CASE REPORT

Liver transplantation for acute liver failure accompanied by severe acute pancreatitis

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SUMMARY

The role of liver transplantation (LT) in acute liver failure (ALF) complicated by severe acute pancreatitis is still unclear. We here report a case of deceased-donor LT for idiopathic ALF accompanied by severe acute pancreatitis. A 58-year-old man with no history of liver disease presented with idiopathic ALF and acute pancreatitis. After careful consideration, he received a liver from a deceased donor. Following surgery, the patient's liver function rapidly reverted to normal level and the acute pancreatitis simultaneously subsided. The patient later developed a pancreatic pseudocyst, which was treated successfully with combination interventional radiology. LT can be considered for ALF associated with severe acute pancreatitis if there is no clinical evidence of an absolute contraindication for organ transplantation, such as systemic or local infection. Moreover, we recommend a close follow-up by ultrasonography to allow early detection and treatment of pancreatic pseudocysts following surgery.

BACKGROUND

Acute pancreatitis is a recognised complication of acute liver failure (ALF).¹⁻⁴ Various mechanisms behind this association, including direct injury to pancreatic acinar cells by causative agent of ALF and indirect physiological effects, have been reported.^{4 5} In the setting of ALF, regardless of its pathogenesis, acute pancreatitis is associated with multiple-organ system dysfunction and a significantly increased risk of mortality. Thus, in this setting, the treatment decisions for ALF, particularly in terms of determining the appropriateness of liver transplantation (LT), become more difficult.³

In this article, we report on a patient who developed ALF complicated by severe acute pancreatitis. The patient's ALF, along with the acute pancreatitis, was treated successfully by deceased-donor LT, and a postoperative pancreatic pseudocyst was effectively managed by interventional radiology.

CASE PRESENTATION

The patient provided written consent for this case to be published.

A 58-year-old man with no history of liver disease was admitted with idiopathic acute liver dysfunction. He did not have any history of viral hepatitis, alcohol abuse, gall stone disease or drug use relevant to liver damage.

The serological test results for hepatitis A, B and C virus; cytomegalovirus; human T-lymphotropic virus 1; HIV and Epstein-Barr virus were all negative.

INVESTIGATIONS

Despite conservative treatments for 15 days, the patient had marked mental confusion and was diagnosed as having grade 3 hepatic encephalopathy. He was consequently placed on the liver transplant waiting list under the diagnosis of idiopathic ALF. During the same period, the patient's serum amylase level increased to 3000 IU/mL without any symptoms. CT showed massive ascites with atrophy of the liver and oedema of the pancreas and retroperitoneum (figure 1). CT findings suggested Balthazar grade C-D.⁶ His serum total bilirubin, creatinine, albumin, amylase levels and international normalised ratio were 25.1 mg/dL, 1.6 mg/dL, 2.2 g/dL, 453 IU/dL and 1.98, respectively, while undergoing renal replacement therapy support and artificial liver support. The model for end-stage liver disease (MELD), Child-Pugh and Acute Physiology and Chronic Health Evaluation II scores were 40, 11 and 15, respectively. His age, unknown aetiology of hepatic failure, duration of jaundice before the onset of encephalopathy (15 days) and serum bilirubin fulfilled four out of five points of the King's College Hospital (KCH) criteria.

Eleven days after being placed on the transplant waiting list (15th day from the ALF diagnosis), the patient received a whole graft liver transplant from a deceased donor with a compatible blood type (O to B). The graft weight was 1300 g, which corresponded to a 1.72% graft-to-recipient body weight ratio.

Intraoperatively, liver atrophy with massive clear ascites and oedema of the pancreas and retroperitoneum were observed, which were consistent with the CT findings. No operative findings suggestive of pancreatic necrosis, infection or abscess formation were noted in the recipient. Graft implantation was performed using the piggyback technique and biliary reconstruction involving a single duct-to-duct anastomosis with an external stent. The cold ischaemia time was 319 min, and the warm ischaemia time was 37 min.

DIFFERENTIAL DIAGNOSIS

Classically, the differential diagnosis of acute pancreatitis accompanied by ALF includes alcohol abuse and gallstone related. Acute pancreatitis was also reported to develop secondary to viral hepatitis and drug-induced hepatic failure. However, this condition also occurs in the patients of indeterminate ALF. The other point in the differential diagnosis was whether the pancreatitis had a common aetiology with ALF or if it developed in

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Figure 1 Preoperative CT scan of the recipient showed massive ascites and oedema of the pancreas and retroperitoneum, without any findings suggestive of pancreatic necrosis.

the context of worsening multiple-organ dysfunction. This is addressed in the Discussion section.

TREATMENT

The patient received emergency re-exploration for abdominal haemorrhage on the first postoperative day. He regained consciousness and was taken off the ventilator on day 2 and was moved out of the intensive care unit on day 5 after the LT. Pathology of the excised liver showed submassive necrosis of the hepatocytes, without evidence of autoimmune hepatitis (figure 2).

Postoperatively, he was managed using our standard protocol of immunosuppressive agents, including tacrolimus, mycophenolate mofetil and steroids.

