Single-Session Treatment of Portal Vein Thrombosis Using Combined Pharmacomechanical Thrombolysis

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ABSTRACT

A patient with portal hypertension developed thrombosis of her transjugular intrahepatic portosystemic shunt (TIPS) and the portal vein. The Trellis device (Bacchus Vascular, Santa Clara, CA) was used to achieve rapid lysis of the portal vein thrombus and help restore portal and TIPS patency in a single session.

KEYWORDS: Portal hypertension, portosystemic shunt, portal vein thrombosis

Objectives: Upon completion of this article, the reader should be able to appreciate a potential role of modern devices in treating portal vein thrombosis.

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Portal vein thrombosis (PVT) is a serious condition that can be difficult to manage, often requiring multiple days to clear the thrombus. The wide variety of interventional approaches that have been tried is evidence that no one technique has been found to be optimal. As available tools improve, the ease and rapidity of treating PVT may increase. This case demonstrates use of a newer device to allow complete clearance of PVT in a single session.

CASE REPORT

The patient is a 68-year-old woman with diabetes and a history of coronary artery disease, chronic obstructive pulmonary disease, and cirrhosis secondary to nonalcoholic steatohepatitis. She had a history of esophageal varices diagnosed by endoscopy but no history of bleeding, and her primary problem was refractory ascites.

When she had first developed severe ascites, she underwent a 12 L paracentesis and then required a large-volume paracentesis every 4 to 5 weeks. Between paracenteses she had rapid reaccumulation of her ascites, which led to symptoms of discomfort, shortness of breath, decreased mobility, and decreased appetite. Laboratory results were as follows: bilirubin, 0.4 mg/dL; albumin, 3.3 g/dL; creatinine, 1.3 mg/dL; international normalized ratio, 1.31; and platelet count, 161. Her Model End-Stage Liver Disease (MELD) score was 12.

The transjugular intrahepatic portosystemic shunt (TIPS) was done in standard fashion except that the middle hepatic vein was used as a starting point due to the acute angulation from the inferior vena cava (IVC) into the right hepatic vein. The portal system was accessed through a branch of the left portal vein. The TIPS was created using a 10-mm diameter × 8 cm long VIATORR stent graft (W.L. Gore, Flagstaff, AZ). The

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stent was then dilated with a 10-mm balloon. Portal venography demonstrated good flow through the TIPS with no evidence of filling defects (Fig. 1). The portosystemic gradient was lowered from a pre-TIPS level of 25 mm Hg down to 11 mm Hg. During the TIPS a paracentesis was done with removal of ~4 L of ascites. She did well and was discharged to home 2 days later. Although she felt fine with no light-headedness or other symptoms, review of the nursing records revealed that she was occasionally hypotensive with a blood pressure of ~80/40. She was sent home on 100 mg of spironolactone and 60 mg of furosemide per day.

One month after her initial TIPS, the patient was admitted to an outside facility because of severe fatigue and massive recurrent ascites. She was found to be hypotensive with her lowest blood pressure documented to be 77/61 mm Hg. Her oral intake had been very poor, and it was felt that she was dehydrated. She was admitted to the intensive care unit and briefly required intravenous pressor support during fluid resuscitation. She was also found to have acute renal failure with a serum creatinine of 2.0 mg/dL. Diagnostic paracentesis was performed and was negative for spontaneous bacterial peritonitis.

The patient was transferred to our institution for further management. Physical examination revealed massive ascites. She had mild diffuse abdominal tenderness on palpation but normal bowel sounds, no perito-

neal signs, and rectal exam was guaiac negative. Sonography demonstrated significant ascites plus thrombosis of the shunt, the right portal vein, and main portal vein (Fig. 2). Her admission laboratories were not significantly different from the time of discharge with just a slight increase in her total bilirubin to 1.0 mg/dL.

