Diagn Interv Radiol 2008; 14:221–224

CT findings in fatal primary intestinal tuberculosis in a liver transplant recipient

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ABSTRACT
Tuberculosis is a rare post-transplant infection that can present an atypical and misleading clinical picture. The possibility of tuberculosis must be taken into account when a transplant patient has fever and severe abdominal complaints with no clear evidence of another infection. We report a patient with primary intestinal tuberculosis, which was not accompanied by pulmonary, peritoneal, or solid-organ involvement. To our knowledge, this is the only reported case to date of intestinal tuberculosis post liver transplantation.

Key words: • *tuberculosis, gastrointestinal* • *liver transplantation* • *computed tomography*

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Received 13 March 2007; revision requested 27 July 2007; revision received 27 July 2007; accepted 5 September 2007.

Tuberculosis (TB) is a serious opportunistic infection in transplant recipients, with an incidence in organ transplant recipients ranging from 0.35% in developed countries to 15% in endemic areas. Most reports of post-transplantation TB have been in renal transplant patients (1). Reports of infection after transplantation of other organs are rare, and, to our knowledge, only few cases of TB after liver transplantation have been reported (2). TB after transplantation has a mortality rate of as high as 40%. The majority of *Mycobacterium tuberculosis* infections occur within 12 months after transplantation (3).

In this report, we present the computed tomography (CT) findings of a liver transplant patient with fatal primary intestinal TB, and correlate the CT findings with the results of a detailed histological evaluation.

Case report

A 55-year-old woman underwent orthotopic liver transplantation (OLT) in 2004 for decompensated cirrhosis secondary to chronic hepatitis. Following surgery, she received standard immunosuppressive agents, including prednisolone and tacrolimus. The patient was well until two months prior to admission, when she began to experience fever and abdominal pain. She was admitted to our hospital with fever, abdominal pain, and diarrhea. Her temperature was 39ºC.

Physical examination showed abdominal tenderness but otherwise normal findings. ELISA for IgG and IgM antibodies to cytomegalovirus, Epstein-Barr virus,*Toxoplasmosis gondii*, herpes simplex virus-1, and human immunodeficiency virus were negative. Blood, sputum, feces, and urine cultures also were negative. The laboratory results were: red blood cells, 3.5x 10^6 /µl; hemoglobin, 8.6 g/dL; white blood cells, 9.6x10^3/µl; platelets, 381x10^3/µl; serum creatinine, 1.36 mg/dL; urea, 47 mg/dL; sodium, 128 mmol/L; chloride, 90 mmol/L; magnesium, 0.51 mmol/L; calcium, 2.1 mg/dL; fibrinogen, 561 mg/dL; erythrocyte sedimentation rate, 56 mm/h; alanine transaminase, 8 u/L; aspartate transaminase, 12 u/L; total bilirubin, 0.47 mg/dL; direct bilirubin, 0.17 mg/dL; total protein, 6.5 g/dL; and alkaline phosphatase, 216 u/L. Electrocardiogram showed no abnormalities.

There was no history of exposure to TB, or radiological evidence of prior pulmonary TB on chest X-ray. Colonoscopy revealed two superficial ulcerations with a diameter of a few millimeters in the distal transverse colon, while the other segments of the colon were normal. Evaluation of the terminal ileum showed edema and ulcers. The biopsies obtained from this site showed mixed inflammation, granulomas, and a giant cell in the lamina propria (focal active infectious reaction).

Abdominal contrast-enhanced CT (with oral and intravenous contrast) obtained at venous phase showed concentric mural thickening affecting the ileocecal region, the terminal ileum, and the distal ileal loops. CT

