IMAGES IN LIVER TRANSPLANTATION

Hepatic Encephalopathy After Liver Transplantation in a Patient with a Normally Functioning Graft: Treatment with Embolization of Portosystemic Collaterals

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Portosystemic encephalopathy is one of the most important complications of liver cirrhosis. The restoration of normal hepatic function and the reduction of portosystemic shunts by means of a liver graft are followed by the resolution of hepatic encephalopathy. We report the case of a patient with a normal functioning graft that developed recurrent encephalopathy after transplantation. The patient was successfully treated by embolization of a large portosystemic shunt between the superior mesenteric vein and both gonadal veins, this causing an inversion of the superior mesenteric vein flow.

CASE REPORT

A 58-year-old male with alcoholic liver cirrhosis was referred to our center for liver transplantation in April 2006. Liver cirrhosis had been diagnosed in October 2005, and he had remained abstinent since then. At diagnosis, he had jaundice, edema, and ascites. Despite 6 months of abstinence, his Model for End-Stage Liver Disease score at referral for transplantation was 20. Three months later, he had his first episode of hepatic encephalopathy, with rapid improvement after diuretic withdrawal and treatment with oral lactulose. He had no more episodes of encephalopathy before transplantation. In the pretransplant assessment, a patent portal vein, with slow hepatopetal flow, was found in a Doppler ultrasound examination. An abdominal computed tomography scan showed a cirrhotic liver without hypervascular lesions; the portal vein diameter was 12 mm, and important collateral circulation was found.

He underwent liver transplantation in August 2006 with a whole cadaveric graft from a 70-year-old woman. Portal vein flow at the beginning of the surgery was 200 mL/minute; it increased to 1000 mL/minute after graft reperfusion. His postoperative course was uneventful, and he was discharged 6 days after transplantation. He developed posttransplant diabetes mellitus, requiring insulin therapy. In the following months, he had moderate tremor, secondary to tacrolimus, that improved when the tacrolimus dose was reduced. Five months after transplantation, he had a moderate increase in serum aminotransferase values (up to 5 times the upper limit of normal range). A liver biopsy showed a moderate portal and lobular inflammatory infiltrate and mild portal fibrosis. Liver function tests spontaneously improved without changes in immunosuppressive therapy (tacrolimus, 4 mg/day, and prednisone, 7.5 mg/day).

Ten months after transplantation, the patient was admitted to the hospital with a 2-day history of disorientation. On physical examination, the patient was disoriented and had inappropriate speech; asterixis was evident, and no sign suggestive of focal neurological

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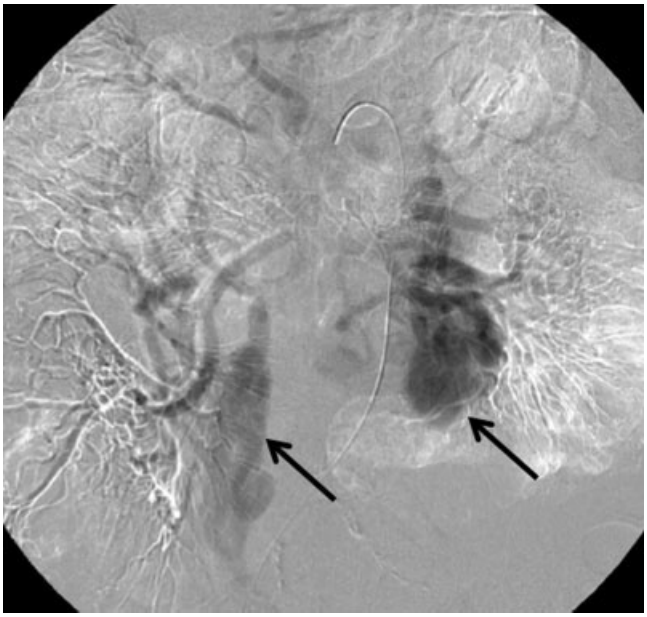

Figure 1. Late venous phase of a superior mesenteric arteriogram. The superior mesenteric vein is not opacified. The flow is diverted toward large collateral veins (arrows).

