Urgent Living-Donor Liver Transplantation in a Patient With Concurrent Active Tuberculosis: A Case Report

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ABSTRACT

Background. Although active tuberculosis (TB) is considered a contraindication for liver transplantation (LT), this is the only treatment in patients with liver failure and concurrent active TB. We report a case with successful urgent living-donor LT for irreversible liver failure in the presence of active TB.

Case Presentation. A 48-year-old man, with a history of decompensated alcoholic liver cirrhosis, was presented with stupor. At admission, his consciousness had deteriorated to semi-coma, and his renal function also rapidly deteriorated to hepatorenal syndrome. A preoperative computed tomography scan of the chest revealed several small cavitary lesions in both upper lobes, and acid-fast bacillus stain from his sputum was graded 2+. Adenosine deaminase levels from ascites were elevated, suggesting TB peritonitis. A first-line anti-TB drug regimen was started immediately (rifampin, isoniazid, levofloxacin, and amikacin). An urgent living-donor LT was performed 2 days later. After LT, the regimen was changed to second-line anti-TB drugs (amikacin, levofloxacin, cycloserine, and pyridoxine). The sputum acid-fast bacillus stain tested negative on postoperative day 10. His liver function remained well preserved, even after the reversion to first-line anti-TB treatment. The patient recovered without any anti-TB medication–related complications and was discharged.

Conclusions. LT can be prudently performed as a life-saving option, particularly for patients with liver failure and concurrent active TB.

TRANSPLANT candidates are at high risk of acquiring tuberculosis (TB). Although transplantation is contraindicated in candidates with active TB, patients with undetected cases can inadvertently undergo this procedure [1]. However, because most first-line anti-TB drugs are hepatotoxic, the treatment of TB after liver transplantation (LT) is rendered more difficult. Considering the adverse outcomes, active TB should be treated before LT because potent immunosuppression is unavoidable after LT [2]. TB infection in transplant candidates is not rare, and appropriate management of patients with pre-existing TB undergoing LT is challenging [3]. Although elective LT is generally contraindicated in our hospital, urgent LT is an inevitable choice for irreversible acute liver failure (ALF).

We present here a case of a patient having active TB who underwent successful urgent living-donor liver transplantation (LDLT) for irreversible liver failure.

CASE PRESENTATION

A 48-year-old man was transferred to our center with stupor consequent to decompensated alcoholic liver cirrhosis. At admission, his stupor had deteriorated to semi-coma. Moreover,

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he had developed acute renal failure and severe ascites. A preoperative computed tomography (CT) scan of the chest revealed several small cavitary lesions in both upper lobes, and acid-fast bacillus (AFB) stain from sputum was graded 2+ (>10/100 fields) (Fig 1). A huge amount of ascites, peritonitis, and advanced liver cirrhosis was observed in a CT scan of the abdomen (Fig 2). The level of adenosine deaminase from ascites was elevated, suggesting TB peritonitis. The laboratory findings on admission were total bilirubin 5.2 mg/dL, prothrombin time 13.8%, serum albumin 2.3 g/dL, and creatinine 1.34 mg/dL. The Model for End-Stage Liver Disease score was 32, and the Child-Turcotte-Pugh score was 14, class C.

The patient was immediately started on an anti-TB drug regimen: rifampin 450 mg, isoniazid 300 mg, and levofloxacin 500 mg through a nasogastric tube and amikacin 250 mg nebulizer twice a day from 2 days before surgery. Although the patient was registered on cadaveric donor waiting lists, an urgent LDLT was performed on day 4 of the hospital stay due to his rapid mental deterioration (Fig 3). The patient received a modified right lobe graft from his 19-year-old son. The graft volume was 820 g, and the graft-recipient-weight ratio was 1.43%. We targeted the level of immunosuppressant at one half the usual dose to prevent aggravation of infection; the level of tacrolimus was maintained at 6 to 8 ng/mL with mycophenolate mofetil 1000 mg/d until the second postoperative week, after which the dose of immunosuppressants was gradually adjusted as graft function stabilized.

