

Portal Biliopathy Treated With Living-donor Liver Transplant: Index Case

Subash Gupta,¹ Ashish Singhal,¹ Neerav Goyal,¹ Vivek Vij,¹ Manav Wadhawan²

Abstract

Portal biliopathy refers to abnormalities of the entire biliary tract in patients with extrahepatic portal vein obstruction. Most of the patients are asymptomatic. However, more than 80% of patients show characteristic morphologic features on endoscopic retrograde cholangiopancreatography. Symptomatic cases usually require therapy. The proposed therapies include endoscopic dilatation and stenting of the common bile duct, portosystemic shunt with splenectomy, meso Rex bypass, and occasionally, bilioenteric bypass. In patients with failed stenting and nonshuntable anatomy, liver transplant may be the only option, provided an adequate inflow can be achieved to the graft. To the best of our knowledge, only 2 cases have been reported, and these have undergone deceased-donor liver transplant for portal biliopathy. We report an index case treated successfully with living-donor liver transplant.

Key words: *Thrombosis, Mesenteric, Biliary, Obstruction, Portal*

Portal biliopathy refers to abnormalities of the entire biliary tract including extrahepatic and intrahepatic bile ducts, cystic duct, and gall bladder, owing to impediment of hepatopetal splanchnic venous blood flow by a partial or complete obstruction of spleno-mesenteric portal axis.¹⁻³ It leads to dilatation of periportal veins within the hepatic pedicle including

paracholedochal veins of Petren and/or epicholedochal plexus of Saint, which provide an anatomic basis for the development of choledochal and gall bladder varices leading to portal biliopathy. It is not associated with any primary liver disease.^{1,2} Symptoms associated with portal biliopathy could be secondary to prehepatic portal hypertension, diminished portal blood flow to the liver, spontaneous portosystemic shunting, which was prominent in this patient, and biliary obstruction. However, the majority of the patients remain asymptomatic. Symptomatic biliary obstruction and other symptoms such as splenomegaly, major upper-gastrointestinal bleeding, growth retardation, and neuropsychiatric disease were reported in 5% to 18% of patients.¹⁻³ On endoscopic retrograde cholangiopancreatography, 81% to 100% show biliary strictures of various lengths and degrees as caliber irregularity, ectasia, indentations, angulations, clustering, and pruning of the intrahepatic ducts.²⁻⁶ The present patient had characteristic features of stricturing on endoscopic retrograde cholangiopancreatography.

The proposed therapies include endoscopic dilatation and stenting of the common bile duct, portosystemic shunt with splenectomy, and rarely biliary-digestive bypass.^{2, 3, 7-10} Recently, introduction of the meso Rex bypass has caused a paradigm shift in management of extrahepatic portal vein obstruction.¹¹ However, despite various treatment options, liver transplant remains the only choice in some patients. Alternatively, owing to relatively preserved liver functions in these patients, disease severity based organ allocation policies, and associated technical difficulties, only 2 cases have undergone deceased-donor liver transplant.¹²⁻¹³ Here, we report an index case of portal biliopathy treated successfully with a living-donor liver transplant.

From the Departments of ¹Surgical Gastroenterology and Liver Transplantation, and ²Gastroenterology and Hepatology, Indraprastha Apollo Hospital, New Delhi, India
Address reprint requests to: Subash Gupta, Department of Surgical, Gastroenterology and Liver Transplantation, Indraprastha Apollo Hospital, Sarita Vihar, New Delhi-110076, India
Phone: +91 11 2987112 Fax: +91 11 41611010 E-mail: guptasubash@hotmail.com

Case Report

Between September 2006 and December 2009, 239 orthotopic liver transplants were done, of which, 232 were living-related and 7 were deceased-donor liver transplants. We recently treated a 26-year-old Indian man from the United States who presented with growth retardation during childhood, recurrent episodes of cholangitis for the past 11 years, upper gastrointestinal hemorrhage, and generalized weakness for the past 4 years. At the age of 15 years, ultrasonography revealed portal vein thrombosis and splenomegaly with associated features of hypersplenism. Consequently, he underwent a splenic artery embolization. One year later, he developed obstructive jaundice. Endoscopic retrograde cholangiopancreatography showed concentric stenosis of the common bile duct and intrahepatic ducts with no evidence of stones. Subsequently, he had recurrent episodes of obstructive jaundice with cholangitis managed by multiple endoscopic retrograde cholangiopancreatography and stenting. In last 4 years, he had recurrent episodes of upper-gastrointestinal hemorrhage treated by endoscopic variceal ligation. During the last 2 years, he had 2 episodes of life-threatening sepsis owing to cholangitis requiring immediate stent exchange and admission to intensive care units elsewhere.