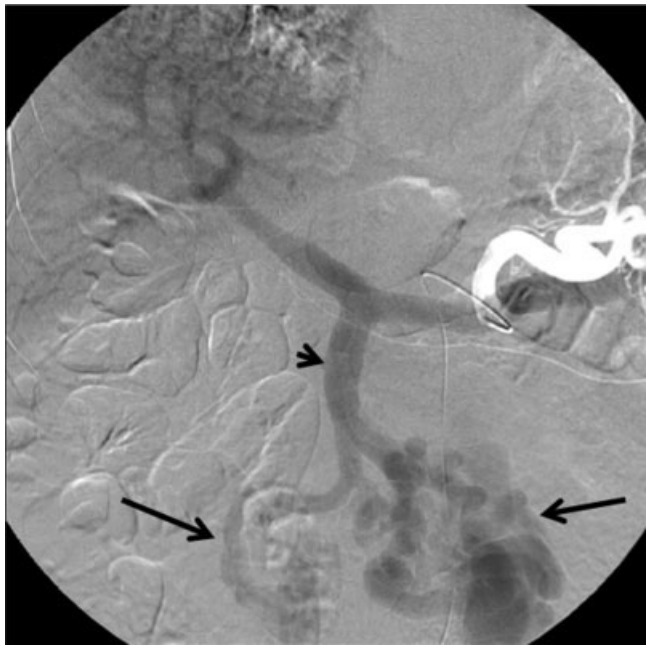

Figure 2. Late venous phase of a splenic arteriogram. There is hepatofugal flow toward the superior mesenteric vein (arrowhead). The flow is diverted toward large collateral veins (arrows).

damage was found. Serum urea, creatinine, and liver function tests were normal. Serum ammonia levels were 197 μg/dL. A brain magnetic resonance scan did not reveal changes when compared with a scan performed before liver transplantation (T1-weighted hyperintensity of basal ganglia was present in both examinations). Doppler ultrasound revealed patency of both the portal vein (with a flow of 15 cm/second) and the hepatic artery. The patient was treated with oral lactulose, and the clinical picture improved in less than 24 hours. An uncomplicated urinary tract infection was also diagnosed, and ceftriaxone treatment was indicated. He was discharged 3 days after admission; oral lactulose was prescribed at discharge.

Two weeks later, the patient was admitted again with disorientation and somnolence. On physical examination, asterixis was again evident. Serum ammonia levels were 202 μg/dL, and liver function tests were normal. An electroencephalogram was consistent with metabolic encephalopathy (lentification and occasional triphasic waves). Nuclear magnetic resonance spectroscopy revealed a marked glutamine increase and a decrease in myo-inositol suggestive of hepatic encephalopathy.[1] A urine culture was negative, and the patient did not have any other apparent cause or precipitant of this episode of encephalopathy.

With the aim of detecting occult portosystemic collaterals, abdominal angiography was performed. The venous phase of the superior mesenteric arteriogram showed that the venous return from jejunal, ileal, and colonic veins was deviated to gross varices draining to inferior vena cava (Fig. 1). The splenic angiography showed that a large proportion of venous flow was stolen from the superior mesenteric vein to the previously mentioned varices (Fig. 2). A retrospective examination

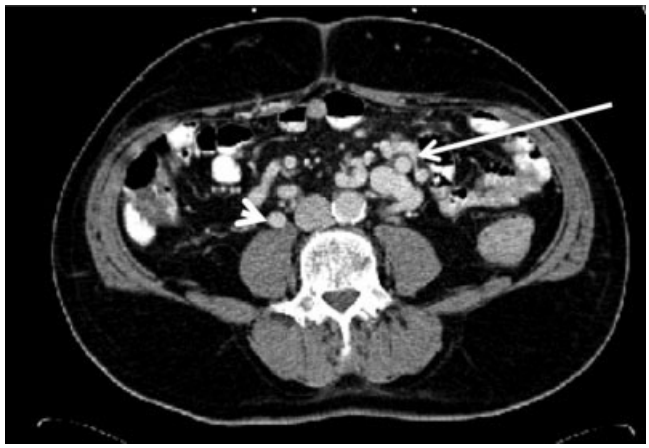

Figure 3. Computed tomography performed before liver transplantation. Collaterals in the territory of the left gonadal vein are clearly depicted (arrow). An enlarged right gonadal vein can also be seen (arrowhead).

of the abdominal computed tomography scan performed before transplantation showed the presence of huge collaterals in the retroperitoneum (Retzius veins)[2] that connected these varices to both gonadal veins and a large left renal vein (Fig. 3).

