

Successful Management of Necrotizing Pancreatitis by Percutaneous Necrosectomy After Orthotopic Liver Transplant for Paracetamol Induced Acute Liver Failure: A Case Report

Rajiv Lochan, Richard M. Charnley, Jeremy J. French, Ahmed Al-Mukhtar, Mark Hudson, Derek M. Manas, Steve A. White

Abstract

Objectives: Acute pancreatitis, which can develop after any whole-organ transplant, is often associated with immunosuppression. Pancreatitis that complicates a liver transplant can be a significant problem that results in a high mortality rate.

Materials and Methods: We describe the successful use of minimally invasive techniques to treat severe acute pancreatitis. To our knowledge, this is the first reported case in which major laparotomy was precluded by the use of percutaneous necrosectomy to manage necrotizing pancreatitis in a liver transplant recipient. We also briefly review the published literature on severe acute pancreatitis in liver transplant recipients.

Results: Our patient, who had a Model for End-Stage Liver Disease score of 39 when transplanted and an Acute Physiology and Chronic Health Evaluation II score of 19 when infected necrosis in his pancreas was diagnosed, recovered completely after 92 days of hospitalization. He underwent 2 percutaneous drainage procedures and 3 percutaneous necrosectomies to treat his pancreatic complication. A review of the literature revealed that severe acute pancreatitis significantly increases morbidity and mortality in liver transplant recipients. Unlike necrotizing pancreatitis, which develops outside the context of liver transplant

where there is a distinct shift towards minimally invasive procedures, infected necrosis associated with fulminant liver failure or a liver transplant is usually treated with open necrosectomy.

Conclusions: Severe acute pancreatitis in liver transplant recipients should be managed exactly as it is in patients who have not received a liver transplant. Anatomically guided minimally invasive necrosectomy appears to be beneficial, especially when patients are critically unwell, as they are following a liver transplant.

Key words: Liver transplant, Necrotizing pancreatitis, Percutaneous necrosectomy

Acute pancreatitis (AP) is a major complication after liver transplantation. Severe AP in a liver transplant patient is associated with significant morbidity and greatly increased mortality. Infected necrotizing pancreatitis cannot be successfully treated with standard management techniques. Debridement with a minimally invasive approach serves the interests of the patient best, particularly after major abdominal surgery such as a liver transplant and the associated risks of immunosuppressive therapy. This report describes the successful use of and rationale for percutaneous necrosectomy in a recipient of an orthotopic liver transplant. To our knowledge, this is the first such case reported.

Case report

A 22-year-old man with acute fulminant liver failure caused by a paracetamol overdose was admitted to the Freeman Hospital, Newcastle upon Tyne, United Kingdom. He reported a recent history of cocaine abuse but there was no history of alcohol

From the Department of Hepato-Pancreato-Biliary and Organ Transplant Surgery, Freeman Hospital, Newcastle upon Tyne, United Kingdom

Address reprint requests to: Mr. Steve White, MD, FRCPS, FRCS (Gen Surg), Consultant, Hepato-Pancreato-Biliary and Liver Transplant Surgeon, The Freeman Hospital, Newcastle upon Tyne, Tyne and Wear, UK NE7 7DN

Phone: +0191 2137074 Fax: +0191 223 1483 E-mail: steve.white@nuth.nhs.uk

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consumption. Hours after transfer, his condition deteriorated significantly: encephalopathy developed, and he required ventilatory support. His calculated Model for End-Stage Liver Disease score was 39, and he was added to the “super-urgent” category to receive a liver transplant. A suitable liver became available from a non-heart-beating (category 3) donor. This patient subsequently underwent a routine orthotopic liver transplant. At the conclusion of that surgery, the small bowel appeared dusky but viable, and a repeat laparotomy was scheduled to be performed 24 hours later. During that procedure, the gut was found to be viable and otherwise unremarkable. It was clear that the transplanted liver was functioning well, and the results of a liver biopsy after perfusion of the transplanted liver revealed minimal macrovesicular steatosis.

Over the next few days, the patient required continuous venovenous hemofiltration and became increasingly unwell. He exhibited an increasing white blood cell count, tachycardia, vomiting, and abdominal distension. A further laparotomy was performed on postoperative day 4, during which areas of fat necrosis were identified within the small bowel mesentery but no other abnormality or discrete collection was noted. Serum amylase levels at admission and during the immediate post-operative period were within the normal range (chart 1). A diagnosis of acute severe pancreatitis was made, and supportive management that included continuous venovenous hemofiltration, ventilation, enteral nutrition, and care in the intensive care unit was continued. The patient then underwent a contrast-enhanced computed tomographic scan of his abdomen so that the severity and extent of his pancreatic inflammation could be assessed. This

confirmed that his pancreas was enhancing well; however, it was edematous (computed tomographic severity index, 2). His treatment with ventilation and continuous venovenous hemofiltration was continued. Over the next few days, his liver function worsened, and the following peak values were recorded: bilirubin, 308 $\mu\text{mol/L}$; alanine transaminase, 200 U/L; and alkaline phosphatase, 240 U/L. The results of a repeat liver biopsy confirmed minimal cellular rejection. The patient continued to receive supportive care, he began to recover and ventilation was discontinued. He returned to ward on postsurgical day 54 subsequently renal replacement therapy was also discontinued.