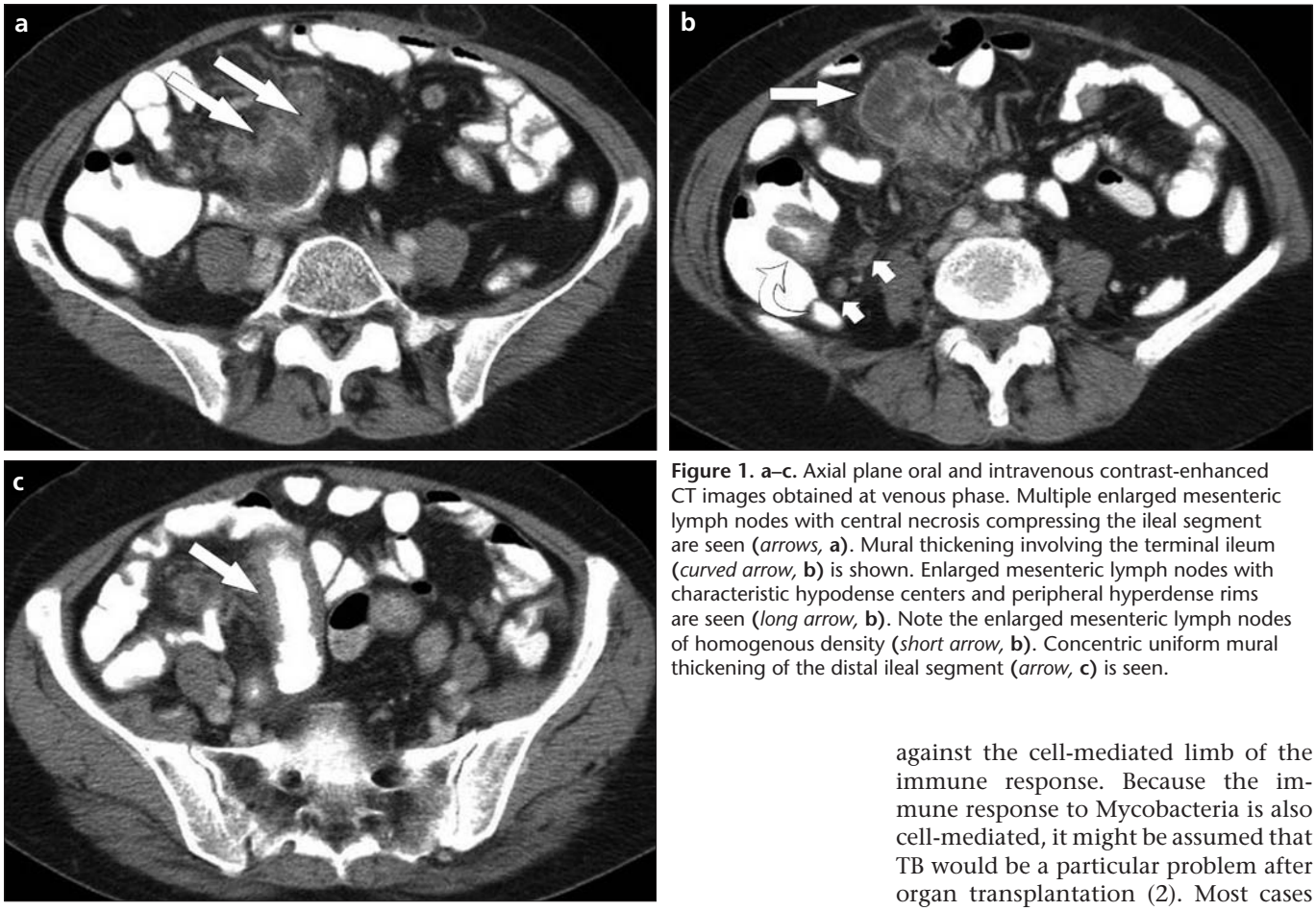

Figure 1. a–c. Axial plane oral and intravenous contrast-enhanced CT images obtained at venous phase. Multiple enlarged mesenteric lymph nodes with central necrosis compressing the ileal segment are seen **(***arrows,* **a)**. Mural thickening involving the terminal ileum **(***curved arrow,* **b)** is shown. Enlarged mesenteric lymph nodes with characteristic hypodense centers and peripheral hyperdense rims are seen **(***long arrow,* **b)**. Note the enlarged mesenteric lymph nodes of homogenous density **(***short arrow,* **b)**. Concentric uniform mural thickening of the distal ileal segment **(***arrow,* **c)** is seen.

also showed multiple enlarged nodes with hypodense centers and peripherally enhanced rims in the adjacent mesentery (Fig. 1). Multiple normal-sized retroperitoneal and mesenteric lymph nodes of homogenous density also were noted. Mesenteric and pericecal fat showed minimal haziness. There was no evidence of ascites, omental thickening, or peritoneal or solid organ involvement.

The result of a pretransplant tuberculin skin test was not known. In addition, it was unknown whether she had received TB prophylaxis. Sputum smear for acid-fast bacilli and subsequent TB culture were both negative.

In the next few days, the general condition of the patient deteriorated; therefore, a diagnostic laparotomy was performed. Laparotomy showed multiple mesenteric lymph nodes, and wall thickening and inflammation of the ileum and cecum. Short-segment ileal resection was performed.

