Early prevention and treatment of biliary tract complications after orthotopic liver transplantation

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OBJECTIVE: To investigate the prevention and treatment of biliary complications after orthotopic liver transplantation (OLT).

METHODS: OLT was performed in 18 patients with end-stage liver disease, including 6 patients with primary liver cancer. Except 1 patient was infused only through the portal vein, others were infused through the portal vein and hepatic artery of the donor. The biliary tract was reconstructed using choledochocholedostomic anastomosis in 17 patients, and using Roux-en-Y choledochojejunostomic anastomosis in 1 patient.

RESULTS: Four patients with biliary complication were found. In one patient, biliary leakage was found around the T-tube on day 14 postoperatively, and disappeared after re-opening of the tube. In one patient undergoing Roux-en-Y choledochojejunostomic anastomosis, biliary leakage was found on day 12 postoperatively and reoperation was performed. The T-tube was removed from the anastomosis after reoperation, and abdominal infection was controlled, but high fever recurred on day 49 postoperatively. The patient died on day 52 postoperatively. Autopsy revealed biliary leakage and biliary tract necrosis. In another patient, biliary leakage was found on day 3 after operation, and was treated by adequate drainage. Four months after operation, biliary sludge in the common tract was found and treated successfully with oral chemolysis. But biliary sludge or stone recur on one and half year after OLT. Spincterotomy and basket extraction were performed via endoscopic retrograde cholangiopancreatography, and the biliary sludge or stone was cleared out. In case 4, biliary drainage tube cholangiogram showed anastomotic stenosis one month after operation. Three months later, biliary sludge or stone was found beyond anastomotic stenosis. After oral chemolysis (ursodeoxycholic acid) and irrigation with heparinized saline solution via the biliary drainage tube, the biliary sludge disappeared.

CONCLUSIONS: To reduce the incidence of biliary complications, adequate infusion of the hepatic artery, complete slushing of the biliary tract, and reduction of injury to the blood supply of the donor biliary tract are essential. Most biliary complications can be treated successfully by non-operative treatment or minimally invasive operation.

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Key words: orthotopic liver transplantation; biliary complication; treatment; prevention

Introduction

In early-stage of liver transplantation, biliary complications are a leading cause of surgical morbidity and mortality. The reported morbidity ranges from 30% to 50%, and the mortality from 20% to 30%, caused by biliary tract reconstruction

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after orthotopic liver transplantation (OLT).[1-3] In 1977, Calne characterized biliary tract reconstruction as the "technical Achille's heel" of liver transplantation.[1] In recent years, the improvement of organ preservation technology, refinement of procurement and surgical techniques, and advances of immunosuppressive treatment have lowered the incidence of biliary tract complications; but the morbidity remains high.[1-3] This study aimed to sum up our experience in early prevention and treatment of biliary complications in 18 patients after OLT.

Methods

Illustrative cases

The 18 patients (16 were men and 2 women) were subjected to standard traditional procedure or piggyback orthotopic liver transplantation. These recipients received ABO-compatible organs. Indications for transplantation included primary liver cancer ($n = 6$), hepatitis B ($n = 6$), Wilison's disease ($n = 3$), primary biliary cirrhosis ($n = 2$), and cryptogenic cirrhosis ($n = 1$). The methods for biliary reconstruction were end-to-end choledochocholedochostomy ($n = 17$) and Roux-en-Y choledochojejunostomy (RY, $n = 1$). Three recipients died within two months, and 12 had been surviving for more than 6 months. Fifteen patients were given a regimen of combined tacrolimus-steroid and cellcept, and 3 patients were given a regimen of combined cyclosporine-steroid and cellcept. Abdominal ultrasonography was performed on the first postoperative day to confirm vascular patency. In the patient undergoing choledochocholedochostomy, T-tube was clamped when liver function returned to normal 2 weeks after transplant. Cholangiography was performed before the tube was clamped under antibiotic prophylaxis. Four patients developed biliary complications.

