ELSEVIER

Rescue of a Marginal Liver Graft by Sequential Treatment With Molecular Adsorbent Recirculating System and Transjugular Intrahepatic Portosystemic Shunt: A Case Report

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ABSTRACT

A 53-year-old man with alcoholic liver cirrhosis underwent orthotopic liver transplantation (OLT) using a marginal graft. Persistent cholestasis post-OLT was successfully treated using a molecular adsorbent recirculating system (MARS). Afterwards, the patient developed refractory ascites, which was controlled by a transjugular intrahepatic portosystemic shunt (TIPS). TIPS reduction and eventually occlusion was necessary due to the development of encephalopathy. Despite TIPS occlusion, the ascites did not relapse probably because of the onset of other adaptive mechanisms. MARS and TIPS used sequentially were capable of rescuing a liver graft, thereby avoiding the morbidity and mortality associated with early retransplantation and sparing a liver graft from the donor pool.

THE MOLECULAR ADSORBENT recirculating system (MARS) is a well-known treatment option for patients with acute or acute-on-chronic liver failure and as a bridge to transplantation. The transjugular intrahepatic portosystemic shunt (TIPS) is fairly effective for the management of pretransplant ascites due to cirrhosis. Experiences with MARS and TIPS after orthotopic liver transplantation (OLT) are more limited. Herein we have described a case that illustrates the possibility to treat persistent cholestasis by MARS and refractory ascites by TIPS after OLT. These 2 techniques were used sequentially in the same patient, thereby avoiding the morbidity and mortality associated with early retransplantation and sparing a liver graft from the donor pool.

CASE REPORT

A 53-year-old man with a Model for End-Stage Liver Disease (MELD) score of 28 received a full-size OLT because of alcoholic cirrhosis. The donor liver originated from a 72-year-old man who had died from a subarachnoid hemorrhage. Donor liver tests were unremarkable, except for an elevated gamma-glutamyl transferase (160 U/L). The total warm and cold ischemia times were 50 and 720 minutes, respectively. The post-OLT course was complicated by severe, prolonged liver cholestasis (hyperbilirubinemia of 20–30 mg/dL and alkaline phosphatase of 1000 U/L), but with preserved coagulation and synthetic capacity. In addition, encephalopathy, as well as renal and respiratory failure required temporary dialysis and ventilator assistance. Six weeks post-OLT, the patient was discharged from the intensive care unit and admitted to the ward although severe cholestasis remained present. Magnetic resonance imaging (MRI) showed normal arterial, venous, and biliary tract patency. Liver biopsy showed no rejection but severe ductular bilirubinostasis. At 2 months post-OLT, the patient was treated with 3 sessions of MARS with dramatic improvement in cholestasis and an excellent clinical response. However, a few weeks later, ascites gradually developed and became refractory to diuretics, albumin replacement, and repeated large-volume paracentesis. At 5 months post-OLT, an hepatic and portal venogram in combination with hepatic venous pressure gradient measurements excluded an outflow or an inflow obstruction, but documented the existence of portal hypertension. The right atrial pressure was 2 mm Hg; the inferior caval pressure, 9 mm Hg; the right hepatic vein pressure, 13 mm Hg; and the hepatic wedge pressure, 30 mm Hg. A liver biopsy at 5 months post-OLT showed substantial portoportal fibrosis and phlebosclerosis in association with ductular and parenchymal bilirubinostasis. We then performed a TIPS. During follow-up the onset of encephalopathy necessitated a TIPS reduction at 23 days thereafter, eventually followed by a TIPS occlusion at 68 days

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Table 1. Experience With TIPS After OLT