Embolization of these collateral veins was decided and then performed; bilateral femoral vein access was used. After catheterization of the left femoral vein, a catheter was introduced through the left gonadal vein, which received its flow from a large-caliber tortuous retroperitoneal collateral. In parallel with this catheter, a second catheter was advanced, and the flow was sub-

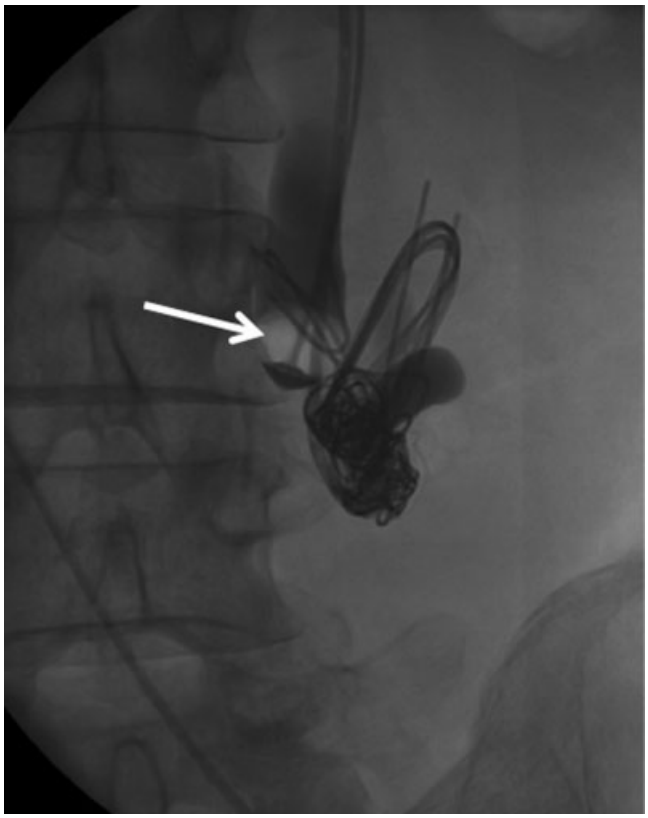

Figure 4. Left gonadal vein phlebography performed after its embolization with coils and segments of guide wire. An occlusion balloon catheter (still inflated) is seen (arrow).

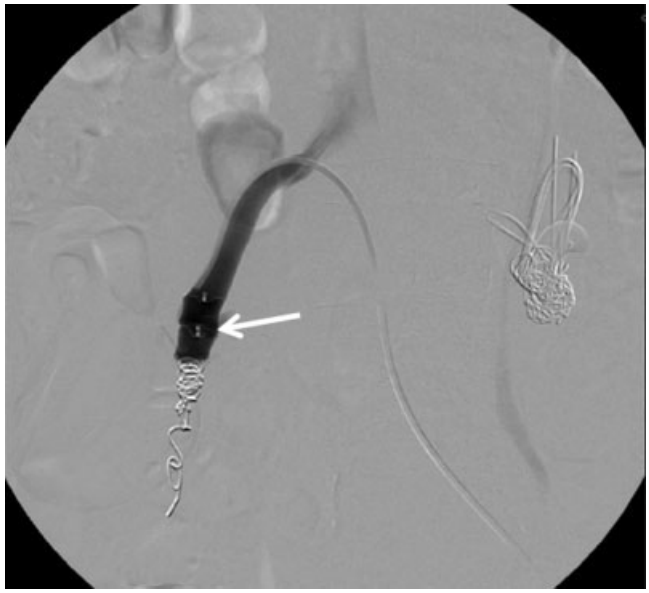

Figure 5. Right gonadal vein phlebography performed after its embolization with coils and Amplatzers (arrow).