Gross examination of the resected specimen demonstrated ulcers on the mucosal surface. The nonulcerated mucosa appeared edematous. Regional mesenteric lymph nodes were enlarged, containing areas of caseous necrosis.

Microscopic examination of the specimen revealed ulceration and granulomas. The lymph nodes contained epithelioid granulomas with central necrosis. Ziehl-Nielsen stain demonstrated abundant acid-fast bacilli consistent with *M. tuberculosis*; thus, a diagnosis of intestinal TB was established (Fig. 2).

Antituberculosis therapy with isoniazid (300 mg), ethambutol (1.5 g), and rifampicin (600 mg) was started. The patient's clinical condition deteriorated despite the antituberculosis therapy, and she died of septic shock a few days later.

Discussion

Immunosuppressive therapy increases the incidence of infection; the spectrum of pathogens and the clinical course of these infections are also different from those in the immunocompetent host. Current immunosuppressive protocols are directed mainly against the cell-mediated limb of the immune response. Because the immune response to Mycobacteria is also cell-mediated, it might be assumed that TB would be a particular problem after organ transplantation (2). Most cases of TB in transplant patients have been reported among renal transplant patients (1–11). Reports of infection after transplantation of organs other than kidney are rare, and, to our knowledge, only few cases of TB after liver transplantation have been reported (2).

The causative organism is usually *Mycobacterium tuberculosis hominis* or atypical Mycobacteria (*M. avium intracellulare*), the latter being associated with acquired immune deficiency syndrome. In the study of Singh and Paterson, only 7–10% of liver transplant patients had TB two or more years after transplantation (4). In our patient, intestinal TB occurred in the second year post transplantation.

Autopsies of patients with pulmonary TB demonstrated intestinal involvement in 55–90% of fatal cases, while pulmonary involvement was seen in only 15% of patients with intestinal TB (5, 6). In our patient, autopsy was not performed.

In the abdomen, TB may affect the intestinal tract, lymph nodes, peritoneum, and solid viscera (7). As many as two-thirds of patients with abdominal TB may have lymphadenopathy or

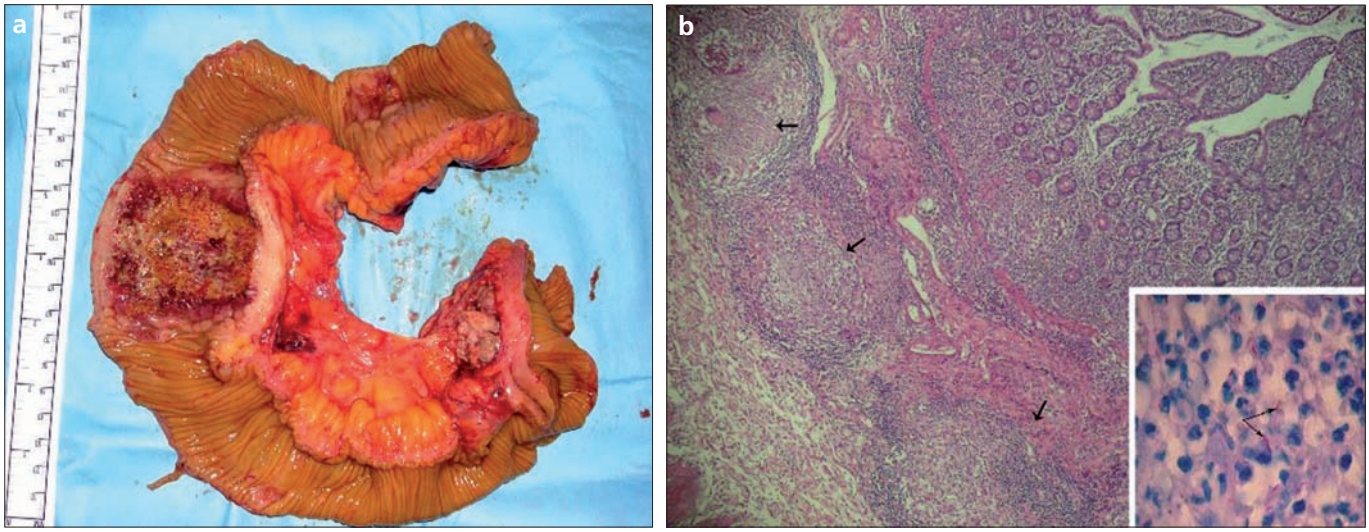

Figure 2. a, b. The specimen **(a)** demonstrating the ulcerative form of tuberculosis. Photomicrograph **(b)** (original magnification, x100; hematoxylin-eosin stain) of resected intestinal specimen revealing submucosal caseous necrosis, epitheloid granulomas, and Langhans' giant cells *(arrows)*. Inset: abundant acid-fast organisms *(arrows)* are seen within the granulomas (original magnification, x1000; Ziehl-Nielsen stain).