Accordingly, the patient was listed for a deceased-donor liver transplant at another hospital in the United States. However, he has been on the wait list for 20 months, and still he could not get an organ because of a low model for end-stage liver disease (MELD) score of 10. When he presented at our center, he was malnourished, icteric, and had hepatosplenomegaly (Table 1). Contrast-enhanced computed tomography of the abdomen showed

splenomegaly, a relatively normal-looking liver with a stent in situ, a thrombosed intrahepatic and extrahepatic portal vein, a splenic vein, and a superior mesenteric vein, with large, multiple collaterals in the superior mesenteric vein (Figures 1 and 2). Magnetic resonance cholangiopancreatography showed multiple intrahepatic and extrahepatic biliary strictures. Repeat endoscopic retrograde cholangiopancreatography showed multiple strictures in the biliary tree. Considering his young age, intractable symptoms, failure of endoscopic therapy, nonfeasibility of other treatment options, poor quality of life, and nonavailability of deceased-donor organ, the option of a living-donor liver transplant was given to him. Simultaneously, all the technical difficulties involved in his case and his need for life-long immunosuppression and their potential adverse effects were discussed. To establish portal inflow, a preoperative decision was made to use infracolic collateral visible on computed tomography scan, or if that failed, then we would do a cavoportal hemitransposition.

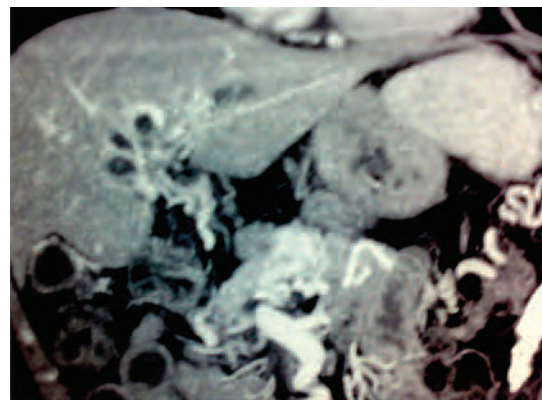


Figure 1. Computed tomography scan showing thrombosed portal vein with large, multiple periportal and perisplenic collaterals.

Table 1. Pretransplant laboratory values.

Hematology	TLC	3000
	Platelet	100 000
LFT	Bilirubin T/D	25.6/14.8 $\mu\text{mol/L}$
	ALP	625 U/L
	SGOT	75 IU/L
	SGPT	68 IU/L
	Albumin	39 g/L
	PT	10.1 s
	aPTT (T/C)	>120/30

Abbreviations: ALP, alkaline phosphatase; aPTT (T/C), activated partial thromboplastin time; LFT, liver function tests; PT, prothrombin time; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase; TLC, Total leucocyte count

Operative details

Hepatoduodenal ligament dissection was difficult with the fibrotic portal vein until but was completed after we located the hilum and an enlarged hepatic artery. The common bile duct was thin, fibrotic, and irregular, and was surrounded by multiple, dilated, and friable collaterals. Donor surgery was started after we identified a 1-cm wide anastomosable collateral inferior to the pancreas in an infracolic compartment. The recipient hepatectomy was accomplished without any splanchnic congestion. This was achieved by preserving the inferior vena cava, maintaining flow of the collaterals, and

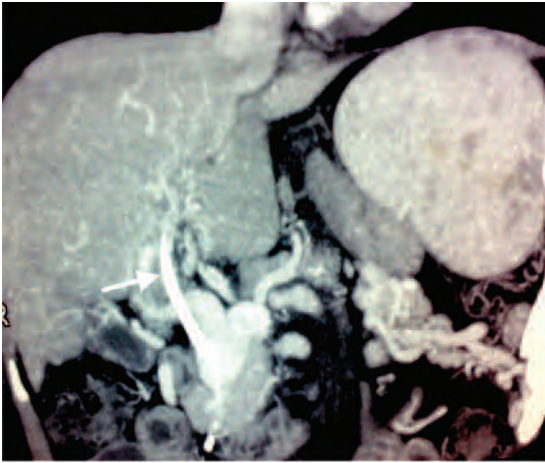


Figure 2. Computed tomography scan showing splenomegaly with large, multiple periportal and perisplenic collaterals (arrowhead showing biliary stent in-situ).

clamping only the hepatic veins and artery. A standard right lobe graft (a right lobe without the middle hepatic vein) was recovered from his 48-year-old mother. The graft weighed 698 grams, and there was a single right hepatic artery, a portal vein, and a hepatic duct; cold ischemia time was 40 minutes.