Case 1

A 62-year-old man with primary biliary cirrhosis and chronic hepatic failure was subjected to OLT using standard traditional procedure. The donor was a brain dead patient showing ABO-compatible and a value of $<10\%$ for lymphocyte test. The donor organ was infused only through the portal vein, and the biliary was infused 200 ml solution. The operation time lasted 7.5 hours, the heat ischemia time 3 minutes, and the cold ischemia time 9 hours and 37 minutes. The immunosuppressive agents used included cyclosporine, steroid and azathiopine. On day 3 after operation, the patient suffered from pneumonia of the left lobe. Antibiotics were prescribed and the pneumonia disappeared on day 5. Rejection occurred on day 8 and was controlled with a large dose of steroid. Twelve days after operation, the patient was complicated by fever, ileus, and bile-like liquid from the drainage of the abdominal cavity. Reoperation revealed bile leakage around the anastomosis, from which the T-tube dislocated when abscess occurred locally, T-tube was removed, and infected lesion was slushed clearly. The symptoms of the recipient were relieved. Fourty days after operation, the patient experienced fever, weakness, and loss of appetite. The increased serum levels of billirubin, γ-glutamyl transferase (γ-GT), and alkaline phosphatase (AKP) were suggestive of rejection. A large dose of steroid was given to relieve the symptoms. On day 49, however, jaundice became darker; the patient became confused and died on day 52 after operation. Autopsy demonstrated normal hepatic artery, but biliary leakage around the anastomosis, coagulatory necrosis of the biliary duct, and lots of biliary casts in the bile duct at the presence of hepatocellular cholestasis.

Case 2

An 18-year-old unmarried woman was admitted to our department because of Wilson's disease. She was subjected to OLT using piggyback procedure. The donor was a brain dead patient with ABO-compatible and lymphocytes <10%. The donor organ was infused through the portal vein and hepatic artery, and the biliary tract was infused with 500 ml solution. The operation time was 7 hours, the heat ischemia time 6 minutes, and the cold ischemia time 5 hours and 30 minutes. Immunosuppressants included tacrolimus, steroid and cellcept. On day 3 after operation, bile-like liquid

was drained from the right subphenic area and the porta hepatis, but the patient had no fever. B-ultrasonography demonstrated liquid in the superphenoic area and the porta hepatis. On day 20, the bile-like liquid from the right drainage tube tended to be less, and the tube was removed gradually. T-tube photography showed the contrast medium tracking around the T-tube and exhibiting a triangular shape (8×9 cm). On day 45, T-tube cholangiography showed less liquid in the abdominal cavity, and on day 90, the T-tube was pulled out gradually, and the liquid disappeared. Four months after operation, the patient experienced jaundice and fever. B-ultrasonography demonstrated strong echo in the common bile duct, anti-bacterial treatment and oral chemolysis were given to relieve the symptoms. One and half year after operation, the patient presented with acute cholangitis again, leading to shock and acute renal failure. B-ultrasonography demonstrated lots of biliary sludge or stones in the extended bile duct. Ultrasound-guided percutaneous transhepatic cholangiodrainage (PTCD) was performed, and the symptoms relieved rapidly. When symptoms disappeared, intraluminal chemolytic agents via PTCD were used twice per week. The biliary sludge reduced markedly, but three weeks later it had to be halted because of the recurrence of acute cholangitis and hemobilia. Therefore, spincterotomy and basket extraction were performed via endoscopic retrograde cholangiopancreatography. The biliary sludge or stones were cleared out, the jaundice disappeared, and no cholangitis occurred for half a year.

Case 3

A 23-year-old unmarried man with chronic hepatic failure received OLT using piggyback procedure. The donor was a brain dead patient with ABO-compatible and lymphocytes <10%. The donor organ was infused through the portal vein and hepatic artery, and the biliary duct was infused with 500 ml solution. The operative time was 6 hours, the heat ischemia time 3 minutes, and the cold ischemia time 6 hours and 30 minutes. Immunosuppressants used included tacrolimus, steroid, and cellcept. Two weeks after operation, B-ultrasonography demonstrated liquid around the T-tube. T-tube cholangiography showed the contrast medium tracking around the T-tube and exhibiting a triangular shape (8×6 cm). On day 90, the liquid in the abdominal cavity disappeared and the T-tube was removed gradually.

