CLINICAL CASE

Long-term survival after portal vein arterialization for portal vein thrombosis in orthotopic liver transplantation

Survie à long terme après artérialisation de la veine porte pour thrombose portale au cours d’une transplantation hépatique orthotopique

S. Bonnet a, A. Sauvanet a,*, O. Bruno b, D. Sommacale a, C. Francoz c, F. Dondero a, F. Durand c, J. Belghiti a

Summary  Portal vein thrombosis is a relatively common finding during liver transplantation. The management of portal vein thrombosis during liver transplantation is technically demanding and ensures adequate portal flow to the liver graft. Eversion thromboendovenectomy and bypass using a patent splanchnic vein and cavoportal hemitransposition are the most often used procedures to treat portal vein thrombosis. There have been anecdotal reports of portal vein arterialization. We report a case of portal vein arterialization during orthotopic liver transplantation for decompensated cirrhosis. When thromboendovenectomy failed to restore sufficient portal flow and completion of arterial anastomosis between the recipient hepatic artery and the donor celiac trunk, a calibrated end-to-side anastomosis between the donor splenic artery and the donor portal vein was performed. With a 6-year follow-up, there are no symptoms related to portal hypertension, liver function is normal. However, an aneurismal dilatation of the portal branches has progressively developed. Calibrated portal vein arterialization is a possible option for portal vein thrombosis in liver transplantation, allowing long-term patient and graft survival.

© 2009 Elsevier Masson SAS. All rights reserved.

Résumé  Une thrombose portale est assez fréquemment présente au moment d’une transplantation hépatique orthotopique. La prise en charge d’une thrombose portale au cours d’une transplantation hépatique orthotopique est techniquement difficile et nécessite d’assurer un

* Corresponding author.
E-mail address: alain.sauvanet@bjn.ap-hop-paris.fr (A. Sauvanet).

0399-8320/© 2009 Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.gcb.2009.05.013

Introduction

The incidence of portal vein thrombosis during liver transplantation varies from 2 to 26% [1—5]. Initially, portal vein thrombosis was considered to be an absolute contraindication for liver transplantation due to technical difficulties and disappointing results in particular inadequate hepatopetal flow to the liver graft [4]. Several techniques have been proposed to treat this complication: eversion thromboendovenectomy [3], bypass [2,6], use of blood inflow from the inferior vena cava or the left renal vein [7—10], combined liver-small bowel transplantation [11] and portal vein arterialization [12—18]. Among these approaches, eversion thromboendovenectomy is the most frequently used but, like bypass, it requires a patent vein in the portal system. Portal vein arterialization is considered to be a salvage solution because it results in non-physiological vascular perfusion in the liver which is deprived of hepatotrophic splanchnic-derived factors [19]. Portal vein arterialization has been reported in a few patients but without long-term results [12—18]. We report the case of a patient who underwent portal vein arterialization after portal eversion thromboendovenectomy failed during orthotopic liver transplantation with a 6-year follow-up.

Case report

A 47-year-old man with decompensated alcoholic cirrhosis underwent orthotopic liver transplantation in October 2001. The patient had been placed on a waiting list 6 months before orthotopic liver transplantation because of gastrointestinal bleeding due to portal hypertension associated with ascites and encephalopathy. Abdominal computed tomography performed at the time of listing showed a patent portal vein, oesophageal varices and splenorenal shunts. Intraoperatively, a troncular portal vein thrombosis was diagnosed. Dissection of the portal vein and intraoperative ultrasound showed diffuse thrombosis extending inferiorly to both the superior mesenteric and splenic veins. A direct eversion thromboendovenectomy was attempted but was considered incomplete.

Orthotopic liver transplantation was performed according to the piggyback technique. An end-to-end portal venous anastomosis between recipient and donor was performed but resulted in a poor portal flow after portal unclamping. An attempt at additional thrombectomy in the recipient portal system failed. There was no variceal vein large enough for portal vein reconstruction. The left renal vein was not accessible because of its retroaortic position (Fig. 1). There were numerous venous collaterals posterior to the duodenopancreatic area due to portal hypertension. Therefore, dissection of the inferior vena cava for cavoportal transposition was declined due to the risk of haemorrhage. Finally, we decided to perform portal arterIALIZATION to improve blood flow in the graft portal vein. This technique was chosen because it was technically simpler and also avoided additional warm ischemia due to iterative clamping of the portal vein.

Reconstruction of the arterial blood flow into the graft was achieved by an end-to-end anastomosis between the recipient common hepatic artery and the donor celiac trunk. The portal vein of the graft was clamped laterally, thus preserving portal flow to the graft. Portal vein arterilization was then performed by anastomosing the donor splenic artery end-to-side to the donor portal vein. The graft portal vein was circumferentially reinforced around the arterial anastomosis with a circular ring of the donor aorta. The arterioporal anastomosis was calibrated under doppler ultrasound control to limit blood flow into the portal vein.