Before beginning the graft implant, we lengthened the collateral isolated for portal inflow on the bench. An approximately 10-cm long venous graft was required to establish an inflow from the infracolic collateral to the graft portal vein. This was made by using a 5-cm long internal jugular vein recovered from the donor. The internal jugular vein was anastomosed to the inflow collateral and was brought to the supracolic compartment anterior to the pancreas through a retrocolic tunnel. Another 5-cm long venous jump graft recovered from explanted liver middle hepatic vein was used to lengthen it to the donor portal vein.

The graft implantation was begun by closing the caval orifices of the recipient's left and middle hepatic veins. The right hepatic vein caval orifice was plastied, and a hepatic vein anastomosis was performed. Reperfusion of the graft was done after completion of the anastomosis between the jump graft and the donor portal vein (Figure 3). Caval clamping time and warm ischemia time were 32 minutes and 28 minutes. End-to-end hepatic arterial anastomosis and Roux-en-Y hepaticojejunostomy were done using $\times 3.5$ loupe magnifications. Intraoperative Doppler ultrasonography showed triphasic flow in the hepatic vein and normal flow in hepatic artery and portal vein, with peak systolic velocity of 28 cm/sec and 69 cm/sec. The patient was

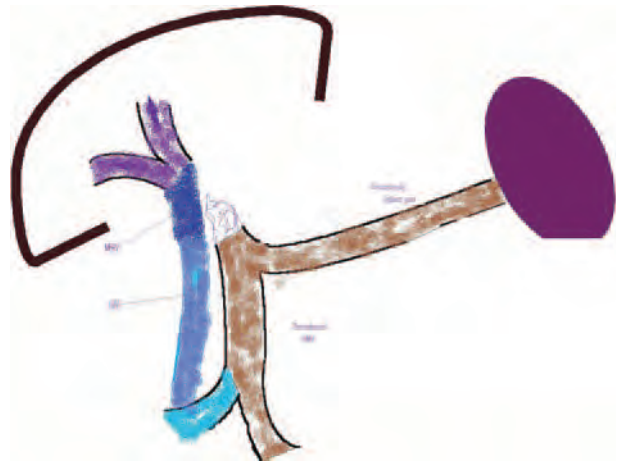


Figure 3. Diagrammatic representation of surgical procedure.

given 5 units of packed red cells and 3 units of fresh frozen plasma during the operation. The operative time was 11 hours 45 minutes.

Doppler ultrasonography for the first 5 postoperative days showed triphasic flow in the hepatic vein, and persistently well-maintained flow in the hepatic artery and the portal vein with a peak systolic velocity of 38 cm/sec and 54 cm/sec on the fifth postoperative day. Computed tomographic angiography of the abdomen showed a well-perfused hepatic allograft with patent vasculature. The patient was discharged in stable condition on the 12th postoperative day. He was discharged on tacrolimus, mycophenolate mofetil, and prednisone. The donor had an uneventful recovery with normal liver function test results on the fifth postoperative day. He was discharged on seventh postoperative day.

Histopathologic examination of the explanted liver showed markedly dilated intrahepatic and extrahepatic biliary tree with segments of stricture. The lining of the epithelium was partly ulcerated and the subepithelium showed dense infiltration of lymphomononuclear cells, admixed with neutrophils and eosinophils. The wall of bile duct showed prominent fibrosis and the duct lumina was filled with inspissated bile. His liver parenchyma showed periportal fibrosis and a fibrotic intrahepatic portal venous system. Also, there was evidence of chronic cholecystitis. At the time of this writing (28 months after surgery), the patient is doing well with stable liver function results, a weight gain of > 15 kg, patent portal inflow (Figure 4), and good quality of life.

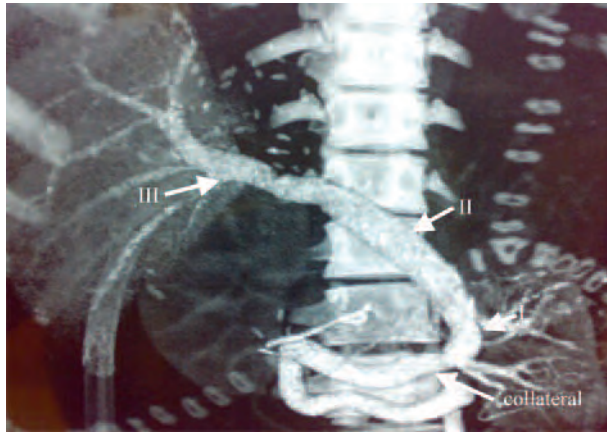


Figure 4. Computed tomography angiogram (after transplant) showing patent portal inflow (I-donor internal jugular vein jump graft; II-explanted liver middle hepatic vein graft; III-donor liver portal vein).

