CASE REPORT

Successful living donor liver transplantation of fulminant liver failure due to isoniazid prophylaxis

Tuğrul Çakır,¹ Cengiz Ara,² Hacı Vural Soyer,² Süleyman Koc²

¹Antalya Training and Research Hospital, Antalya, Turkey
²Department of General Surgery, Faculty of Medicine, Inonu University, Malatya, Turkey

Correspondence to
 Dr Tuğrul Çakır,
 tugrul-cakir@hotmail.com

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SUMMARY

Progressive liver failure is rarely seen in tuberculosis chemoprophylaxis with isoniazid. We present a case of a 32-year-old woman admitted to our clinic reporting abdominal pain, nausea and vomiting for 2 days. The initial diagnosis was fulminant toxic hepatitis due to isoniazid chemoprophylaxis, which was treated successfully with living donor transplantation. Tuberculosis continues to be a significant public health problem. Isoniazid-related hepatotoxicity is extremely rare in adults. The only treatment in cases of fulminant liver failure is orthotopic liver transplantation from a deceased or living donor. If a deceased donor is not available or the patient refuses this treatment, living donor transplantation is the only choice. Although rare, isoniazid used as protective therapy for pulmonary tuberculosis can lead to fulminant liver failure. When cadaveric liver transplantation is not available, living donor liver transplantation is vital.

BACKGROUND

Isoniazid chemoprophylaxis is the standard treatment for preventing the spread of active tuberculosis from patients to uninfected individuals with whom they are in close contact.^{1–3} During treatment of tuberculosis, chemoprophylactic agents can have a wide range of side effects of the liver, ranging from a slight increase in transaminases to diffuse necrosis of the liver. Many metabolites of isoniazid are responsible for the hepatic toxicity that develops during chemoprophylaxis.⁴ Because liver damage is dose related with isoniazid chemoprophylaxis, it is usually of a hepatocellular type, and the majority of cases develop in the first 4–8 weeks of treatment.⁵ Progression to irreversible liver failure is very rare.² In these cases, the current approach is orthotopic liver transplantation.^{6–8} If only a few cadavers are available, or the patient refuses cadaveric organ transplantation, the only remaining choice of treatment is living donor liver transplantation (LDLT).

Our patient had fulminant liver failure resulting from isoniazid chemoprophylaxis and she refused a cadaveric liver transplantation. Consequently, we performed a successful LDLT.

CASE PRESENTATION

A 32-year-old woman was admitted to our gastroenterology clinic reporting abdominal pain, nausea and vomiting for 2 days. The initial diagnosis was toxic hepatitis and she was followed for 15 days. On the seventh day of treatment, reduced consciousness and delirium developed. The patient's

father had been treated for active pulmonary tuberculosis and all of the family members in close contact with him were examined, underwent pulmonary radiographs and tuberculin skin testing with purified protein derivative (PPD), and were started on isoniazid chemoprophylaxis at a dose of 300 mg/day for 5 months.

On presentation, the patient weighed 52 kg and was 160 cm tall. The physical examination revealed poor general status, tendency to sleepiness and jaundiced appearance of the entire body. Neither hepatosplenomegaly nor ascites was noted on palpation and abdominal ultrasonography. Laboratory testing revealed aspartate aminotransferase (AST) 821 U/L, alanine transaminase (ALT) 539 U/L, gamma glutamyl transferase 166 U/L, albumin 2.8 g/dL, total bilirubin 9.5 mg/dL, direct bilirubin 4.8 mg/dL, C reactive protein 0.434 mg/dL, blood urea nitrogen 5 mg/dL, creatinine 0.5 mg/dL, haemoglobin 8 g/dL, white cell count 7000/μL, platelets 308 K/μL, prothrombin time 26s, partial thromboplastin time 27%, international normalised ratio 2.3 and ammonia 239 μg/dL. Arterial blood gases were pH 7.32, pCO₂ 34 mm Hg, HCO₃ 21 mmol/L, SO₂ 91.9% and bicarbonate 18 mg/dL. Multidetector CT revealed that the liver margins were regular and the parenchyma was homogenous; no ascites was observed. Fulminant liver failure was diagnosed and the patient was taken to the intensive care unit and monitored. With regard to aetiopathogenesis, no viral hepatitis, α1 antitrypsin, ferritin, ceruloplasmin, transferrin or metabolic diseases were observed. The use of isoniazid was halted as it was thought that the acute liver failure was associated with its use. Despite medical treatment and three bouts of plasmapheresis, no improvement was obtained. The end-stage liver disease score was 19 on presentation and it increased to 24. In this case, there was no interval from the end of isoniazid prophylaxis to liver failure: liver failure occurred during the fifth month of isoniazid prophylaxis.