Figure 1 Preoperative computed tomography. Left renal vein in retroaortic position (white arrow).
vein (Fig. 2). However, portal pressure and arterial flow were not measured intraoperatively. Reperfusion of the liver graft was excellent after a period of 12 hours of cold ischemia. Postoperatively, Doppler ultrasonography on days 1, 3, 5 and 7 showed a patent hepatic artery and satisfactory pulsative portal flow. Prothrombin time increased from 38 to 66%, whereas serum bilirubin level decreased from 85 to 37 micromoles/L at days 1 and 5, respectively. The peak in serum transaminases level was observed at day 1: alanine aminotransferase 1250 IU/L (normal < 40) and aspartate aminotransferase 1560 IU/L (normal < 40). Anticoagulation therapy with curative intent was begun using low molecular weight heparin. The patient was reoperated on day 12 due for biliary anastomotic leakage treated by a leak suture and T-tube insertion. The subsequent postoperative course was uneventful with no significant ascites. At discharge (day 38), liver function tests were within the normal range including, 7 micromoles/L of conjugated bilirubin, aspartate aminotransferase 65 IU/L (normal < 45), alanine aminotransferase 55 IU/L (normal < 45), alkaline phosphatase 338 IU/L (normal < 130), gamma-glutamyl-transferase 374 IU/L (normal < 55). Prothrombin time was decreased due to fluindione therapy.

Intrahepatic arterial resistance index obtained by Doppler ultrasonography was 0.68, unchanged compared to the previous postoperative control. The intrahepatic portal vein was permeable with good arterialized hepatopetal blood flow (speed: 15 cm/s). Three-dimensional computed tomographic angiography showed a diffuse aneurismal dilatation of the portal vein and its intrahepatic branches (Fig. 4) and the presence of some varices in the territory of the inferior mesenteric vein. There was no ascites or argument for biliary anastomotic restenosis.

Nine months after orthotopic liver transplantation, the patient developed cholangitis with liver abscess. At Doppler ultrasonography, the hepatic arterial resistive index was 0.69 and an anastomotic biliary stenosis was suspected. Retrograde cholangiography confirmed an isolated anasto-

Figure 2 Schematic representation of vascular reconstruction. Ao: aorta; rCT: recipient's celiac trunk; SMA: recipient’s superior mesenteric artery; RRA: recipient’s right renal artery; rCHA: recipient’s common hepatic artery; rSA: recipient’s splenic artery; dCT: donor’s celiac trunk; dCHA: donor’s common hepatic artery; dSA: donor’s splenic artery with thrombosis; RbHA: donor’s right branch of hepatic artery; LbHA: donor’s left branch of hepatic artery; PV: recipient’s portal vein with thrombosis; SV: recipient’s splenic vein with thrombosis; SMV: recipient’s superior mesenteric vein with thrombosis.
The incidence of portal vein thrombosis during orthotopic liver transplantation ranges from 2 to 26% [1–5]. Portal vein thrombosis can be classified according to its extension and its severity into four grades ranging from partial to complete thrombosis, with or without extension into the superior mesenteric vein [1,2]. Initially, portal vein thrombosis was considered a contraindication for orthotopic liver transplantation due to technical difficulties and inadequate hepatopetal portal flow resulting in poor long-term results [4]. Even if portal vein thrombosis is an unfavourable condition for performing orthotopic liver transplantation, the development of new surgical techniques has made it possible to overcome this condition which is no longer considered an absolute contraindication to orthotopic liver transplantation. In two recent series, portal vein thrombosis was associated with difficult surgery and portal re-thrombosis, but did not result in increased overall morbidity and mortality [5,7].

Several surgical techniques have been described to treat portal vein thrombosis. Eversion thromboendovenectomy consists of dissecting the thrombus from the everted venous wall until adequate blood flow is obtained [3]. Eversion thromboendovenectomy is the most frequently used technique but it can be unsuccessful when the thrombosis extends upstream from the splenomesenteric junction. In this setting, either a jump graft to a patent proximal superior mesenteric vein can be performed or an anatomical venovenous bypass with the coronary vein or any vein of the splanchnic territory that provides sufficient blood flow [2,6]. Finally, a patent vein in the portal system is needed for eversion thromboendovenectomy, jump graft and venous bypass. When the thrombosis involves the whole portal system and no collaterals are available, an alternative solution is to obtain portal flow to the graft from the inferior vena cava [7,9,10] or the left renal vein [8]. Cavoportal hemitransposition consists of anastomosing the recipient inferior vena cava to the donor portal vein usually with caval calibration whereas renoportal anastomosis is performed between the native left renal vein and the graft portal vein [1,8]. These two techniques are frequently associated with postoperative ascites (in up to 60% of cases) and portal thrombosis (in up to 25% of cases), with a trend towards greater morbidity after cavoportal than after renoportal transposition [1,8], so they can not be considered to be routinely indicated in case of diffuse portal thrombosis. A more aggressive option is the combined liver-small bowel transplantation which remains a technical and immunological challenge [11].

