Transpl Int (1998) 11 [Suppl 1]: S251–S254

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Biliary complications secondary to late hepatic artery thrombosis in adult liver transplant patients

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Abstract Biliary complications (BC) are the usual presentation of late hepatic artery thrombosis (HAT) of the liver graft. Our aim was to study the clinical features and outcome of BC secondary to HAT compared to BC which occurred in liver transplant (LT) patients with patent vessels. We present a retrospective study of 224 LTs performed in 204 patients between 1988 and 1996. The mean recipient × s age was 51 years. A choledochocholedochostomy without T-tube was used as biliary reconstruction in most cases (67%); in 12%, a choledochojejunostomy was performed. An iliac conduit was necessary in 15% of cases and back-table arterial reconstruction was performed in 10% of cases of anatomic variants in graft arteries. Different donor, recipient and intraoperative variables, as well as treatment and outcome, were studied in the two groups of patients presenting BC with or without HAT. BC occurred in 38 cases (17%) whereas HAT was diagnosed in 11 cases (4.9%). Therefore, 23% of BC encountered after LT were secondary to HAT. Nine cases of late HAT manifested as BC, septicaemia (88%) and hepatic bilomas (8 cases). Percutaneous or surgical drainage of hepatic bilomas was performed in all cases, followed by retransplantation in six cases (66%). BC secondary to HAT appeared later than the rest of BC. Donor age was the only significant predisposing factor found in our study. Graft survival is significantly reduced as most patients needed retransplantation. In conclusion, BC secondary to HAT presented later in livers from older donors in the form of biliary sepsis and hepatic biloma. Retransplantation was ultimately required in most cases and graft survival was significantly diminished.

Key words Biliary complications · Hepatic artery thrombosis · Liver transplantation · Hepatic biloma · Retransplantation

Introduction

Early hepatic artery thrombosis (HAT) is a rare complication after liver transplantation (LT) in adults. If it is not diagnosed and treated immediately, it produces graft ischaemia and extrahepatic biliary tract necrosis. Usually, graft loss and retransplantation are the consequences of this complication. However, when HAT occurs late after LT, clinical manifestations are characterised by septicaemia, biliary complications (BC) and hepatic bilomas. The aetiology and pathogenesis of late HAT are probably different. The aim of this retrospective study was to compare the incidence, risk factors, clinical presentation, treatment and outcome of BC secondary to late HAT with the rest of BC which occurred after LT.

Materials and methods

In the period between October 1988 and January 1996, 224 LTs were performed in 203 adult patients in our Unit. Patient characteristics are presented in Table 1.

Biliary anastomosis

An end-to-end choledochocholedochostomy was performed in 87% of LTs whereas in 13% of cases, the recipient common bile duct was not suitable and a Roux-en-Y choledochojejunostomy was fashioned. In our early experience, a biliary drainage, T-tube or stent, was routinely left in all LTs. However, very soon, we decided to avoid biliary drainages in almost all cases due to frequent complications, such as bile leaks, collections or peritonitis, that occurred after drainage removal. Our technique and results of duct-to-duct and duct-to-jejunum anastomoses without drainage have already been reported [1, 2]. Briefly, a catheter was introduced in the donor cystic duct and brought down to the duodenum through both donor and recipient common bile ducts, thereby assessing the papilla's permeability. A biliary anastomosis was fashioned with absorbable monofilament material while the catheter was kept as a stent in the common bile duct. Once the anastomosis was finished, the catheter was pulled back to the cystic duct. Then, saline and a contrast medium were injected and a cholangiogram was taken to check the anastomosis. In cases of low implantation of the cystic duct, the septum between the cystic and hepatic ducts was divided and a wide orifice was obtained to perform the biliary anastomosis with the same technique.

Arterial anastomosis

Commonly, a Carrel patch of the donor coeliac axis was anastomosed to the bifurcation of the recipient hepatic and gastroduodenal arteries. In 34 cases, a fragment of donor iliac artery was interposed between the aorta and the donor coeliac axis. Arterial reconstructions in bench surgery were necessary in 24 cases of anatomic variants in graft arteries. Vascular and biliary patencies were checked regularly by means of Doppler ultrasound. Angiograms and/or cholangiograms (endoscopic or percutaneous) were done at any time vascular or BC were suspected.