On postoperative day 56, he became extremely unwell, and his Acute Physiology and Chronic Health Evaluation 2 score was 19. He exhibited signs of systemic sepsis and underwent another contrast enhanced computed tomographic scan of his abdomen, which showed a pancreatic collection in the body and tail of the pancreas (computed tomography severity index, 7) (Figure 1). This was initially managed with percutaneous drainage (Figure 2), which seemed to improve his clinical condition remarkably. However, several days later it was apparent that the sepsis was not controlled by simple drainage, and a formal percutaneous necrosectomy was performed. This procedure is performed in the operating theater under a general anesthetic, consists of dilating the drain tract (Figures 3 and 4) into the pancreatic necrosis under fluoroscopic guidance. A nephroscope is then inserted down the drain tract, and solid necrotic material is removed by instruments 3 mm in diameter that are advanced down the operating shaft

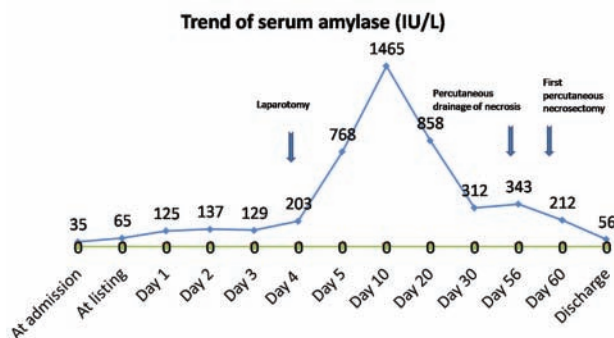


Chart 1. Serial amylase trend.



Figure 1. Pancreatic collection in the body and tail of the pancreas (CT Severity Index - 7 points)

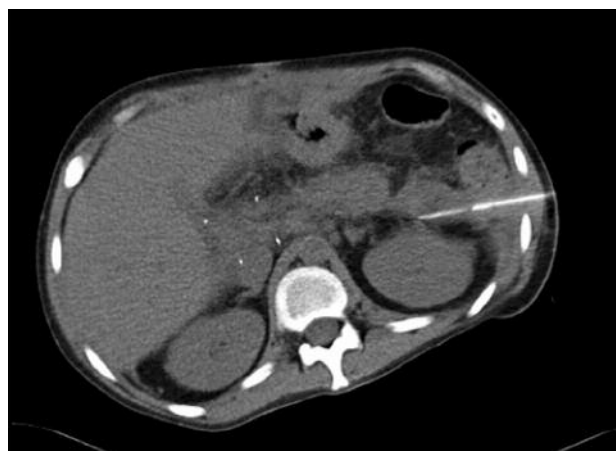


Figure 2. CT guided percutaneous drainage

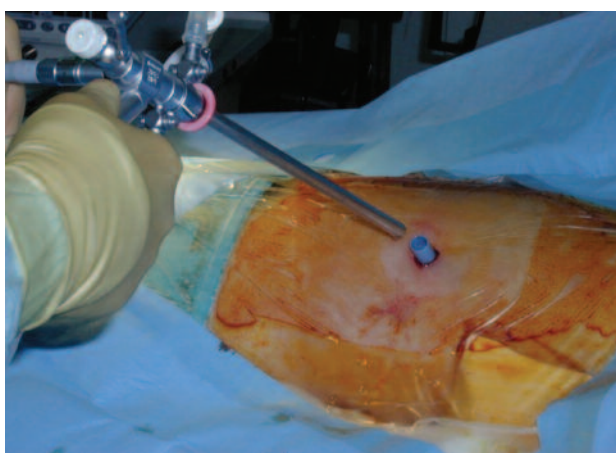


Figure 3. A nephroscope is being used down the drain track and solid necrotic material is removed using 3 mm diameter instruments passed down the operating shaft of the nephroscope



Figure 4. Complete resolution of pancreatic necrosis

of the nephroscope. Percutaneous necrosectomy was performed twice during the next 10 days. The need for repeat procedures was determined by the patient's clinical condition, inflammatory markers, and the results of cross-sectional imaging. After each percutaneous intervention, the patient required further high dependency care for 2 days so that his

vital signs could be closely monitored. He did not require organ support during that period. More importantly, percutaneous necrosectomy prevented the need for major laparotomy, with all associated risks of morbidity and possible mortality, in a liver transplant recipient.

