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CLINICAL OBSERVATIONS IN HEPATOLOGY

Effects of Restoring Portal Flow With Anticoagulation and Partial Splenorenal Shunt Embolization

Nicolas M. Intagliata,[1] Wael E. Saad,[1,2] and Stephen H. Caldwell[1]

Spontaneous portosystemic shunt (PSS) from portal hypertension is associated with portal vein (PV) stasis and chronic hepatic encephalopathy (HE).[1] Embolization of PSS is effective in select cases of refractory HE, but is relatively contraindicated in patients with portal vein thrombosis (PVT) (Table 1).[2-8] This procedure redirects significant blood flow back through the PV and has been reported to improve liver function.[5,9] We present a case of a new PVT in a cirrhosis patient with refractory HE thought secondary to PSS. This was treated sequentially with 6 months anticoagulation to achieve PV patency, followed by partial coil embolization of a large PSS. One year later, imaging revealed a 54% increase in liver volume.

Case Report

A 46-year-old man with cirrhosis secondary to primary sclerosing cholangitis followed for ~8 years had been noted to decline over 1 year prior to presenting with acute onset abdominal pain and worsening HE. Computed tomography (CT) revealed an atrophic liver with a new PVT in a diminutive PV and increased size of previously identified splenorenal shunt (SRS). Endoscopy revealed no esophageal varices and small, low-risk gastric fundal varices. The Model for Endstage Liver Disease (MELD) score prior to warfarin therapy was 12 (Table 2). Anticoagulation was started with warfarin to a goal international normalized ratio (INR) of 2-3. He continued to require hospitalization for HE despite adherence to medical therapy. Follow-up imaging 4 months after starting warfarin revealed interval partial recanalization of the main diminutive PV with a residual large SRS and atrophic liver. The patient continued to struggle with severe HE and therapeutic shunt obliteration was pursued.

A hepatic venogram and catheterization of SRS was performed to evaluate hemodynamic response to shunt occlusion in anticipation of future embolization. This study revealed a patent main diminutive PV with sluggish velocities (peak velocity in the main PV 6.9 cm/s). The large SRS demonstrated an average flow volume of 325 mL/min. Test balloon occlusion of the SRS resulted in an increase in main PV peak velocity to 90.1 cm/s. Next, a partial coil embolization of the SRS was performed resulting in ~30% decreased flow (Fig. 1). Concurrent PV ultrasound demonstrated conversion of hepatofugal blood prior to the procedure (25 cm/s) to hepatopetal flow (20 cm/s).

The patient did very well, with a significant reduction in fatigue and marked improvement in cognition. Biochemical indices improved (Table 2). Ascites and high-risk esophageal varices have not developed to date, while the platelet level has remained unchanged. A follow-up CT scan 9 months after this procedure revealed a 54% increase in liver volume (Fig. (Fig. 2).

Discussion

This case represents successful sequential therapy of a PVT with anticoagulation to reestablish patency,

Table 1. Reported Series Evaluating Therapy for Encephalopathy With Shunt Embolization in Cirrhosis

Study	Study Design	Study Subjects
Uflacker et al. 1987[7]	Case series	5
Fukuda et al. 2001[8]	Case series	11
Zidi et al. 2007[3]	Case series	7
Mukund et al. 2012[6]	Case series	7
Laleman et al. 2013[2]	Multicenter retrospective cohort	37
Singh et al. 2013[4]	Case series	10
An et al. 2014[5]	Single center retrospective case control	17

Abbreviations: CT, computed tomography; HE, hepatic encephalopathy; INR, international normalized ratio; MELD, Model for Endstage Liver Disease; PSS, portosystemic shunt; PV, portal vein; PVT, portal vein thrombosis; SRS, splenorenal shunt.

From the [1]University of Virginia Health System, Division of Gastroenterology and Hepatology, University of Virginia, Charlottesville, VA; [2]University of Michigan Health System, Division of Interventional Radiology, University of Michigan, Ann Arbor, MI.

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Address reprint requests to: Nicolas Intagliata, M.D., PO Box 800708, Charlottesville, VA 22908. E-mail: intagliata@virginia.edu; fax: 434-244-7529.