Table 1 Patient characteristics (*BC* biliary complications, *HAT* hepatic artery thrombosis, *UW* University Wisconsin solution, *NS* not significant)

	Total	BC	BC and HAT	*P* value
Number of transplants	224	35	15	
Number of patients	203	29	9	
Mean recipient age (years)	51	49	46	NS
Mean donor age (years)	36	32	50	0.003
Sex (% males)	66	76	89	NS
Main indications (%)				
Postnecrotic cirrhosis	60	51	56	NS
Malignant tumour	20	24	44	
Cholestatic disease	6	10	–	
Fulminant hepatitis	3.5	10	–	
Mean preservation time (min)	447	498	588	NS
Preservation solution (% UW)	88	90	89	NS
Split liver transplant	3	2	1	
Biliary reconstruction (%)				
Choledochocholedoco-stomy + T-tube	20%	41%	22%	NS
Choledochocholedocostomy	67%	37%	56%	
Choledochojejunostomy	12%	20%	22%	
Arterial reconstruction				
Back-table surgery	10%	10%	33%	NS
Iliac conduit	15%	20%	33%	

Table 2 Clinical features of biliary complications *(BC)*

	BC (38 cases)	BC and HAT (9)	*P* value
Obstructions	17	2	0.02
Extrinsic compression	4	–	
Anastomotic strictures	8	–	
Non-anastomotic strictures	1	–	
Choledocholithiasis (stones, sludge)	5	2	
Bile leaks	12	–	0.04
Anastomotic leak	5	–	
T-tube exit	7	–	
Hepatic bilomas	0	8	0.000
Bacteraemia/sepsis	5 (16%)	8 (88%)	0.001
Time of presentation (mean)	58 days	190 days	0.005

Results

BC occurred in 38 cases (17%) whereas HAT was diagnosed in 11 cases (4.9%). Only one patient presented early HAT, requiring retransplantation for graft necrosis.The rest of HAT manifested as BC, sepsis, cholangitis and/or hepatic bilomas. Therefore, 23% of BC encountered after LT were secondary to HAT.

The type of BC and clinical manifestations are shown in Table 2. BC without HAT occurred earlier; predominant clinical signs were liver dysfunction, bile duct dilatation or extrahepatic bile collections diagnosed by ultrasound and, rarely, cholangitis. This principal aetiology was a technical failure; anastomotic bile leak, obstruction secondary to anastomotic stricture due to local ischaemia, redundant common bile duct, mucocele of cystic duct. Other sources of BC were split livers; two patients presented partial and total extrahepatic bile duct necrosis requiring an hepatojejunostomy and intrahepatic cholangiojejunostomy, respectively. One of them presented later with an hepatic biloma secondary to HAT requiring percutaneous drainage. The third source of complications was T-tube removal, which produced biliary collections and peritonitis. Biliary stones or sludge were diagnosed in five patients.

Table 3 Treatment and outcome

	BC	BC and HAT	*P* value
Reoperations	20 (68%)	7 (77%)	NS
Drainage	1	3	
Necrosectomy + hepatectomy	0	1	
Anastomosis reconstruction	10	–	
Hepaticojejunostomy	10	3	
Non-surgical treatment	17% (5)	66% (6)	0.009
ERCP	2	–	
Percutaneous drainage	4	7	
Retransplantations	6 (20%)	6 (66%)	0.016
Total for technical complications	3 (10%)	6 (66%)	0.002
Three-year patient survival	55%	30%	NS
Three-year graft survival	49%	19%	0.01

Clinical manifestations of HAT were septicaemia from biliary microorganisms (*Streptococcus faecalis, Pseudomonas, Escherichia Coli*), mild liver dysfunction and, mainly, hepatic bilomas secondary to partial hepatic necrosis. These BC appeared significantly later than BC without HAT.

Factors which could have influenced HAT in these nine patients were the use of an iliac graft from an old donor with arteriosclerosis (2 cases), anastomosis of the iliac graft to an ateromatous recipient aorta (1), recurrence of Budd-Chiari syndrome (1), severe acute graft rejection (1), split liver (1), hypertension and hypercholesterinaemia (1), unknown (2).

The treatment and outcome for the patients evaluated are summarised in Table 3. Most patients with BC required surgery. When graft arteries were patent, these complications were managed by revision of the anastomosis or conversion to Roux-en-Y choledochojejunostomy. Four cases of abdominal bile collections secondary to T-tube removal were treated by percutaneous drainage. Two cases of common bile duct lithiasis were removed endoscopically and papillotomy was performed.

Surgical or percutaneous drainage of hepatic bilomas was performed in all cases of HAT. In two cases, obstruction of the common bile duct by sludge was present and an hepaticojejunostomy with debris removal was carried out. One patient presented a thrombosis of both the left hepatic artery and portal vein with left hepatic lobe necrosis. A left hepatectomy was performed but later a total HAT appeared, requiring retransplantation.

