Treatment of Hepatic Artery Thrombosis After Orthotopic Liver Transplantation

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OBJECTIVES: This study evaluated conservative treatment for delayed hepatic artery thrombosis after orthotopic liver transplantation (OLT).

METHODS: Whole-graft OLTs (n = 108) and live donor liver transplants (LDLTs; n = 140) were performed in 237 patients between October 1991 and July 2002. Seven episodes of hepatic artery thrombosis were identified in six patients. Among the six patients, three had received whole-graft OLT and three had received right-lobe LDLT. Treatment included retransplantation, thrombectomy plus thrombolysis, and conservative treatment of hepatic and biliary complications.

RESULTS: Five patients survived after treatment. Among the three LDLT recipients who received conservative treatment, two had subsequent collateral formation and one had spontaneous recanalization of arterial inflow. Of the three recipients of whole-graft OLT, the first died because of hepatic failure and technically difficult retransplantation, the second had thrombectomy plus thrombolysis but had recurrence of thrombosis that spontaneously recanalized during conservative treatment, and the third patient had successful retransplantation for graft failure.

CONCLUSION: In the absence of hepatic failure, conservative treatment appears to be effective for patients with hepatic artery thrombosis. Collateralization is more likely to develop after LDLT than after whole-graft OLT.

Introduction

Hepatic artery thrombosis (HAT) after orthotopic liver transplantation (OLT) remains a life-threatening complication. Although a few patients survive without symptoms, most patients with HAT experience serious morbidity, and the mortality rate is high. Treatment of HAT usually requires surgical intervention, with retransplantation considered the standard therapy. However, retransplantation is limited by both organ availability and the patient’s condition. Urgent revascularization with thrombectomy and a combination of thrombectomy with revision of anastomosis has been successful in some patients with an early diagnosis. A number of patients with delayed HAT are not immediately diagnosed, and surgical revascularization in these patients does not give good results because of condensed adhesion around and organization of clots in the vessel. Conservative treatment is often adopted to prepare these patients for retransplantation. The aim of this study was to evaluate conservative treatment as definitive therapy for HAT.

Patients and methods

Between October 1991 and July 2002, 248 OLTs were performed in 237 patients at Queen Mary Hospital, Hong Kong: 108 whole-graft OLTs and 140 live donor liver transplants (LDLTs). In whole-graft OLT, the donor coeliac artery was anastomosed to the junction of the gastroduodenal artery and
common hepatic artery. For LDLT, a microvascular technique was employed to anastomose the donor artery to either the right or left hepatic artery. No preventive anticoagulant was used postoperatively. Of 13 patients who had previously undergone transarterial oily chemoembolization (TOCE), five received whole-graft OLT and eight received LDLT. Seven episodes of HAT were identified in six patients. HAT was confirmed using Doppler ultrasonography and angiography in all cases. Anticoagulant was not given during conservative treatment.

Results

Details of the patients with HAT are shown in the Table. Six patients developed HAT. Patient 4 had two episodes of HAT. Thus, four HAT episodes occurred after whole-graft OLT and three after LDLT (Table). Two of the eight LDLT recipients (25%) who had previously undergone TOCE developed HAT, while HAT occurred in only one of the 105 LDLT recipients (1%) who had not previously had TOCE (Chi-squared test, 16.634; p = 0.013). In the whole-graft OLT group, there was no significant difference between patients with and without previous TOCE (0/5 vs 3/103). Before the diagnosis was confirmed, all patients had impaired liver function and various symptoms, except Patient 4, who was asymptomatic during the two episodes of HAT. Two patients were diagnosed early (Patients 4 and 6) after whole-graft OLT. Both received urgent laparotomy. One (Patient 4) was treated successfully using thrombectomy plus intra-arterial injection of urokinase. After 43 days, however, this patient had recurrent HAT and was treated conservatively. Patient 6 had multiple hepatic necroses and organized clots in the hepatic artery, which were not amenable to recannulation. The patient recovered after retransplantation.