She was brought to the fluoroscopy suite, and a temporary peritoneal catheter was placed to drain ascites. From a right internal jugular approach a marking pigtail catheter was advanced across the TIPS into the portal vein. Portal venography (Fig. 3) confirmed thrombosis of the TIPS and portal vein. A 30-cm 9F vascular sheath was advanced into the upper end of the thrombosed TIPS. Through the sheath a Trellis infusion catheter (Bacchus Vascular, Santa Clara, CA) with a 15-cm infusion length was positioned so that one occlusion balloon was in the patent segment of splenic vein beyond the thrombus and the other occlusion balloon was in the upper end of the TIPS (Fig. 4). Thus the infusion segment spanned the occluded portal vein and most of the TIPS. Between the occluding balloons, 8 mg of tissue plasminogen activator (tPA) was injected. The Trellis motor drive was turned on to oscillate the sinusoidal wire and disperse the tPA throughout the thrombus. After 10 minutes the wire oscillation was stopped, and liquefied thrombus was then aspirated.

Repeat portography revealed a small amount of residual clot in the splenic vein and some persistent occlusion at the cephalad end of the TIPS. It was also noted during catheter manipulations that there was moderate resistance through the caudal end of the VIATORR. It became apparent that there was some kinking of the existing VIATORR where it turned from

Figure 1 Portal venogram after transjugular intrahepatic portosystemic shunt creation showing a widely patent portal vein and shunt.

Figure 2 Ultrasound demonstrating no flow in the transjugular intrahepatic portosystemic shunt. Although some flow is seen in a portal vein branch, other images showed nearly occlusive portal vein thrombosis.

Figure 3 Splenic venogram shows thrombus throughout the portal vein and occlusion of the transjugular intrahepatic portosystemic shunt.

the left portal vein toward the main portal vein. It was decided to deploy another stent across the portal end of the TIPS to provide better support against kinking. Because residual mural thrombus was likely, a stent graft was used to prevent thrombus from penetrating through stent interstices. A 10 mm × 80 mm Fluency stent graft was deployed starting slightly further into the main portal vein and overlapping the existing VIATORR. This was dilated to 10 mm.

Flow through the shunt was still suboptimal as assessed during fluoroscopic test injections of contrast. Contrast injection through the vascular sheath positioned within the TIPS demonstrated persistent stenosis at the hepatic vein caval junction (Fig. 5). A second 10 mm × 60 mm Fluency covered stent was used to span across this stenosis and extend the shunt right to the IVC. An Arrow-Trerotola percutaneous thrombectomy device (Arrow International; Reading, PA) device was then inserted to macerate the residual clot in the splenic vein. Following this there was brisk antegrade flow through the shunt (Fig. 6), and no significant residual thrombus was seen in the portal vein. During the procedure, 8 L of clear yellow fluid was also aspirated from the patient's abdomen. No intraoperative complications were encountered.

Postprocedure she had a difficult course. For the first 24 hours postreoperation she felt well, but the next evening she became hypotensive and dyspneic. Chest radiograph showed diffuse patchy infiltrates in both lungs, and the patient was initially thought to be fluid overloaded. Her respiratory failure progressed and required

Figure 4 Spot film showing the Trellis catheter in position. The two occlusion balloons are used to isolate the segment where the thrombolytic agent was infused.

Figure 5 Venogram done after lysis shows a residual stenosis (arrow) at the hepatic vein caval junction.

Figure 6 Venogram poststenting of the hepatocaval stenosis shows a widely patent shunt. There was no residual thrombus in the main portal vein. The defect along the inferior aspect is inflow of unopacified blood from mesenteric branches.

intubation and mechanical ventilation. Bronchoscopy revealed findings of diffuse alveolar hemorrhage. Given the lack of other causes, the hemorrhage was felt to have occurred as a complication of the thrombolysis even though her respiratory distress did not develop until 24 hours after the TIPS lysis. Over the ensuing weeks she also had episodes of bacteremia requiring antibiotics, hypotension requiring pressor support, and acute renal failure that resolved without needing dialysis. With supportive care she gradually improved and was extubated 13 days after the thrombolysis procedure. A Doppler ultrasound done 2 weeks after the thrombolysis showed a patent TIPS and portal venous system (Fig. 7). Given her overall poor state of health and because she was not a liver transplantation candidate, the family decided not to pursue further aggressive medical therapy. Thus when she was discharged a few days later she went to a hospice setting and did not return for further follow-up.