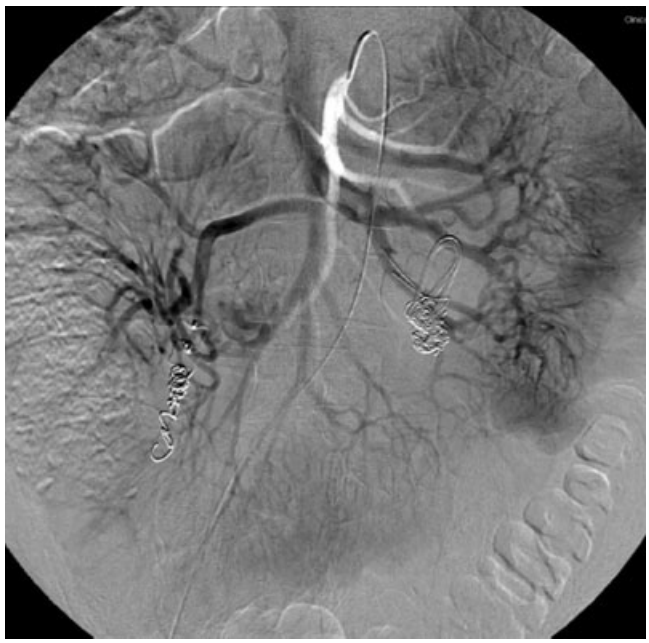

Figure 6. Late venous phase of a superior mesenteric arteriogram. The superior mesenteric vein is now opacified and presents hepatopetal flow.

sequently stopped. Segments of mobile core guide and different caliber coils were used to completely occlude the left shunt (Fig. 4). Afterwards, the right gonadal vein was catheterized and completely occluded with several coils and two 12-mm occluding Amplatzer devices (Fig. 5).

One month later, a new angiogram from the superior mesenteric artery showed that venous mesenteric vein flow was patent and hepatopetal and that there was no flow to varices or collateral veins (Fig. 6). The venous phase of a splenic angiograph showed the absence of reverse flow directed toward the superior mesenteric artery (Fig. 7). Ten months after the embolization, the patient remains free of new episodes of encephalopathy.

DISCUSSION

Hepatic encephalopathy is usually a complication of acute and chronic liver disease, but it has also been reported in patients with major portosystemic shunts without cirrhosis.[3] In patients with liver cirrhosis, the restoration of normal liver function after liver transplantation is usually followed by the resolution of encephalopathy, despite the persistence of portosystemic shunts. In the case reported here, the development of hepatic encephalopathy was unexpected because graft function was normal. High ammonia levels, electroencephalogram changes, improvement with lactulose and magnetic resonance spectroscopy, and the exclusion of other structural or metabolic causes strongly suggest that the clinical picture was consistent with hepatic encephalopathy related to the presence of such shunts. Finally, the absence of new episodes of encephalopathy after their embolization confirmed that suspicion.

In liver transplant recipients, large collateral veins may steal flow from the portal vein because they may remain patent even with a very low portosystemic pres-

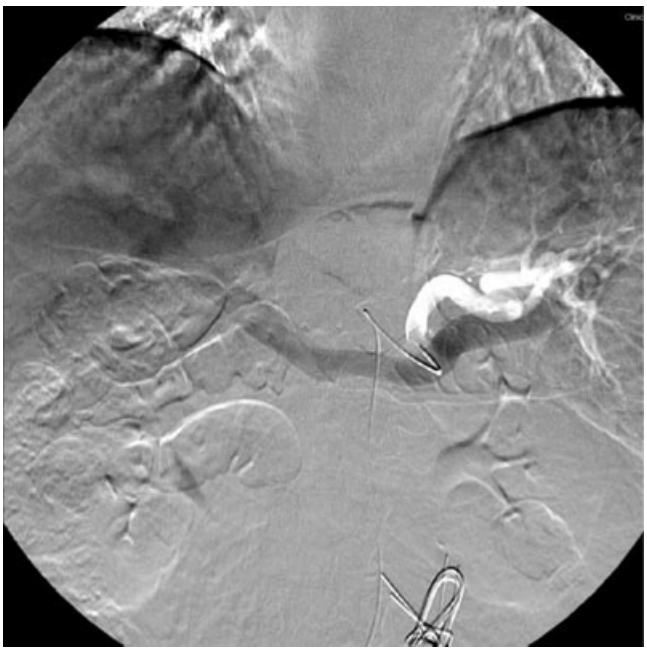

Figure 7. Late venous phase of a splenic arteriogram. There is no hepatofugal flow toward the superior mesenteric vein.