peritoneal disease in addition to intestinal involvement. In the present case, there was no ascites, omental thickening, or any findings of peritoneum or solid organ involvement.

The most frequent site of intestinal involvement is the ileocecal junction, followed by the ileum, cecum, ascending colon, jejunum, appendix, duodenum, stomach, sigmoid colon, and rectum (4, 5, 8). In gastrointestinal disease, fever and varying severity of gastrointestinal bleeding (ranging from heme-positive stools to massive bleeding) have been reported as the usual presenting symptoms (4).

Tubercle formation and caseous necrosis are characteristically seen in the bowel wall which incites an inflammatory response. Ulceration of the overlying mucosa results in the more common ulcerative form of the disease. The hyperplastic form is the second type which features florid bowel wall thickening. A combination of the two results in the ulcero-proliferative type (8, 9). Although mucosal changes are best evaluated with barium examinations, evidence of extramucosal disease is both indirect and incomplete. Abdominal CT shows extramucosal changes directly, can also reveal mucosal changes, and is considered essential for the evaluation of peritoneal, nodal, and visceral involvement (7, 8). CT is therefore ideal in defining the true extent of disease, assessing complications and for follow-up (8).

The most common CT finding is mural thickening affecting the ileocecal region, either limited to the terminal ileum or cecum, or, more commonly, simultaneously involving both regions. This mural thickening is usually concentric, but is occasionally eccentric and predominantly affects the medial cecal wall. Ileocecal involvement is usually associated with enlarged nodes in the adjacent mesentery. The mesenteric, mesenteric root, celiac, porta hepatis, and peripancreatic nodes are characteristically involved, reflecting the lymphatic drainage of the small bowel. In the majority of patients (40–70%), CT shows enlarged nodes with hypodense centers and peripherally enhancing rims, explained by the usual findings of an extensive perinodal inflammatory reaction and central caseous necrosis (7).

Radiologic features are not pathognomonic for TB, but can be strongly suggestive when considered along with the clinical presentation and immune status of the patient. Similar patterns may be seen with metastases of malignant neoplasms (e.g., head and neck squamous carcinomas), Whipple's disease, lymphoma following chemotherapy, and infection with *M. avium intracellulare*. Other CT patterns of lymph node morphology include: (i) conglomerate mixed density nodal masses, (ii) enlarged nodes of homogenous density and (iii) increased number (>3 in one CT section) of normal sized or mildly enlarged mesenteric nodes of homogenous density. Calcification of nodes may be seen occasionally (6, 7).

Intestinal TB can resemble Crohn's disease. In addition, *Yersinia enterocolitica* can produce mesenteric adenopathy with ulcerations and thickening of the bowel mucosa. In the differential diagnosis, such rare diseases as adenocarcinoma of the small bowel, ameboma, syphilis, and lymphogranuloma venereum can be considered (5).

TB in organ transplant recipients may develop after reactivation of old quiescent disease, nosocomial exposure, or transmission by cadaveric or living donors with TB. In our patient, there was no history of exposure to TB, or radiological evidence of prior pulmonary TB on chest X-ray. The result of pre-transplant tuberculin skin test was not known. In addition, whether she had received TB prophylaxis was unknown. Autopsy was not performed. We assumed that de novo infection might have been responsible for the clinical picture.

In conclusion, TB is a rare post-transplant infection that can present atypically, with a misleading clinical picture. Establishing the correct diagnosis is crucial because untreated disease has a significant mortality rate. The possibility of TB must be taken into account when a transplant recipient has fever and severe abdominal complaints with no clear evidence of another infection. There is no pathognomonic radiological sign for the

diagnosis; however, several features including mural thickening in the ileum and cecum, and enlargement of adjacent mesenteric lymph nodes are suggestive radiological findings. The most reliable diagnostic method for mycobacterial infection of the gastrointestinal tract is the histopathologic examination of the specimens obtained at laparotomy (5).

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