by perforation of the adjacent thickened ileum, we resected ~7 cm of distal ileum, being careful not to disrupt the enteric or vascular pancreatic graft anastomoses. Kinyoun stain of the abscess cavity revealed acid-fast bacilli (Fig 2), and frozen section analysis demonstrated necrotizing granulomas (Fig 3), consistent with TB. Continuity of the small bowel was reestablished, and an intra-abdominal drain was placed adjacent to the abscess cavity.

Postoperatively, anti-TB therapy with isoniazid, rifabutin, ethambutol, and pyrazinamide was used. Results of induced sputum cultures demonstrated acid-fast bacilli by polymerase chain reaction. Mycobacteria TB complex polymerase chain reaction of the small bowel was positive for the IS6110 locus, confirming the diagnosis. A CT scan of the chest subsequently demonstrated scattered noncalcified pulmonary nodules (Fig 4) not seen on her chest radiograph at the time of admission. She was discharged on postoperative day 25 with a plan for 9 months of anti-TB therapy.

DISCUSSION

TB is often difficult to diagnose in immune-suppressed patients. Intestinal TB is very rare in any patient population, and when it does occur, the most frequent sites of infection are the ileocecal junction, ileum, cecum, ascending colon, jejunum, appendix, duodenum, stomach, sigmoid, and then rectum [3]. The most common finding on a CT scan is mural thickening of the bowel, and 40% to 70% of patients have lymphadenopathy with hypodense centers and peripherally rim-enhancing fluid collections. Our patient's bowel exhibited concentric mural thickening adjacent to a rim-enhancing fluid collection. In our patient, radiographic findings on plain chest radiograph were nonspecific, as is typical [4].

A retrospective review of the 20-year experience at a single institution with TB in solid organ transplant recipients demonstrated rates of 0.47%, 0.22%, 1.1%, and 0.54% among kidney, liver, kidney-pancreas, and heart recipients, respectively [5]. The mean posttransplant time to diagnosis was 21 months, and 47% of cases were pulmonary TB, 28.6% were extrapulmonary TB, and 23.8% were disseminated. Although it is estimated that one third to one half of all cases are actually disseminated at the time of

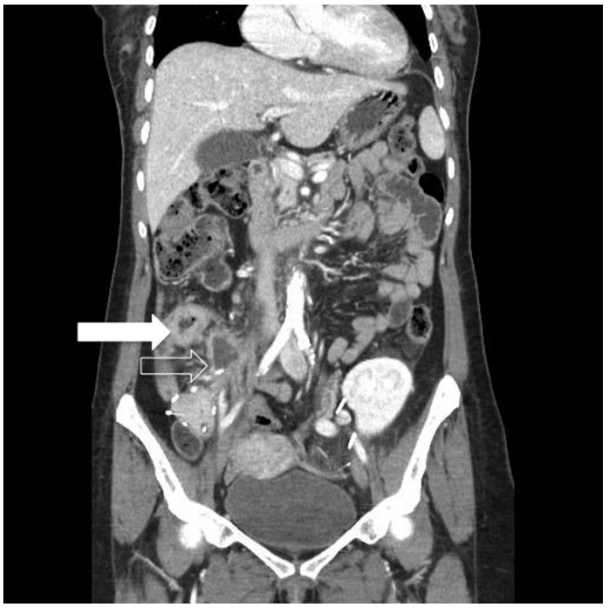

Fig 1. Coronal sections of the computed tomography scan demonstrating the heterogeneous fluid collection (open arrow), adjacent to the normal-appearing pancreas graft and the thickened small intestine (solid white arrow).

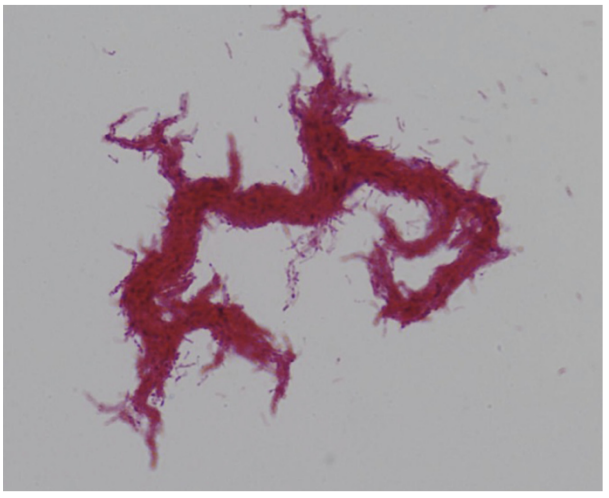

Fig 2. Kinyoun stain of abdominal tissue demonstrating acid-fast bacilli.