Grade 3 encephalopathy developed on the 10th day and the decision to perform a liver transplantation was made. The patient was added to the emergency cadaveric waiting list and a suitable cadaveric liver was found after 5 days. However, the patient's family rejected the proposed cadaveric organ transplantation, so they were screened for LDLT. The patient's general status worsened. The patient and a living donor were admitted for surgery simultaneously. At surgery, the patient's liver was extremely hard and pale (figure 1). A right lobe LDLT was performed (figure 2). No problems occurred during the surgery. The pathology of the removed liver was reported as submassive necrosis of the liver.

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Figure 1 Operative appearance of the fulminant liver failure is seen.

TREATMENT

We performed a LDLT as the surgical procedure.

OUTCOME AND FOLLOW-UP

The patient was monitored in the intensive care unit for 4 days and extubated on the second postoperative day. She was given tacrolimus-based immunosuppression. The tacrolimus blood levels were maintained at 10–15 ng/mL during the first month and 5–10 ng/mL thereafter. Methylprednisolone (10 mg/kg) was started intraoperatively and the dosage was then tapered to reach 1 mg/kg/day for 2 weeks postoperatively, and 0.25 mg/kg/day for 3 months postoperatively. Tuberculosis prophylaxis was not given. After 20 days of uneventful postoperative follow-up, the patient was discharged from hospital and resumed her normal life without any problems.

DISCUSSION

Tuberculosis continues to be a significant public health problem. Our country, Turkey, has implemented a control programme following the WHO protocol. Preventive treatment is administered to individuals who are in contact with patients with active

tuberculosis and those with latent tuberculosis infection.¹ To protect adults, isoniazid is given at a dosage of 5 mg/kg/day to a maximum of 300 mg/day for a minimum of 6 months.^{1 2} In the case presented here, protective treatment of 300 mg/day isoniazid was started because of close contact with a patient with active tuberculosis. When the transaminases and bilirubin increase fivefold in the absence of another reason, with nausea, vomiting and jaundice, drug-associated hepatitis should be considered and the medication should be stopped.⁹ In our case, the isoniazid treatment was stopped because liver failure developed in the fifth month of treatment. Isoniazid-related hepatotoxicity is extremely rare in adults.² In this case, the AST levels had increased 2-fold, the ALT 10-fold and the bilirubin 9-fold. Although the isoniazid was stopped, there was no response to the medical and hepatic support therapy, and fulminant hepatic failure developed. To treat fulminant liver failure, cadaver or living donor transplantation should be performed immediately.¹⁰ In countries with low rates of organ donation, as in our country, and in cases where the patient or their families refuse cadaver organ transplant for whatever reason, the only treatment choice for fulminant liver failure is LDLT.¹¹ In our case, a right lobe liver transplant from a living donor was performed because the patient's family would not permit liver transplant from a cadaver.

Learning points

- ▶ Isoniazid is used as protective therapy for tuberculosis prophylaxis.
- ▶ Isoniazid can lead to fulminant liver failure.
- ▶ In cases where cadaveric liver transplantation cannot be performed, living donor liver transplantation is of vital importance.

Competing interests None declared.

Patient consent Obtained.

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Figure 2 Surgical procedure of living donor liver transplantation is seen.

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