A computed tomographic scan 2 weeks later indicated complete resolution of pancreatic necrosis, and the percutaneous drain was removed. At the patient's 3-months follow-up examination, the results of liver function tests were within the normal range and revealed no evidence of pancreatic exocrine insufficiency or diabetes.

Discussion

AP after a liver transplant is a rare but devastating complication. In a large retrospective cohort of pediatric patients ($n = 634$) who underwent a liver transplant, AP occurred in 26 children (4%), 11 of whom died. The overall mortality rate was thus 42% and, 14 (54%) patients developed severe pancreatitis. Five of those 14 patients were treated conservatively, and all died. Nine of the 14 underwent a laparotomy, and more than 50% died (1). A French series also reported a high mortality rate (43%) in patients with severe AP after a liver transplant (2).

In pediatric liver transplant recipients, the following risk factors contribute to the development of AP: the construction of an infrarenal aortic conduit, re-transplant, heavy blood loss, prolonged surgery (1), and the use of steroids (3). AP can also develop after renal, cardiac, or bone marrow transplant. After a renal transplant, viral infections (4) and treatment with immunosuppressive drugs such as azathioprine and cyclosporine (5) are the most frequent causes of AP, but after a liver transplant, the frequent development of biliary sludge, treatment with cyclosporine and steroids are thought to be more important. After a diagnosis of AP, our usual maintenance immunosuppressive protocol of tacrolimus and azathioprine was changed to tacrolimus and mycophenolate mofetil in this patient. In addition, he had received intravenous methylprednisolone when anesthesia was induced before the transplant operation.

Paracetamol poisoning is often associated with hyperamylasemia, which increases with worsening hepatic function, but clinical pancreatitis is rare (6) and the development of hemorrhagic pancreatitis is

even more uncommon (7). Substance abuse is especially important as a risk factor for AP; alcohol abuse (8), cocaine (9) and cannabis (10) have also been reported as causes.

Three degrees of severity of AP are recognised after a liver transplant: level 1 (minor AP), which is characterized by the biochemical elevation of amylase and or lipase in the absence of radiologic or clinical evidence of severe AP; level 2 (clinically severe AP), AP associated with clinical and radiological features of AP and its sequelae; and level 3 which is AP that develops in the very unwell liver transplant patient as part of multi-organ failure and is in most circumstances lethal. This classification system does have prognostic importance, because mortality rates of 0%, 40%, and 100%, respectively, have been noted in those 3 categories (11).

While the diagnosis of AP is certainly extremely important in the setting of liver failure, once AP has been diagnosed, it is paramount to monitor the severity of the disease using clinical, laboratory and radiological means and the APACHE2 score has been found especially useful after liver transplant (11). Prediction and early recognition of the complications of severe AP, such as infected pancreatic necrosis, with early and appropriate intervention is crucial in the successful management of a severely ill patient.

It is increasingly recognized that the complications of an open necrosectomy for AP ie; a large open wound, bleeding, GI fistulation, worsening of organ failure in the immediate post-operative period, combined with long periods of intensive care management all contribute to the prohibitive morbidity and mortality in LTX patients with AP. Consequently various groups with an interest in the management of severe AP have developed innovative specialist minimally invasive necrosectomy techniques that include percutaneous necrosectomy (12), endoscopic transgastric necrosectomy (13) and other laparoscopic approaches (14) to retroperitoneal debridement. With increasing resolution of CT and the ability of interventional radiologists to place percutaneous drains into areas of necrosis, not only into the retro peritoneum adjacent to pancreatic and peri-pancreatic areas but also into collections remote from the pancreas (15), it is now possible to treat these areas percutaneously with meticulous debridement of all necrotic and infected tissue under direct vision without the need for a large abdominal wound. Selected cases may need an endoscopic approach

through the posterior gastric wall or through the duodenum, however this is not common. Since its description by Carter et. al. the percutaneous technique of necrosectomy has been shown to reduce postoperative organ dysfunction (12). Large experiences (16, 17) of percutaneous necrosectomy have been described (16, 17) confirming its safety and efficacy in treating AP. Indeed a retrospective case-controlled study showed that patients who underwent percutaneous necrosectomy had fewer instances of postoperative organ failure and a lower death rate than did patients who underwent open necrosectomy (18). The Pancreatitis, Necrosectomy Versus Step Up Approach (PANTER) trial (19), which compared the results of percutaneous, minimally invasive necrosectomy versus with those of a traditional open necrosectomy, should provide investigators with much-needed level 1 evidence to demonstrate the overall benefit of percutaneous necrosectomy. This case report demonstrates shows that percutaneous necrosectomy can be used in patients who have undergone major abdominal surgery such as a liver transplant which to our knowledge, has not been previously reported.

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