Case 4

A 28-year-old married man was admitted to our hospital because of Wilson's disease, severe neurologic damage, and hepatic insufficiency. He was subjected to OLT using piggyback procedure. A tube of 3-mm in diameter was placed in the bile duct via donor's cyst duct for biliary drainage. The donor was an brain dead patient with ABO-compatible, and lymphocytes <10%. The donor's organ was infused through the portal vein and hepatic artery, and the biliary tract was infused 500 ml solution. The operative time was 4 hours, the heat ischemia time 5 min, and the cold ischemia time 6 hours and 30 minutes. Immunosuppressants included tacrolimus, steroid, and cellcept. One month after operation, the biliary drainage duct was clamped. The serum γ-GT and AKP levels increased, and cholangiograph showed anastomotic stenosis. He was weak, and his neurologic damage was still severe. His subphenic infection was not controlled, and interventional treatment was not prescribed. Three months after operation, B-ultrasonography demonstrated a strong echo. Biliary drainage tube cholangiogram showed a vague irregular filling defect, about 6×4 mm, in the bile duct. Oral chemolysis (ursodeoxycholic acid) and irrigation with heparinized saline via the biliary drainage tube was given one time per day. A week later, biliary drainage tube cholangiogram showed that the vague irregular filling defect in the bile duct disappeared. The patient had not had cholangitis until he died of severe malnutrition and infection.

Discussion

Despite the improvement of surgical techniques, organ preservation and immunosuppressive thera-

py, biliary tract complications remain a significant cause of morbidity and mortality after OLT. The major risk factors for biliary complications include lack of blood supply of the donor bile duct, techniques for anastomosis, and rejection.[3,4] During the operation, it is important to protect the bile duct blood supply of the donor and recipient.[5] The common bile duct receives its blood supply from the retroduodenal, common hepatic, and right hepatic arteries. The branches of these arteries form a plexus around the duct, which is joined by two axial vessels, the 3 o'clock and 9 o'clock arteries. The supraduodenal portion of the common bile duct normally depends upon the branches derived from the gastroduodenal artery, but clearly the common bile duct of liver graft must receive its blood supply entirely from the hepatic artery, making the distal part of the duct prone to ischemic necrosis. Devascularization of the extrahepatic bile duct may result from excessive dissection or stripping of the periductal tissues at the time of organ procurement. Extensive "cleaning" of either donor or recipient's bile duct should be avoided, and in the reimplantation phase active bleeding from the cut ends of both structures should be confirmed before choledochocholedochostomy.[6] In organ procurement, full infusion of the hepatic artery to avoid thrombosis of the microvasculature of the bile duct and complete slush to the biliary tract to avoid necrosis of bile duct epithilial cells are necessary. In this study, a donor organ was infused only with the portal vein, and little solution was used to slush to the biliary tract, resulting in necrosis of the bile duct.

The placement of T-tube in end-to-end choledocholedochostomic anastomosis or choledochojejunostomic anastomosis, which decompresses the bile duct, is able to monitor the quality and quantity of bile produced as an index of hepatic function and to evaluate biliary reconstruction in most liver transplant centers; however it has been the source of complications, such as biliary tract sepsis, early dislodgement associated with leakage, obstruction associated with migration of the tube, and leakage after planned removal of the tube. As reported, the T-tube related complications vary from 9% to 29%.[7] Before the removal of the T-tube, leakage may be caused by its dislodgement and bile duct obstruction by its migration. Even sludge or inspissated, thickened bile is formed. T-tube removal may lead to leakage nearby because the use of immunosuppressants, poor nutritional state and ascites inhibit the formation of the fibrotic tract around the T-tube.[8] In this study, the occurrence of biliary tract complications was associated with T-tube. In Case 1, bile leakage was caused by the dislodgement of T-tube and in Cases 2 and 3, leakage occurred at the site of the T-tube.