A simpler option to improve portal inflow is to arterialize the portal vein directly using a branch from the donor or recipient celiac axis, or an interposed graft between the recipient aorta and the graft portal vein. To our knowledge, portal vein arterialization has been reported in 13 patients during orthotopic liver transplantation [12–18] and even more rarely in auxiliary heterotopic liver transplantation [20]. During orthotopic liver transplantation, portal vein arterialization was indicated for pre-existing diffuse portal vein thrombosis or more rarely for portal vein thrombosis complicating a recent orthotopic liver transplantation (Table 1). In the latter setting, portal vein arterialization was usually associated with thrombectomy of the portal vein. Five of the 13 patients died within a few months after orthotopic liver transplantation from haemorrhage, right heart failure or acute portal thrombosis [12,17]. Four of the five deaths occurred after portal vein arterialization for secondary portal vein thrombosis [12,16–18] whereas only one death complicated the seven portal vein arterializations for primary portal vein thrombosis. Some patients developed complications related to “over-arterialization”, including graft fibrosis due to alterations in liver microcirculation [12,17], right-sided heart decompensation [13] and persistent portal hypertension [16,17]. Conversely, some patients had a favourable outcome with a follow-up ranging up to 36 months, including the only three patients who had portal vein arterialization with surgical or radiological calibration for the purpose of limiting the infrahepatic flow [13,14]. These results of portal vein arterialization for primary portal vein thrombosis seem comparable to that of cavoportal hemitransposition and renoportal anastomosis which are associated with a 74% survival rate [1,8].

Results of portal vein arterialization for primary portal vein thrombosis and our case suggest that limiting arterial flow into the portal system is probably important to improve long-term results of portal vein arterialization during orthotopic liver transplantation. In clinical orthotopic liver transplantation, “over-arterialization” of the liver can result in liver fibrosis [12,17]. Experimentally, “over-arterialization” of the portal vein during orthotopic liver transplantation in a syngenic rat model does not alter liver function but can result in early activation of liver fibrogenesis [21]. In clinical orthotopic liver transplantation, limiting arterial flow after portal vein arterialization has been performed by several groups but there is no agreement about the “ideal” flow in this setting: some authors propose 0.6 to 0.8 L/min [15] while others recommend 1 L/min [14] or even 1.5 to 1.8 L/min [16]. When calibration of
<table>
<thead>
<tr>
<th>Authors (ref)</th>
<th>Age (years)</th>
<th>Indication of PVA</th>
<th>Type of PVA</th>
<th>Postoperative course</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erhard et al. [16]</td>
<td>47</td>
<td>Primary PVT</td>
<td>Jump graft between aorta and graft PV</td>
<td>Portal hypertension</td>
<td>Alive (12)</td>
</tr>
<tr>
<td></td>
<td>29</td>
<td>Secondary PVT</td>
<td>Jump graft between aorta and graft PV</td>
<td>Acute renal failure</td>
<td>Ultimate</td>
</tr>
<tr>
<td>Aspinall et al. [18]</td>
<td>53</td>
<td>Secondary PVT</td>
<td>Jump graft between aorta and graft PV</td>
<td>Encephalopathy grade 4</td>
<td>Dead (2)</td>
</tr>
<tr>
<td></td>
<td>29</td>
<td>Secondary PVT</td>
<td>Jump graft between aorta and graft PV</td>
<td>Septicemia</td>
<td>Alive (10)</td>
</tr>
<tr>
<td>Charco et al. [17]</td>
<td>66</td>
<td>Primary PVT</td>
<td>Recipient HA anastomosed to graft PV</td>
<td>Severe graft dysfunction: re-orthotopic liver transplantation at day 1 with same type of anastomosis</td>
<td>Alive (24)</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>Secondary PVT</td>
<td>Jump graft between aorta and graft PV</td>
<td>Portal hypertension</td>
<td>Dead (4)</td>
</tr>
<tr>
<td>Stange et al. [13]</td>
<td>53</td>
<td>Primary PVT</td>
<td>Recipient HA anastomosed to graft PV</td>
<td>Biliary leakage</td>
<td>Alive (36)</td>
</tr>
<tr>
<td>Settmacher et al. [14]</td>
<td>35</td>
<td>Primary PVT</td>
<td>Recipient HA anastomosed to graft PV + calibration</td>
<td>Multi-organ failure</td>
<td>Alive (36)</td>
</tr>
<tr>
<td></td>
<td>55</td>
<td>Primary PVT</td>
<td>Jump graft between aorta and graft PV + calibration</td>
<td>Right heart failure (treated by coil insertion into recipient hepatic and splenic artery at 3 months)</td>
<td>Alive (30)</td>
</tr>
<tr>
<td>Ott et al. [12]</td>
<td>35</td>
<td>Secondary PVT</td>
<td>Jump graft between aorta and graft PV</td>
<td>Biliary leakage PVT</td>
<td>Dead (2)</td>
</tr>
<tr>
<td></td>
<td>57</td>
<td>Secondary PVT</td>
<td>Jump graft between aorta and graft PV</td>
<td>Right heart failure</td>
<td>Dead (11)</td>
</tr>
<tr>
<td></td>
<td>54</td>
<td>Primary PVT</td>
<td>Recipient HA anastomosed to graft PV</td>
<td>Acute renal failure</td>
<td>Alive (24)</td>
</tr>
<tr>
<td></td>
<td>68</td>
<td>Primary PVT</td>
<td>Jump graft between aorta and graft PV</td>
<td>Chronic rejection: re-orthotopic liver transplantation at 2 years</td>
<td>Alive (1)</td>
</tr>
<tr>
<td>Nivatvongs et al. [15]</td>
<td>70</td>
<td>Primary PVT</td>
<td>Recipient HA anastomosed to graft PV</td>
<td>Portal hypertension with bleeding</td>
<td>Alive (20)</td>
</tr>
</tbody>
</table>