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Table 2. Clinical Course Over Time

	Pre PVT	PVT	Pre-SRS Embolization	Postembolization Until Present
Timeline		0 → 1mth → 6mths CT #1	→ 21mths CT #2	
Total bilirubin (mg/dL)	1.2	1.4	1.6	0.6
Creatinine (mg/dL)	0.7	0.7	0.8	0.8
INR	1.4	1.5	3.0*	2.9*
Albumin (g/dL)	3.3	2.9	3.0	4.0
MELD	11	12	–	–
CTP score	B(7)	B(7)	–	–
Liver volume (mL)	–	–	873	1346
Encephalopathy?	Yes	Yes	Yes	No

*Warfarin-effect of INR does not allow accurate calculation of MELD and CTP. PVT, portal vein thrombosis; SRS, splenorenal shunt; mth, month; INR, international normalized ratio; MELD, model for endstage liver disease; CTP, Childs-Turcotte-Pugh; CT, computed tomography scan.

followed by partial occlusion of a large PSS. A recent multicenter retrospective study was published from Europe demonstrating that embolization of PSS in patients with refractory HE is safe and effective in select cases.[2] This study found that patients with a MELD of less than 11 responded best to therapy. Notably, patients with PVT were excluded.

Since antiquity, as recounted in the Greek myth of Prometheus, the remarkable capabilities of the liver to regenerate have fascinated mankind.[10] Moreover, surgical advancements in partial hepatic resection and living donor liver transplantation have built upon this understanding.[11] Chronic or acute ischemia from thrombosis can result in hepatocyte apoptosis and atrophy, potentially resulting in worsening liver function and progressive liver disease.[12] Recently, Villa et al.[13] showed that prevention of PVT with prophylactic enoxaparin decreased the incidence of PVT, and reduced decompensation events. Reduction in blood flow by micro and macro thrombosis and/or redirection of flow through a PSS (both present in this case) may deprive the liver of important components (growth factors and cytokines) necessary to compensate for chronic injury. Reversal of this process with anticoagulation and redirection of blood flow through the liver may offer important therapeutic benefit.

Whether this case represents true hepatic regeneration is unclear, as we did not conduct functional

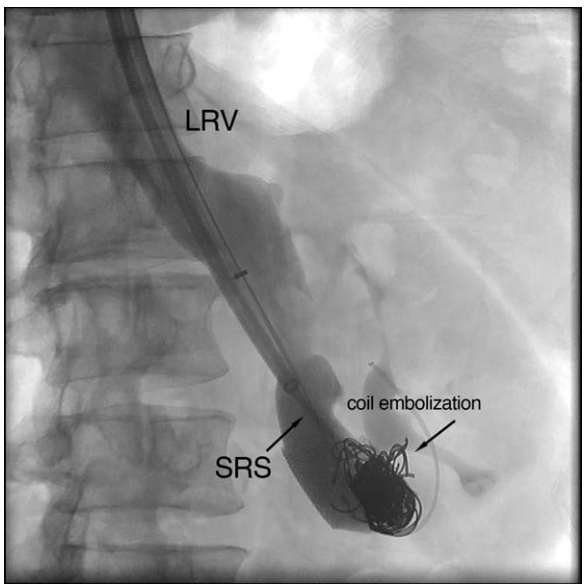

Fig. 1. A retrograde in subtracted venogram of the distal splenorenal shunt (SRS) as it empties into the left renal vein (LRV) after partial coil embolization.

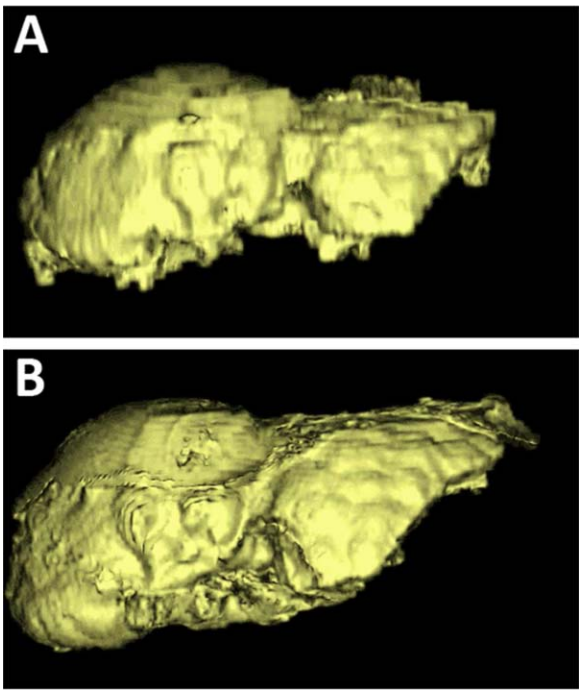

Fig. 2. Liver volume measurement before and after partial shunt embolization. (A) The CT-reconstructed liver volume measured at 873 mL prior to partial shunt embolization. (B) CT-reconstructed liver volume measured at 1,346 mL ~9 months after partial shunt embolization.