sure gradient. These collateral veins may reduce portal flow through a competitive flow-steal phenomenon, thus precipitating portal vein thrombosis.[4] Large spontaneous portosystemic shunts may also have a detrimental effect on graft function.[5] In patients with cirrhosis and hepatic encephalopathy, it has been previously reported that the occlusion of portosystemic shunts improves this condition.[6] Thus, in liver transplant candidates, the occlusion of portosystemic shunts would ameliorate hepatic encephalopathy and avoid all these aforementioned risks. Unfortunately, the closure of these shunts could lead to esophageal or gastric variceal bleeding.[7] This complication is not expected in liver transplant recipients with a normal grafted liver. Therefore, a potential approach to this problem could be the intraoperative ligation or embolization of these shunts in the immediate postoperative period. In a recent article, Aucejo et al.[8] suggested that triple-phase computed tomography should be used for characterizing these portosystemic shunts. They also recommended measuring intraoperative portal vein flow. If postreperfusion portal vein flow is less than 1 L/minute, shunt ligation should be indicated to avoid the risk of postoperative portal vein thrombosis.[8]

Portosystemic shunts, although detected in sectional studies (computed tomography or magnetic resonance), should be evaluated by conventional angiography, which allows not only their demonstration but also the recognition of their precise routes of connection. When identified, they can be embolized, as demonstrated in this case, with specific methods such as the use of large-caliber occluding devices (Amplatzer or wire segments) or the reduction of their flow with simultaneous occluding techniques (balloon catheters).[9]

In conclusion, large portosystemic shunts may persist after liver transplantation in patients with cirrhosis if they are not ligated during transplant surgery. These shunts may allow the development of hepatic encephalopathy in the absence of significant liver damage. Embolization of these shunts is a potential and effective treatment for this condition.

REFERENCES

1. Zwingmann C. Nuclear magnetic resonance studies of energy metabolism and glutamine shunt in hepatic encephalopathy and hyperammonemia. J Neurosci Res 2007;85: 3429-3442.
2. Ibukuro K, Tsukiyama T, Mori K, Inoue Y. Veins of Retzius at CT during arterial portography: anatomy and clinical importance. Radiology 1998;209:793-800.
3. Ferenci P, Lockwood A, Mullen K, Tarter R, Weissenborn K, Blei AT, and the Members of the Working Party. Hepatic encephalopathy. Definition, nomenclature, diagnosis, and quantification: final report of the working party at the 11th World Congress of Gastroenterology, Vienna, 1998. Hepatology 2002;35:716-721.
4. Bilbao JI, Arias M, Herrero JI, Iglesias A, Martinez-Regueira F, Alejandre PL, et al. Percutaneous transhepatic treatment of a posttransplant portal vein thrombosis and a preexisting splenorenal shunt. Cardiovasc Intervent Radiol 1995; 25:323-326.
5. De Carlis, Del Favero E, Rondinara G, Belli LS, Sansalone CV, Zani B, et al. The role of spontaneous portosystemic shunts in the course of orthotopic liver transplantation. Transpl Int 1992;5:9-14.
6. Zamora CA, Sugimoto K, Tsurusaki M, Yamaguchi M, Izaki K, Taniguchi T, et al. Portosplenic blood flow separation in a patients with portosystemic encephalopathy and a spontaneous splenorenal shunt. J Vasc Interv Radiol 2004;15: 875-879.
7. Shah SR, Pramesh CS, Desmukh HL, Mathur SK. Splenic artery embolization for variceal hemorrhage following blocked distal splenorenal shunt. Hepatogastroenterology 2003;50:1167-1168.
8. Aucejo FN, Hashimoto K, Quintini C, Kelly D, Vogt D, Winans C, et al. Triple-phase computed tomography and intraoperative flow measurements improve the management of portosystemic shunts during liver transplantation. Liver Transpl 2008;14:96-99.
9. Bilbao JI, Arias M, Longo JM, Alejandre PL, Betes MT, Elizalde AM. Embolization of nonvariceal portosystemic collaterals in transjugular intrahepatic portosystemic shunts. Cardiovasc Intervent Radiol 1997;20:149-153.