PVA: portal vein arterialisation; primary PVT: portal vein thrombosis pre-existing to orthotopic liver transplantation; secondary PVT: portal vein thrombosis complicating orthotopic liver transplantation; PV: portal vein; HA: hepatic artery.

Arterioporal anastomosis is not performed during orthotopic liver transplantation, intrahepatic portal flow can be limited by secondary angiographic coil embolization of the arterial branch anastomosed to the portal vein [13,14]. In our case, we surgically created a stenosis limiting hyperarterialization while maintaining good portal perfusion and also maintained betablocker therapy after orthotopic liver transplantation to reduce splanchnic blood pressure. In a 6-year follow-up, the patient did not develop any clinical signs of portal hypertension or heart failure. An arterial steal syndrome was suspected in our patient due to portal arterialization when biliary stenosis was diagnosed 9 months after orthotopic liver transplantation. However, the steal syndrome seems very unlikely because of the absence of signs of diffuse ischemic-like cholangiopathy at retrograde cholangiography. The absence of biliary re-stenosis 5 years after stent removal and normal arterial resistive index also support this hypothesis.

Although to our knowledge this 6-year follow-up is the longest reported follow-up after portal vein arterialization for portal vein thrombosis, the long-term safety of this technique has not been demonstrated. First, liver function tests
have progressively deteriorated in the 3 years after orthotopic liver transplantation but we did not perform recent liver biopsy to exclude liver fibrosis. Second, from 3 to 6 years after orthotopic liver transplantation, although the periportal aortic ring prevented dilatation of the portal vein, progressive dilatation of intrahepatic portal branches has occurred and has developed into a real aneurismal dilatation. To our knowledge, this is the first case of aneurismal dilatation of the intrahepatic portal branches after portal arterialization during orthotopic liver transplantation.

In conclusion, during orthotopic liver transplantation with portal vein thrombosis, portal vein arterialization combined with arterial calibration may result in long-term patient and graft survival and should be considered as an alternative technique when both evasion thromboendovenectomy and bypass are not feasible. In this setting, cavoportal transposition and renoportal transposition are also acceptable options despite a significant risk of postoperative ascites and portal thrombosis [8]. Renoportal transposition seems particularly indicated when portal thrombosis is associated with splenorenal shunts which increase blood flow into the left renal vein and also avoids the risk of thrombosis upstream from caval calibration [8]. However, renoporal transposition is technically impossible when the left renal vein is in a retroaortic position. This case of portal vein arterialization and the literature show that the best results with this technique are obtained when portal vein thrombosis is pre-existing to orthotopic liver transplantation. However, the progressive aneurismal dilatation of intrahepatic portal branches which was observed in our patient and a possible risk of liver fibrosis as described clinically [12,17] or experimentally [21] suggests that portal vein arterialization should be also used with caution.

Contributors

SB, AS, OB, DS, CF, FD0 were all involved in the treatment of the patient and data collection. SB, AS and FD0 wrote the first draft of the manuscript FD0 and JB: scientific supervision.

Conflicts of interests

None.

References