The remaining four patients (Patients 1–3 and 5) had delayed HAT diagnosed between postoperative Day 21 and 105. Patient 1, who was confirmed with HAT on Day 105 after whole-graft OLT, had incomplete collateral formation at the hepatic hilum shown by angiography (Figure 1). Urgent retransplantation was attempted owing to hepatic failure, but it was not successful because of difficult dissection and massive bleeding. The patient died soon after the operation. Patients 2, 3 and 5, who had received LDLT, presented with one or more morbidities when the diagnosis was confirmed. They were treated using percutaneous drainage of the biloma and abscess, dilatation of the biliary tract and systemic antibiotics. The symptoms were gradually alleviated and liver function improved. Two (Patients 2 and 3) had been placed on the waiting lists for retransplantation. However, after 38 and 85 days of treatment, respectively, revascularization with collaterals was detected by Doppler ultrasonography and angiography (Figure 2). Retransplantation was considered unnecessary and the patients recovered with normal liver function after 124 and 156 days of conservative treatment, respectively. Patient 5 underwent many episodes of hepatic and biliary complications. Multiple procedures were undertaken. After long-term (6 months) conservative treatment, spontaneous recanalization of the hepatic artery was detected by both Doppler ultrasonography and enhanced computerized tomography (CT) scan and the patient’s situation was much improved.

Discussion

Revascularization is essential for salvage of the graft after HAT. One report showed that collaterals were formed as early as 2 weeks after transplantation.7 The sources of collateralization are thought to be the intrahepatic left or right hepatic artery, superior mesenteric artery, splenic artery, inferior phrenic artery, left gastric artery and the arteries of the omentum and Roux-en-Y limb.7–10 Complete revascularization was found in four of the five patients with delayed HAT out of the seven HAT episodes in our study. Interestingly, three of these were LDLT recipients while only one was a whole graft recipient. The other delayed HAT after whole-graft OLT had incomplete collaterals. This result is compatible with the report that reduced-size grafts were more likely to form arterial collaterals.4 Wozney et al reported that 43% of paediatric arterial occlusions after OLT developed collaterals while no collaterals were observed in adults.7 The difference in collateralization between adults and children may be due partially to the different surgical methods adopted, as children received reduced-size grafts more frequently than adults in Wozney et al’s series. The possible mechanism of the prevalence of collateralization in reduced-size graft or LDLT is that the arterioles at the liver transection surface act as conduits for collateral vessel regeneration.11 Another possibility is that the tissues around the coeliac branches in LDLT are intact compared to those in whole-graft OLT, and the length of donor artery is much shorter in LDLT than in whole-graft OLT. Collaterals are more probably and rapidly established across the anastomosis if the tissues surrounding the artery are intact and the length of donor hepatic artery from the anastomosis to the liver hilum is short.

There is no established treatment of choice for delayed
Table. Data of six patients with hepatic artery thrombosis (HAT)

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>OLT Gender/age (yr)</th>
<th>Preoperative diagnosis</th>
<th>Previous TOCE</th>
<th>Graft</th>
<th>Presentation at time HAT confirmed</th>
<th>Occurrence after OLT (d)</th>
<th>Treatment for HAT</th>
<th>Outcome of hepatic artery</th>
<th>Outcome of Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>94 M/48</td>
<td>Hepatitis B cirrhosis</td>
<td>No</td>
<td>Whole</td>
<td>Deranged LFT, fever, epigastric pain, graft failure</td>
<td>105</td>
<td>Dilatation and stent insertion at structured bile duct anastomosis, systemic antibiotics, failed re-OLT</td>
<td>No change</td>
<td>Died</td>
</tr>
<tr>
<td>2</td>
<td>171 F/63</td>
<td>Hepatitis B cirrhosis, HCC</td>
<td>2 sessions</td>
<td>Right lobe LDLT</td>
<td>Deranged LFT, RFT, fever, septic shock</td>
<td>21</td>
<td>Drainage of biloma, systemic antibiotics</td>
<td>Revascularized by collateralization</td>
<td>Asymptomatic with normal LFT and RFT</td>
</tr>
<tr>
<td>3</td>
<td>126 M/47</td>
<td>Fulminant hepatic failure</td>
<td>No</td>
<td>Right lobe LDLT</td>
<td>Deranged LFT, fever, septic shock, hypoglycaemia, hepatic abscess</td>
<td>102</td>
<td>Drainage of abscess, dilatation of structured HJ anastomosis, PTBD, systemic antibiotics</td>
<td>Revascularized by collateralization</td>
<td>Asymptomatic with normal LFT</td>
</tr>
<tr>
<td>4</td>
<td>177 M/49</td>
<td>Hepatitis B cirrhosis</td>
<td>No</td>
<td>Whole</td>
<td>Deranged LFT</td>
<td>9</td>
<td>Thrombectomy and intra-arterial injection of urokinase</td>
<td>Recurrent HAT with deranged LFT, spontaneous recanalization</td>
<td>Asymptomatic with normal LFT</td>
</tr>
<tr>
<td>5</td>
<td>213 M/47</td>
<td>Hepatitis B cirrhosis, recurrent HCC after right posterior hepatectomy</td>
<td>1 session</td>
<td>Right lobe LDLT</td>
<td>Deranged LFT, hepatic abscess, stricture of bile duct anastomosis</td>
<td>24</td>
<td>Drainage of abscess, dilatation and stent insertion at bile duct stricture, endoscopic sludge clearance, systemic antibiotics</td>
<td>Spontaneous recanalization</td>
<td>Generally stable, intermittent fever due to intra-hepatic bile duct stricture</td>
</tr>
<tr>
<td>6</td>
<td>221 M/26</td>
<td>Wilson’s disease, 3rd OLT for rejection</td>
<td>No</td>
<td>Whole</td>
<td>Deranged LFT, fever, graft failure</td>
<td>2</td>
<td>Failed thrombectomy, systemic antibiotics, re-OLT</td>
<td>Patent</td>
<td>Asymptomatic with normal LFT</td>
</tr>
</tbody>
</table>