Discussion

Various treatment options have been reported for portal biliopathy; however, there is no consensus regarding the optimal or definitive treatment as there are limited reports in the literature. Endoscopic treatment remains the treatment of choice in patients with symptomatic biliary obstruction. It includes an endoscopic sphincterotomy, stone extraction, a mechanical lithotripsy, and endoscopic dilation of the biliary stricture with or without a stent or nasobiliary drain placement. Stents or nasobiliary drains relieve the biliary obstruction and cholangitis, but are likely to be blocked frequently, requiring repeat stent exchange. Our patient had 2 episodes of cholangitis-induced life-threatening sepsis requiring immediate stent exchange. Considering his age and poor quality of life, it was not a suitable option. Nine of 20 patients treated with a plastic stent had complications of cholangitis, cholecystitis, or pancreatitis.^{7-9, 14, 15} In the largest series of 10 patients with mean follow-up of 3.3 years, cholangitis developed in 5 patients and the stents had to be left in place because of inadequate biliary drainage in 7 patients, despite a scheduled stent replacement every 6 months (or earlier) in case of stent occlusion or cholangitis. One death occurred after 2.5 years from secondary biliary cirrhosis.⁷ Durmortier and associates reported persistent cholestasis in 4 of 6 patients requiring secondary surgical treatment in all 4 patients.¹⁵ To our knowledge, use of metallic endobiliary stents for this benign indication has not been reported. Moreover, metallic stents appear to lack usefulness in this situation because of their 5-year patency, and the

relative difficulty of removal if biliary surgery becomes necessary.¹⁶

Portal decompression by transjugular intrahepatic portosystemic shunt insertion,¹⁷ meso Rex bypass,¹¹ or surgical shunt formation (splenorenal or mesocaval)^{11, 18, 19} can be an alternative in patients with persistent symptoms requiring repeat biliary intervention. These procedures have proved effective in anticipating that biliary strictures are reversible, will resolve with portal decompression, and will not require secondary bilioenteric bypass.^{10, 15, 17} Transjugular intrahepatic portosystemic shunt and meso Rex bypass were not feasible in our patient because of an attenuated intrahepatic portal venous system and the likelihood of limited patency with poor portal inflow. Also, the presence of nonshuntable anatomy, multiple biliary strictures, and a high risk for thrombosis of a makeshift shunt preclude the option of a surgical shunt.

Bilioenteric bypass may be another option to relieve biliary obstruction. However, the presence of multiple intrahepatic and extrahepatic biliary strictures in our patient excluded this as an option, as anastomosis placed below the biliary obstruction was likely to be nonfunctional. Moreover, it is impossible to approach the bile duct surgically without any prior portosystemic shunt causing massive hemorrhage from collaterals and death.^{10, 20} Patients not a candidate for any form of portosystemic shunting or meso Rex bypass may benefit from a nonshunt portal hypertension surgical procedure, such as the Sugiura procedure or splenic artery ligation.¹¹ Nevertheless, these operations may be only proposed as a temporary or palliative option for recurrent variceal bleed, and it is likely that the condition will continue to worsen with time.

Liver transplant could be the only option when both endoscopic and surgical treatments have either failed or are not feasible^{4, 9, 11-13} provided an adequate portal inflow can be achieved to the graft. Until now, 2 cases of portal biliopathy have been reported to undergo deceased-donor liver transplant.^{12, 13} It has the potential to cure both the patient's symptoms and complications of portal hypertension, and provide long-lasting relief in a young patient with an otherwise normal life expectancy. The present patient could not get a deceased-donor organ being on the waiting list for about 20 months. This was partly due to his disease severity scoring based on organ

allocation policy, as these patients have preserved synthetic liver functions and a lower MELD score. In this scenario, a living-donor liver transplant was performed. It was technically demanding to establish the portal inflow in the presence of extensive portomesenteric thrombosis and an absence of vascular allografts. We used an infracolic collateral as a portal inflow and lengthened it with 2 venous jump grafts, an internal jugular vein recovered from the donor, and a middle hepatic vein recovered from the explant. One may argue that if a portal inflow could be achieved from a collateral then a portosystemic shunt also could have been done without requiring a transplant. Nevertheless, this patient had poor quality of life from recurrent episodes of cholangitis and in case the shunt had thrombosed, it would rob the patient of a chance at a transplant.