Early-stage leakage usually occurs at the site of T-tube or anastomosis, and late-stage leakage develops following the removal of the T-tube. If leakage develops around the T-tube at the time of clamping, it is necessary to re-open the T-tube until liquid collection around the T-tube disappears. Generally, leakage can be resolved, but some should be investigated whether there are bile duct stenosis, biliary sludge or thickened bile, Oddi's sphincter dysfunction or whether the place of the T-tube is appropriate. If cholangiograms demonstrate that the T-tube adequately diverts bile flow, no percutaneous transhepatic drainage catheter is necessary. Otherwise, a percutaneous trans-hepatic drainage catheter is placed. Leakage after removal of the T-tube was diagnosed using endoscopic retrograde cholangiopancreatography and treated with a nasobiliary catheter or endoscopic sphincterotomy. Anastomotic leakage after choledochocholedochostomy only requires operative repair in patients with complete disruption of suture and those who failed to percutaneous transhepatic drainage. Partial disruption of suture after choledochocholedochostomy or choledochojejunostomy can be treated similarly to leakage before T-tube removal. If the T-tube adequately diverts the bile flow from the anastomotic stoma as demonstrated by cholangiogram, it can be opened to gravity, otherwise a percutaneous transhepatic drainage catheter is placed.[9] In the USA,[10] 24% of 49 transplant programs initially treated T-tube leakage with endoscopic stent or nasobiliary tube, whereas 6% of them were re-operated and 55% were treated conservatively. The prospective use of endoscopic nasobiliary tube or sphincterotomy with internal stent was successful in 94% patients in a year.[11] Ano-

ther group[12] reported the successful treatment after 3–14 days' nasobiliary drainage without sphincterostomy.

Anastomotic bile leakage associated with choledochojejunostomy is more common than with choledochocholedochostomy. When it occurs after choledochojejunostomy, biliary-enteric anastomotic disruption is likely. When it occurs after choledochocholedochostomy, this problem is managed by surgery in 51%, and by endoscopy in 16% medical centers surveyed; some of these centers prefer surgery to choledochojejunostomy.[10] In our study, Case 1 experienced leakage at the biliary-enteric anastomosis, which was not controlled conservatively and reoperation was performed. Leakage in the other two cases after choledochocholedochostomy was controlled by keeping the drainage tube unobstructed and dropping the biloma completely. We consider that leakage at choledochocholedochostomy can be treated conservatively if liquid is fully drained.

The cause of biliary sludge after liver transplantation remains unclear, although rejection, infection and ischemia are considered the pathogenetic cause of biliary sludge. The reported prevalence of sludge ranged from 5.7% to 13%.[13] Sludge produces bile duct obstruction and cholangitis, leading further to obstructive jaundice or cholestasis. It is a potentially life-threatening complication with a mortality of 27%.[13] Surgical, radiological, medical, and endoscopic treatment may be effective to manage sludge after liver transplantation. When cholangiograms indicate possible biliary sludge without signs and symptoms of massive cholestasis or other simultaneous complications such as marked leakage or strictures of the bile ducts or chronic rejection, oral chemolytic treatment can be selected. Barton et al[14] reported that 40% patients had biliary sludge dissolved. Interventional techniques are introduced if sludge does not recede despite oral chemolysis, even if cholestasis increases. When oral chemolysis fails, intraluminal chemolytic agents via PTCD can be used. Zajko et al[15] advocated the use of interventional technique as the primary treatment in liver transplant recipients with bile duct obstruction. The interventional technique includes bile duct irrigation, basket extraction, etc. Evans et al[16] reported successful irrigation with heparinized saline solution in 6 (86%) of 7 patients, but Barton et al[14] found that irrigation is not effective in 4 patients with biliary sludge. As to the patients with biliary sludge that was not desolved with the above treatment, basket extraction is prefered. O'Connor et al[17] reported successful basket extraction in 4 (57%) of 7 patients. Generally, interventional procedures failed more often in nonobstructive sludge (71%) than in obstructive sludge (12%).