Year/Author	Indication (No. of Patients)	TIPS Procedures	Efficacy
1999/Amesur et al[15]	Refractory ascites (6)	12	Ascites 67%
	Variceal hemorrhage (6)		Varices 67%
1999/Lerut et al[11]	Refractory ascites (6)	8	Ascites 100%
	Varices (1)		Varices 100%
	Other (1)		
2005/Van Ha et al[17]	Refractory ascites (5)	6	Ascites 80%
	Variceal bleeding (1)		Varices 100%
2005/Abouljoud et al[14]	Refractory ascites (8)	8	Ascites 87.5%
2005/Vasta et al[18]	Refractory ascites (5)	5	Ascites 80%
2008/Kim et al[16]	Refractory ascites (8)	14	Ascites 57%
	Varices (6)		Varices 50%

thereafter due to persistent encephalopathy. One year after OLT, the patient was clinically well: ascites- and encephalopathy-free with mild cholestasis, which has been treated conservatively.

DISCUSSION

The etiology of post-OLT cholestasis is diverse: ischemia reperfusion injury, small-for-size syndrome, biliary stricture, rejection, liver parenchymal and toxic/multifactorial reasons (drug therapy, parenteral nutrition, etc).[1,2] Investigations via ultrasound, MRI, and liver biopsy usually lead to the correct diagnosis.

Successful MARS treatment has been described for post-OLT graft failure[3–8] as well as for small-for-size syndrome after transplantation of partial liver grafts. In the case described herein, the indication for MARS was persistent cholestasis due to a functional (not anatomical) small-for-size syndrome with liver parenchymal dysfunction, probably multifactorial in origin. MARS was preferred over retransplantation, because of the poor general condition of the patient and the preserved synthetic capacity of his liver graft as evidenced by production of coagulation factors and albumin. MARS treatment in this patient dramatically ameliorated the cholestasis.

Refractory ascites after OLT can be due to anatomical vascular causes (venous outflow or inflow obstruction), small-for-size syndrome, or decreased vascular compliance caused by parenchymal disorders of rejection, hepatitis C, or recurrent disease. Imaging, gradient pressure measurements, and liver biopsy usually lead to a correct diagnosis.[9,10] Treatment options that must be taken into consideration if conservative treatment fails are: retransplantation, a surgical portocaval shunt, a TIPS, and a LeVeen Shunt.[9,11,12] In our case, the cause of ascites, namely, substantial portoportal fibrosis and phlebosclerosis, was diagnosed upon biopsy at 5 months post-OLT, probably due to the marginal quality of the liver graft.

The TIPS procedure has been fairly effective to manage pretransplant ascites due to cirrhosis.[13] Experience with TIPS to control refractory ascites after OLT has been limited to reports including small numbers of patients (Table 1).[11,14–18] Our case confirmed that TIPS can be performed safely and that it effectively controls refractory ascites after OLT. In the setting of refractory ascites and advanced organ dysfunction, the patient should be considered for retransplantation. In our case, we elected to not relist the patient for OLT because his synthesis capacity and coagulation parameters were still adequate. After OLT, shunt stenosis or occlusion seldom occurs, which may be explained by the beneficial effects of immunosuppression on stent endothelialization and by the longer-term patency of expanded-polytetrafluoroethylene (e-PTFE)-covered stents in contrast with classical bare stents.[11,13] After the TIPS procedure, careful immunosuppressive monitoring is necessary because the metabolism of immunosuppressive drugs may be modified as a consequence of the elimination or reduction of the hepatic first pass effect.[11,14,19] In our patient, the ascites disappeared after the TIPS, but because of encephalopathy, it was necessary to perform a TIPS reduction and eventually a TIPS occlusion at 23 and 68 days, respectively, after the initial TIPS procedure. Afterward, the patient's condition improved with only minimal ascites and without further need for paracentesis. It is likely that the TIPS was necessary to temporarily control the ascites. Later occlusion of the TIPS did not lead to a relapse of the ascites, probably because of the onset of other adaptive mechanisms.

In conclusion, this case report illustrated the possibility to treat persistent cholestasis post-OLT by MARS and refractory ascites by TIPS; the 2 techniques can be used sequentially, thereby avoiding the morbidity and mortality associated with early retransplantation and sparing a liver graft from the donor pool.