testing and instead relied on CT-reconstructed volumetric comparison. We are limited by inherent potential inaccuracies of indirect volume measurement and did not account for volume status of the patient. However, we suspect (as evidenced by clinical and biochemical improvement in the patient) some component of hepatic regeneration occurred with the restoration of portal venous flow to the liver.

Redirection of blood flow likely served to reduce stasis and augment better perfusion by way of the diminutive PV. In this case, we believe the combination of anticoagulation and embolization simultaneously reduced HE *and* improved hepatic function. As this procedure can exacerbate portal hypertension, more studies are needed to delineate which particular patients may benefit the most.

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References

1. Riggio O, Efrati C, Catalano C, Pediconi F, Mecarelli O, Accornero N, et al. High prevalence of spontaneous portal-systemic shunts in persistent hepatic encephalopathy: a case-control study. Hepatology 2005; 42:1158-1165.
2. Laleman W, Simon-Talero M, Maleux G, Perez M, Ameloot K, Soriano G, et al. Embolization of large spontaneous portosystemic shunts for refractory hepatic encephalopathy: a multicenter survey on safety and efficacy. Hepatology 2013;57:2448-2457.
3. Zidi SH, Zanditenas D, Gelu-Simeon M, Rangheard AS, Valla DC, Vilgrain V, et al. Treatment of chronic portosystemic encephalopathy in cirrhotic patients by embolization of portosystemic shunts. Liver Int 2007;27:1389-1393.
4. Singh S, Kamath PS, Andrews JC, Leise MD. Embolization of spontaneous portosystemic shunts for management of severe persistent hepatic encephalopathy. Hepatology 2014;59:735-736.
5. An J, Kim KW, Han S, Lee J, Lim YS. Improvement in survival associated with embolisation of spontaneous portosystemic shunt in patients with recurrent hepatic encephalopathy. Aliment Pharmacol Ther 2014; 39:1418-1426.
6. Mukund A, Rajesh S, Arora A, Patidar Y, Jain D, Sarin SK. Efficacy of balloon-occluded retrograde transvenous obliteration of large spontaneous lienorenal shunt in patients with severe recurrent hepatic encephalopathy with foam sclerotherapy: initial experience. J Vasc Interv Radiol 2012;23:1200-1206.
7. Uflacker R, Silva Ade O, d'Albuquerque LA, Piske RL, Mourao GS. Chronic portosystemic encephalopathy: embolization of portosystemic shunts. Radiology 1987;165:721-725.
8. Fukuda T, Hirota S, Sugimura K. Long-term results of balloon-occluded retrograde transvenous obliteration for the treatment of gastric varices and hepatic encephalopathy. J Vasc Interv Radiol 2001;12:327-336.
9. Akahane T, Iwasaki T, Kobayashi N, Tanabe N, Takahashi N, Gama H, et al. Changes in liver function parameters after occlusion of gastrorenal shunts with balloon-occluded retrograde transvenous obliteration. Am J Gastroenterol 1997;92:1026-1030.
10. Court FG, Wemyss-Holden SA, Dennison AR, Maddern GJ. The mystery of liver regeneration. Br J Surg 2002;89:1089-1095.
11. Kele PG, de Boer M, van der Jagt EJ, Lisman T, Porte RJ. Early hepatic regeneration index and completeness of regeneration at 6 months after partial hepatectomy. Br J Surg 2012;99:1113-1119.
12. Shimamatsu K, Wanless IR. Role of ischemia in causing apoptosis, atrophy, and nodular hyperplasia in human liver. Hepatology 1997;26:343-350.
13. Villa E, Camma C, Marietta M, Luongo M, Critelli R, Colopi S, et al. Enoxaparin prevents portal vein thrombosis and liver decompensation in patients with advanced cirrhosis. Gastroenterology 2012;143:1253-1260.