If intervention fails, surgery is advisable. Indications for surgery include ineffective oral and interventional treatment or such biliary complications as nondilatable anastomotic strictures, anastomotic leakage, and T-tube dislocation accompanied by choleperitoneum. Another indication for surgery is an enormous amount of biliary sludge in the presence of cholestasis, particularly the sludge extends from the common bile duct to the intrahepatic bile duct.[18]

Competing interest

The author or authors do not choose to response to the statements listed in Instructions for Authors.

References

1 Starzl TE, Putnam C, Hansbrough J, et al. Biliary complications after liver transplantation: with special reference to the biliary cast syndrome and techniques of secondary duct repair. Surgery 1977;81:212–221.
2 Rerknimitr R, Sherman SE, Fogel EL, et al. Biliary tract complications after orthotopic liver transplantation with choledocholedochostomy anastomosis: endoscopic findings and results of therapy. Gastrointest Endosc 2002;55:224–231.
3 Yang JM, Zhu B. Intrahepatic cholestasis after liver transplantation. HBPD INT 2002;1:176–178.
4 Schlitt HJ, Meier PN, Nashan B, et al. Reconstructive surgery for ischemic type lesions at the bile duct bifurcation after liver transplantation. Ann Surg 1999; 229:137–145.
5 Northover T. The blood supply of human being bile duct. Br J Surg 1979;66:379–384.
6 Donovan J. Nonsurgical management of biliary tract disease after liver transplantation. Gastroenterol Clin

North Am 1993;22:316-336.
7 Randell H, Wachs M, Somberg K, et al. The use of the T-tube after orthotopic liver transplantation. Transplantation 1996;61:258-261.
8 Johnston TD, Gates R, Reddy KS, et al. Nonoperative management of bile leaks following liver transplantation. Clin Transplant 2000;14:365-369.
9 Gholson C, Zibari G, Mcdonald J, et al. Endoscopic diagnosis and management of biliary complications following orthotopic liver transplantation. Dig Dis Sci 1996;41:1045-1053.
10 Vallera RA, Cotton PB, Clavien PA, et al. Biliary reconstruction for liver transplantation and management of biliary complications: overview and survey of current practice in the United States. Liver Transplant Surg 1995;1:143-152.
11 Serman S, Shaked A, Cryer HM, et al. Endoscopic management of biliary fistulas complicating liver transplantation and orther hepatobiliary operations. Ann Surg 1993;218:167-175.
12 Ostroff JW, Roberts JP, Gordon RL, et al. The management of T-tube leaks in orthotopic liver transplant recipients with endoscopically placed nasobiliary tubes. Transplantation 1990,49:922.
13 Portmann B, Wight DGD. Pathology of liver transplantation. In: Calne R, ed. Liver transplantation. London: Grune & Stratton. 1987,437-470.
14 Barton PA, Steininger R, Maier A, et al. Biliary sludge after liver transplantation: treatment with interventional technique versus surgery and/or oral chemolysis. AJR 1995;164:865-872.
15 Zajko AB, Campbell WL, Bron KM, et al. Cholangiography and interventional biliary radiology in adult liver transplantation. AJR 1985;144:127-133.
16 Evans RA, Raby ND, O'grady JG, et al. Biliary complication following orthotopic liver transplantation. Cin Radiol 1990;41:190-194.
17 O'connor HJ, Vichers CR, Buckels JAG, et al. Role of endoscopic retrograde cholangiopancreatography after orthotopic liver transplantation. Gut 1991;32:419-423.
18 Sheng R, Ramirez CB, Zajko AB, et al. Biliary stones and sludge in liver transplant patients: 13-year experience. Radiology 1996;198:243-247.

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