Conclusions

In patients with portal biliopathy, treatment should be determined by the individual patient characteristics with a focus on management of portal hypertension and relief of obstructive jaundice. Living-donor liver transplant can be a viable option in young patients with a nonshunt anatomy and multiple intrahepatic biliary strictures.

References

1. Sarin SK, Agarwal SR. Extrahepatic portal vein obstruction. *Semin Liver Dis.* 2002;22(1):43-58.
2. Sarin SK, Sollano JD, Chawla YK, et al. Consensus on extra-hepatic portal vein obstruction. *Liver Int.* 2006;26(5):512-519.
3. Dhiman RK, Behera A, Chawla YK, Dilawari JB, Suri S. Portal hypertensive biliopathy. *Gut.* 2007;56(7):1001-1008.
4. Dhiman RK, Puri P, Chawla Y, et al. Biliary changes in extrahepatic portal venous obstruction: compression by collaterals or ischemic? *Gastrointest Endosc.* 1999;50(5):646-652.
5. Malkan GH, Bhatia SJ, Bashir K, et al. Cholangiopathy associated with portal hypertension: diagnostic evaluation and clinical implications. *Gastrointest Endosc.* 1999;49(3 Pt 1):344-348.
6. Nagi B, Kochhar R, Bhasin D, Singh K. Cholangiopathy in extrahepatic portal venous obstruction. Radiological appearances. *Acta Radiol.* 2000;41(6):612-615.
7. Sezgin O, Oğuz D, Altıntaş E, Saritaş U, Sahin B. Endoscopic management of biliary obstruction caused by cavernous transformation of the portal vein. *Gastrointest Endosc.* 2003;58(4):602-608.
8. Condat B, Vilgrain V, Asselah T, et al. Portal cavernoma-associated cholangiopathy: a clinical and MR cholangiography coupled with MR portography imaging study. *Hepatology.* 2003;37(6):1302-1308.
9. Vibert E, Azoulay D, Aloia T, et al. Therapeutic strategies in symptomatic portal biliopathy. *Ann Surg.* 2007;246(1):97-104.
10. Chaudhary A, Dhar P, Sarin SK, et al. Bile duct obstruction due to portal biliopathy in extrahepatic portal hypertension: surgical management. *Br J Surg.* 1998;85(3):326-329.
11. Superina R, Shneider B, Emre S, Sarin S, de Ville de Goyet J. Surgical guidelines for the management of extra-hepatic portal vein obstruction. *Pediatr Transplant.* 2006;10(8):908-913.
12. Filipponi F, Urbani L, Catalano G, et al. Portal biliopathy treated by liver transplantation. *Transplantation.* 2004;77(2):326-327.
13. Hajdu CH, Murakami T, Diflo T, et al. Intrahepatic portal cavernoma as an indication for liver transplantation. *Liver Transpl.* 2007;13(9):1312-1316.
14. Thervet L, Faulques B, Pissas A, et al. Endoscopic management of obstructive jaundice due to portal cavernoma. *Endoscopy.* 1993;25(6):423-425.
15. Dumortier J, Vaillant E, Boillot O, et al. Diagnosis and treatment of biliary obstruction caused by portal cavernoma. *Endoscopy.* 2003;35(5):446-450.
16. Lopez RR Jr, Cosenza CA, Lois J, et al. Long-term results of metallic stents for benign biliary strictures. *Arch Surg.* 2001;136(6):664-669.
17. Görgül A, Kayhan B, Dogan I, Unal S. Disappearance of the pseudo-cholangiocarcinoma sign after TIPSS. *Am J Gastroenterol.* 1996;91(1):150-154.
18. Siddiqui MN. Bile duct obstruction due to portal biliopathy in extrahepatic portal hypertension: surgical management. *Br J Surg.* 1999;86(1):138.
19. Arotcarena R, Roulot D, Aubert A, Attali P, Benichou J, Coste T. Successful treatment by mesocaval anastomosis of a common-bile-duct compression by choledochal varices. *J Hepatol.* 1995;23(5):629-630.
20. Bejanin H, Baumann R, Choury A, Fritsch J, Buffet C. Portal cavernoma compressing the bile duct. Apropos of three cases [in French]. *Gastroenterol Clin Biol.* 1993;17(2):134-138.