Along with improvement in his liver function and inflammatory response following surgery, the patient's serum amylase level immediately dropped to a normal level and did not increase again during his postoperative course (figure 3). However, the patient developed a pancreatic pseudocyst on day 19 postsurgery (32 days after diagnosis of acute pancreatitis) (figure 4). Percutaneous drainage of the pancreatic pseudocyst was performed via interventional radiology and an endoscopic nasogastric pancreatic drainage tube was placed. The pseudocyst was completely resolved within 1-month of intervention.

Figure 2 Pathology of the excised liver showed submassive necrosis of the hepatocytes, without evidence of autoimmune hepatitis (H&E stain).

Figure 3 The serum amylase level increased to 3000 IU/mL on day 17 postadmission. The serum amylase and total bilirubin concentrations decreased as a result of renal replacement therapy support and artificial liver support before liver transplantation (LT) and immediately dropped to normal levels after LT. LT, liver transplantation.

Figure 4 Pancreatic pseudocyst diagnosed on postoperative day 19.

OUTCOME AND FOLLOW-UP

The patient developed postoperative biliary stenosis 5 months after surgery, and a biliary stent was placed for ~1 month. Additionally, he had acute cellular rejection 6 months after the transplantation, which was treated with increased doses of immunosuppressive agents and pulse steroid therapy. Despite having good liver function and a stable immunosuppressive status, anorexia continued for more than 6 months after surgery, but it eventually improved. The patient is currently being treated with a maintenance dose of tacrolimus and mycophenolate mofetil and without post-transplantation complications.

DISCUSSION

Although LT is recognised as the only therapeutic option for uncontrollable ALF, the role of this procedure in ALF complicated by severe acute pancreatitis is yet to be determined clearly. Very few articles have described the clinical profiles of this condition and its influence on the decision-making process of whether LT is suitable.^{3 7} Kuo *et al*³ reported that the 1-year survival of patients with fulminant hepatic failure accompanied by acute pancreatitis who received LT was 50%, in contrast to 86% of recipients without acute pancreatitis, indicating that LT may not be warranted in this setting. However, it is difficult to discuss the indication of LT for this condition based on their limited results.

Acute pancreatitis in patients with ALF has been reported regardless of the aetiology of the liver disease.^{1–3} This condition is associated with greater renal dysfunction, higher coma grade and higher arterial lactate level among patients with ALF, and these account for higher MELD score as well as the greater proportion of patients who meet the KCH criteria.⁴ The mechanisms of this condition are yet to be fully elucidated. In the earliest reports, hepatitis viruses and drugs have been considered to have direct effects on pancreatic cells of patients with ALF.^{1 5} However, for ALF of indeterminate cause, such as in the present case, multiple-organ damage due to circulating lysosomal protease or free radicals, which show increased concentration in ALF, are more likely to be the cause of pancreatitis.⁷

Taking into account the time course, in which acute pancreatitis developed on 17th day of admission and only 2 days after the onset of hepatic encephalopathy, this association could occur in the context of acceleration of disease acuity, followed by worsening of overall physiological dysfunction, rather than its common aetiology with ALF.^{4 7}

Moreover, no absolute contraindication for LT, namely systemic or local infection, was demonstrated preoperatively, and the patient's CT scan did not show any findings of pancreatic necrosis, which is associated with a significant risk of infection.⁸ Although the patient's laboratory data were significantly modified by renal replacement therapy support and artificial liver support, he still met the criteria of LT in the MELD score and KCH criteria. For those reasons, we addressed this case as a candidate for deceased-donor LT.

The outcome of LT for patients with severe hepatic failure accompanied by acute necrotic pancreatitis was determined by infectious complications related to pancreatitis, rather than hepatic failure or LT-associated factors.⁷ Early detection and intervention for fluid collection and pancreatic pseudocysts are strongly recommended to avoid fatal abscess formation.^{9 10} We performed bedside abdominal ultrasonography daily for the first month after LT and at every clinic visit after discharge to check the blood flow of the graft and fluid collection in the abdominal cavity. The pancreatic pseudocyst was detected by routine ultrasonography and confirmed by CT.

In summary, LT may be considered as a treatment for ALF accompanied by severe acute pancreatitis if there is no clinical evidence of systemic or local infections or pancreatic necrosis. With more experience in LT for this condition, we may have a better understanding of survival and consideration for indication of LT. In addition, for immunosuppressed patients after LT, a close follow-up ultrasonography is recommended to allow early detection and treatment of pancreatic pseudocysts.

Learning points

- ▶ Acute pancreatitis complicated by acute liver failure (ALF) is related to multiple-organ system dysfunction and a significantly increased risk of mortality.
- ▶ The indication for liver transplantation (LT) for ALF accompanied by severe acute pancreatitis remains controversial because it is generally believed to be associated with a significantly increased risk of mortality.
- ▶ After LT, a follow-up ultrasonography at least once a week or at every clinic visit is recommended to allow early detection and treatment of pancreatic pseudocysts.

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