OLT = orthotopic liver transplantation; TOCE = transarterial oily chemoembolization; LFT = liver function test; HCC = hepatocellular carcinoma; LDLT = live donor liver transplantation; RFT = renal function test; HJ = hepaticojejunostomy; PTBD = percutaneous transhepatic biliary drainage.
Retransplantation is considered the treatment of choice but is not always suitable. Complicated biliary sepsis and difficult dissection during explantation are the major risk factors for operative failure. If extensive perihepatic collaterals have developed in these patients, retransplantation will be met with much more bleeding than the initial OLT. Bhattacharjya et al reported that five of 16 patients with delayed HAT who received retransplantation died within 6 months; one died during surgery. The failure of retransplantation in one of our patients was also ascribed to condensed adhesion and multiple collaterals at the hepatic hilum, which led to difficult dissection and massive bleeding. Thrombectomy is also difficult as the organized clots may closely adhere to the vessel wall in the lumen. Therefore, conservative treatment becomes the only choice in some of these patients. The most common complications secondary to HAT are hepatic abscess, biliary stricture and septicemia. Treatment of these complications requires prolonged and multiple procedures because liquefaction of the infarcted necrosis is a gradual process, biloma from leakage of intrahepatic bile duct necrosis needs continuous drainage until bile leakage stops, and biliary stricture often appears later than the other complications and requires multiple dilatations and stent placements, and may lead to subsequent sludge and stone formation. CT- or ultrasound-guided drainage of the hepatic abscesses in these patients has given good results. Good long-term results have also been obtained in 62.5% to 72% of patients with benign biliary strictures by dilatation and stent placement through the endoscopic or percutaneous transhepatic route. In our practice, a combination of these methods with potent systemic antibiotics solved post-HAT problems one by one, and the grafts were therefore salvaged in four of the five delayed HATs without the need for repeat surgery. Although we treated only a small number of patients, we believe that conservative treatment for delayed HAT after LDLT is the best choice if each of the complications is effectively managed with patience, provided that the patient has no hepatic failure.

Even though investigation of the risk factors for HAT was not the aim of this study, we are interested in discussing the role of TOCE in the development of post-transplant HAT. Richard et al reported that there is no significant difference in HAT incidence between patients with and without preoperative TOCE. However, we found that there was a significantly higher incidence of HAT in patients with preoperative TOCE if they received LDLT, although there was no difference in the whole-graft OLT group. It is obvious that the portion of the artery to which the tip of the TOCE catheter reaches is more likely to be damaged, for the drug concentration is highest there. Emboli and foreign body giant cell reaction have been identified within the walls of the branches of the hepatic artery after TOCE. The use of such a portion or more distal branches for anastomosis with the graft’s artery may lead to stenosis or thrombus formation. During LDLT, the right or left branch of the hepatic artery is frequently used for anastomosis, while the proximal portion of the hepatic artery, which is less affected by TOCE, is used in whole-graft OLT. This may explain the difference in HAT incidence after TOCE in both groups. For patients with previous TOCE who need LDLT, we suggest that transplant surgeons should be aware of the previous TOCE and select another branch such as the gastroduodenal artery for anastomosis.

Figure 1. Superior mesenteric arteriogram demonstrating incomplete collaterals at the hepatic hilum.

Figure 2. Coeliac arteriogram demonstrating bridging collaterals between the gastroduodenal artery and hepatic artery distal to the thrombosis.
References