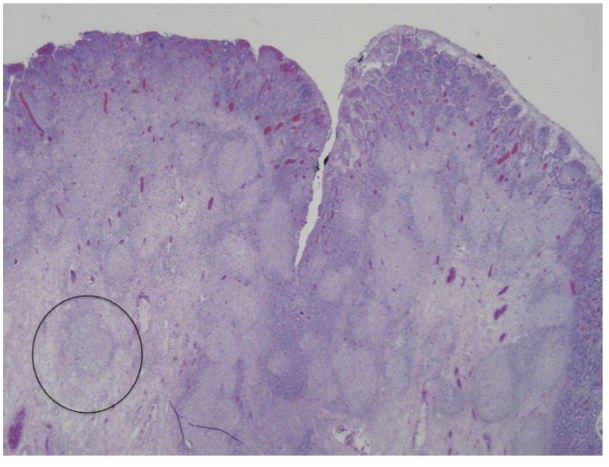

Fig 3. Hematoxylin and eosin stain of the small intestine demonstrating multiple submucosal necrotizing granulomas (one is circled).

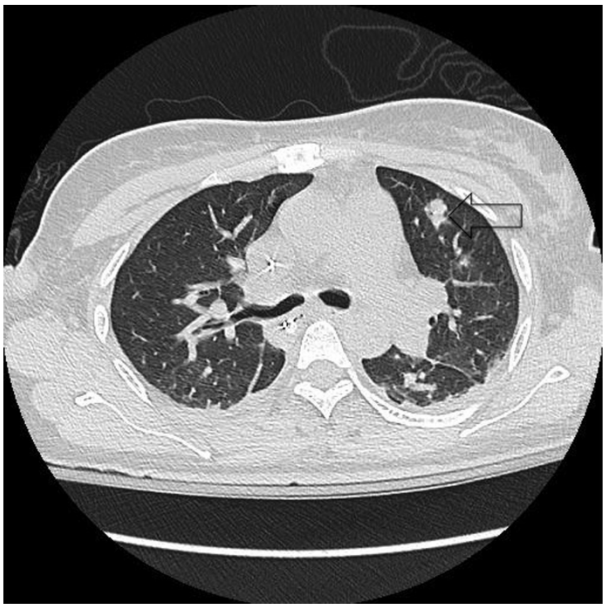

Fig 4. Computed tomography scan of the chest demonstrating noncalcified pulmonary nodule (open arrow).

diagnosis, the diagnosis of TB in the solid organ transplant recipient can be elusive [6]. Classic symptoms such as fever, night sweats, and cough may not be present, as was true for our patient, who experienced only vague abdominal pain and diarrhea.

Once TB has been diagnosed, the Health Department should be contacted and a consultation with a transplant infectious disease specialist should be obtained. Treatment should include negative pressure isolation, search for disseminated disease with a CT scan of the chest, and therapy with isoniazid, rifampin, and pyrazinamide (with the addition of ethambutol or streptomycin, depending on local resistance patterns). Treatment of active TB can be difficult in transplant recipients because rifampin is well known to decrease levels of cyclosporine, tacrolimus, everolimus, and sirolimus, resulting in graft loss in as many as 25% of patients due to drug interactions [4]. Rifabutin is an alternative to rifampin and is thought to cause less cytochrome P450 enzyme induction. Isoniazid is included unless there is a known local resistance or toxicity, as is pyrazinamide. Close monitoring for hepatotoxicity is required. Given the possibility of multidrug-resistant disease in our patient, we included ethambutol after determining the patient had normal results on the ophthalmologic examination. Four-drug therapy is continued for 2 months after diagnosis, but unfortunately, there are few recommendations to guide long-term management. Munoz et al recommend 3-drug therapy for 1 year after diagnosis, with the most worrisome complication of prolonged treatment being hepatotoxicity.

In conclusion, our case, in which TB presented as intestinal perforation, illustrates the need for clinicians to maintain a high index of suspicion for TB in transplant recipients, especially those previously treated for TB or for episodes of rejection.

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