After the LT, the anti-TB treatment was changed to the second-line regimen, to prevent any potential drug-induced liver toxicity: amikacin 7.5 mg/kg, levofloxacin 500 mg, cycloserine 250 mg, and pyridoxine 50 mg. Sputum AFB stain tested negative after 10 days of therapy. The total period of the second-line regimen treatment was ~2 months. The patient's liver function was well preserved even after reverting to the first-line regimen: isoniazid 300 mg, pyrazinamide 1250 mg, ethambutol 800 mg, and pyridoxine 100 mg at 2 postoperative months. The results of liver function tests at the time of reversion to the first-line regimen were slowly on the decline: total bilirubin, 1.7 mg/dL; prothrombin time, 53.4%; aspartate aminotransferase, 52 U/L; alanine aminotransferase, 51 U/L; and serum albumin, 2.9 g/dL.

The patient recovered well with normal liver function as well as successfully treated TB with no adverse drug interactions. There has been no relapse of TB as of the 15-month follow-up.

DISCUSSION

The World Health Organization 2014 Global Tuberculosis Report estimates that 9 million new cases of TB occurred in 2013, compared with 8.6 million in 2012; 1.5 million people die of the disease each year [4,5]. A decreased immune response enhances the risk of developing active *Mycobacterium tuberculosis* (MTB) and is associated with higher disease-specific mortality [6]. MTB causes substantial morbidity and mortality in LT patients [7]. The prevalence of MTB infection in LT recipients is uncertain, with published incidence ranging from 1% to 6% in some case series [7–9]. One study found an overall MTB infection mortality rate of 29% in all solid organ transplantation (SOT) recipients [8], and another study reported a 31% short-term overall, and an 18% MTB infection-specific, mortality rate [7].

For LT patients, 2 issues need to be considered: LT after anti-TB-drug–induced liver failure and TB reactivation after LT. An anti-TB regimen is a leading cause of drug-induced liver disease, which may vary from an asymptomatic presentation to ALF in 0.6% to 2.6% of cases, respectively [10–12]. The range of liver damage can vary significantly, from asymptomatic transaminase elevation in 2% to 28% of cases to ALF in <0.01% of cases [12,13]. Factors associated with increased prevalence of anti-TB treatment–associated liver injury include higher complications due to nosocomial infections and increased disease severity, increased frequency and dosage of anti-TB drugs, differential diagnostic criteria, and genetic factors such as cytochrome P450 2E1 and NAT2 genetic polymorphisms [14–17].

Isoniazid, rifampicin, and pyrazinamide are known hepatotoxic drugs. Hepatotoxicity seems to involve the formation and accumulation of a reactive metabolite rather than a direct effect of the parent drug itself, and it affects some genetic factors such as cytochrome P450 2R1 and NAT2 polymorphisms involved in the metabolic pathways of these drugs [17,18]. The prevalence of isoniazid-induced ALF within the general population is low (between 3.2 and 14 per

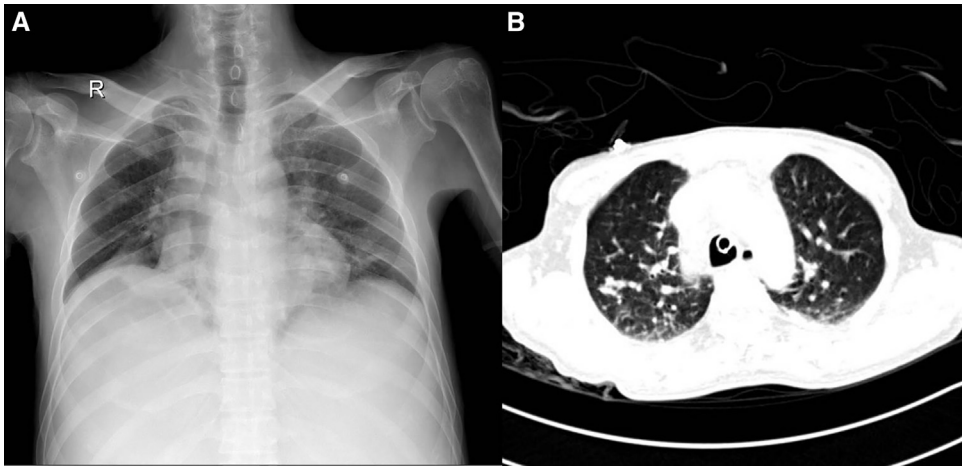

Fig 1. Multiple cavitary lesions in both lungs on preoperative (**A**) chest radiograph and (**B**) computed tomography (CT) scan.