REFERENCES

1. Corbani A, Burroughs AK: Intrahepatic cholestasis after liver transplantation. Clin Liver Dis 12:111, 2008

2. Fusai G, Dhaliwal P, Rolando N, et al: Incidence and risk factors for the development of prolonged and severe intrahepatic cholestasis after liver transplantation. Liver Transpl 12:1626, 2006

3. Bacher A, Zimpfer M: Hot topics in liver intensive care. Transplant Proc 40:1179, 2008

4. Hetz H, Faybik P, Berlakovich G, et al: Molecular adsorbent recirculating system in patients with early allograft dysfunction after liver transplantation: a pilot study. Liver Transpl 12:1357, 2006

5. Kantola T, Koivusalo AM, Hockerstedt K, et al: The effect of molecular adsorbent recirculating system treatment on survival,

native liver recovery, and need for liver transplantation in acute liver failure patients. Transpl Int 21:857, 2008

6. Evenepoel P, Laleman W, Wilmer A, et al: Prometheus versus molecular adsorbents recirculating system: comparison of efficiency in two different liver detoxification devices. Artif Organs 30:276, 2006

7. Laleman W, Wilmer A, Evenepoel P, et al: Review article: non-biological liver support in liver failure. Aliment Pharmacol Ther 23:351, 2006

8. Laleman W, Wilmer A, Evenepoel P, et al: Effect of the molecular adsorbent recirculating system and Prometheus devices on systemic haemodynamics and vasoactive agents in patients with acute-on-chronic alcoholic liver failure. Crit Care 10:108, 2006

9. Taner CB, Nguyen JH: Mesocaval shunt as an alternative treatment for persistent ascites after liver transplantation: case reports. Transplant Proc 40:1534, 2008

10. Nishida S, Gaynor JJ, Nakamura N, et al: Refractory ascites after liver transplantation: an analysis of 1058 liver transplant patients at a single center. Am J Transplant 6:140, 2006

11. Lerut JP, Goffette P, Molle G, et al: Transjugular intrahepatic portosystemic shunt after adult liver transplantation: experience in eight patients. Transplantation 68:379, 1999

12. Mabrut JY, de la Roche E, Adham M, et al: Peritoneovenous diversion using the LeVeen shunt in the treatment of refractory ascites after liver transplantation. Ann Chir 52:612, 1998

13. Maleux G, Nevens F, Wilmer A, et al: Early and long-term clinical and radiological follow-up results of expanded-polytetrafluoroethylene-covered stent-grafts for transjugular intrahepatic portosystemic shunt procedures. Eur Radiol 14:1842, 2004

14. Abouljoud M, Yoshida A, Kim D, et al: Transjugular intrahepatic portosystemic shunts for refractory ascites after liver transplantation. Transplant Proc 37:1248, 2005

15. Amesur NB, Zajko AB, Orons PD, et al: Transjugular intrahepatic portosystemic shunt in patients who have undergone liver transplantation. J Vasc Interv Radiol 10:569, 1999

16. Kim JJ, Dasika NL, Yu E, et al: Transjugular intrahepatic portosystemic shunts in liver transplant recipients. Liver Int 28:240, 2008

17. Van Ha TG, Funaki BS, Ehrhardt J, et al: Transjugular intrahepatic portosystemic shunt placement in liver transplant recipients: experiences with pediatric and adult patients. Am J Roentgenol 184:920, 2005

18. Vasta F, Luca A, Miraglia R, et al: Transjugular intrahepatic portosystemic shunt in adult liver recipient with delayed graft function. Transplant Proc 37:2626, 2005

19. Senzolo M, Patch D, Cholongitas E, et al: Severe venoocclusive disease after liver transplantation treated with transjugular intrahepatic portosystemic shunt. Transplantation 82:132, 2006