Recurrence of sepsis and hepatic bilomas were the main indications for retransplantation, which was finally carried out in six out of nine patients. Two patients died without retransplantation from septic complications and fulminant hepatitis B, whereas three died after retransplantation from portal vein thrombosis, recurrent Budd-Chiari syndrome and multiorgan failure in the early postoperative period. Four patients are alive, only one without retransplantation. An arteriogram performed in this patient showed rearterialisation of the graft through collaterals.

Comparison of patients with BC with and without HAT showed that graft survival was significantly lower when HAT was present because most cases needed retransplantation. Patient survival was also lower, although not significantly different.

Discussion

BC are still an important and frequent problem after LT. The incidence varies from 5% to 38% depending on the definition of BC and the characteristics of the different series [3–5]. BC secondary to technical failures occur early after LT, usually during the first 3 months. A prompt diagnosis is essential to avoid long-term graft and patient morbidity and mortality. A revision of the anastomosis or conversion to choledochojejunostomy are the techniques of choice to solve these problems, but the incidence is decreasing as more expertise is gained. Biliary drainages are another important source of problems. Frequently, biliary leakage occurs after T-tube removal, even if it is delayed more than 3 months. In our experience, BC decreased after biliary drainages were abandoned, particularly after some modifications of the technique were introduced [2].

Ischaemic-type BC in patients without vascular thrombosis have a different pathogenesis; severe rejection associated with ABO incompatibility, preservation times longer than 12 h in University of Wisconsin solution and chronic ductopenic rejection are the most commonly reported causes [6]. Non-anastomotic biliary strictures can be treated with percutaneous dilatation or stenting, although retransplantation is usually necessary. A high incidence of BC have been reported in split LT due to extrahepatic biliary necrosis secondary to devascularisation after extensive dissection of the hilum and splitting of the arteries between the two partial grafts. This troublesome problem may be overcome with the technique of in situ splitting of the liver. Some patients present lithiasis and sludge a long time after LT, even without clear evidence of biliary strictures. The presence of lithogenic bile after transplantation or papilla dysfunction could be the origin [7].

The incidence of HAT varies from 2% to 20% in adult LT to 25% in paediatric LT. Hepatic necrosis with fulminant hepatic failure and extrahepatic necrosis of the biliary system are the common consequences of early presentation of HAT. Retransplantation is usually necessary to rescue these patients, although intrahepatic cholangiojejunostomy has been proposed as a possible alternative, particularly in children [8], when extrahe-

patic biliary necrosis is the main problem and graft parenchyma is still preserved.

In the adult population, late HAT occurring months or years after LT is now discovered more frequently. A Doppler ultrasound examination performed after a LT patient presents liver dysfunction or, more often, fever and biliary sepsis, leads to the finding of an hepatic biloma and suspicion of HAT, which is confirmed later by other imaging studies [9–11]. Cholangiography shows in these cases an altered intrahepatic biliary system with multiple strictures and dilatations. It is of great importance to check the vascular patency in any patient who presents with a BC a long time after LT. Percutaneous drainage should be the first treatment of biliary sepsis originating in these intrahepatic, infected bile collections, together with adequate antibiotic treatment. In only a few cases, mainly children, graft salvage is achieved with a conservative approach. When recurrent sepsis or hepatic bilomas appear in spite of medical treatment and interventional radiology, retransplantation should be indicated [11]. The more benign or sometimes asymptomatic course of this complication can be explained by the gradual occlusion of the arterial supply to the graft that allows arterial collateral flow to develop [12]. Arterial occlusion secondary to intimal hyperplasia and endothelial injury has probably a multifactorial origin; immunological or graft rejection, late consequences of graft ischaemia from preservation damage, or increased atherogenic risk of many LT patients. Arterial hypertension, hypercholesterolaemia, obesity, diabetes and arteriosclerosis are present in many patients before, as older recipients are transplanted, or after LT, as side effects of immunosuppressive treatment. Furthermore, older donors of 60 years or even up to the 80 years are nowadays accepted due to the scarcity of donors. Probably, a toll is paid regarding an increased incidence of ateromatous arterial thrombosis. In fact, in our experience, the donor age is the only significant factor for increased risk of late HAT. Arterial reconstructions with iliac grafts from these older donors is one of the major factors. Arterial grafts harvested from young donors should be kept in a Tissue Bank to be used in case an iliac graft is needed to revascularise a liver graft from an older donor with ateromatous arteries.

In conclusion, HAT should be suspected in any LT patient who presents a BC late after LT in the form of hepatic bilomas or biliary sepsis. Medical treatment and drainage by interventional radiology are the first-line treatment but, eventually, nearly all patients with this complication will need retransplantation. Late HAT appears more frequently in grafts from older donors.

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