DISCUSSION

PVT can be caused by a wide variety of conditions. It occurs in 0.6 to 16% of cirrhotic patients but can result from other local or systemic factors such as pancreatitis, tumor invasion, postoperative changes, or a hypercoagulable state.¹ The natural history of PVT is still somewhat unclear, but with acute PVT, reported mortality varies

Figure 7 Ultrasound done 2 weeks postlysis shows a widely patent portal vein. Good flow through the shunt was also documented.

from 0 to 76% with bowel infarction and variceal bleeding being some of the major causes of death.¹ PVT is an uncommon occurrence after TIPS; however, when it occurs, it can magnify the recurrent symptoms caused by shunt occlusion. It also significantly increases the difficulty of shunt revision, which otherwise would normally be an outpatient procedure.

Numerous interventional techniques for restoring portal vein patency have been reported, including pharmacological lysis, mechanical thrombectomy, and combination strategies. Thrombolytic drugs have been introduced by transmesenteric arterial infusion²⁻⁴ and by direct access into the portal vein via both percutaneous transhepatic and transjugular intrahepatic approaches.⁴⁻⁸

Transarterial infusion has the advantage that the superior mesenteric artery (SMA) can be catheterized more easily than trying to gain direct portal access, and it eliminates the risk of a puncture through the liver capsule. Theoretically, the drug may distribute to the entire portal system when injected into the SMA. However, as with any nonselective infusion technique, if the drug is not infused directly into the thrombus, it may bypass the thrombus as it passes into collaterals. This may explain the lower efficacy of SMA infusion compared with direct portal infusion. One study showed either partial or complete lysis in 93% of patients who underwent direct portal infusion versus response in only 50% of patients when the infusion was via the SMA. SMA infusions also take a long time to lyse the portal thrombus, with infusion times ranging from 16 hours up to 11 days.^{2,3}

As mentioned, direct portal infusions can be done via a transhepatic or transjugular approach. Transhepatic access is technically easier to achieve, and the shorter tract leads to better control of catheters. The main

disadvantage is the transcapsular puncture, which adds the risk of intra-abdominal hemorrhage. Tract embolization at completion can decrease the risk of bleeding. The transhepatic access also assumes that once portal vein patency has been restored, the outflow through the liver will be adequate to prevent stasis and rethrombosis. This may be a poor assumption if there is high resistance to portal flow due to severe cirrhosis or residual small-branch portal thrombosis.

The transjugular approach avoids the puncture through the liver capsule, provided the access needle is not advanced too caudally. It has also been recommended that creation of a TIPS can be useful to improve venous outflow, which will help maintain portal blood flow.⁹ Transjugular approach for portal lysis was clearly dictated in this case by the pre-existing TIPS. Infusion catheters can also be introduced surgically through a mesenteric vein. Because this is more invasive, the main indication for this technique would be in combination with surgical resection of infarcted bowel.¹⁰

Despite direct infusion into the portal vein, mean infusion times until completion still range around 23 to 43 hours.^{4,5} Pulse spray technique may decrease the lysis time but still may take more than a day to achieve complete lysis.⁶ To further speed lysis, mechanical thrombectomy devices can be used to macerate or remove clot. The ability to introduce mechanical devices is another advantage of direct portal access over arterial infusion.

One of the major concerns about using thrombolysis for PVT is the risk of triggering hemorrhage from varices or partially ischemic bowel. Thus mechanical thrombectomy devices are also appealing because they may allow avoidance of lytic drugs or at least reduce doses. Multiple mechanical devices have been used including the Oasis (Boston Scientific, Natick, MA), the AngioJet (Possis Medical, Minneapolis, MN), the Amplatz thrombectomy device (Boston Scientific, Natick, MA), an impeller catheter, the Trerotola PTD, balloon embolectomy, basket embolectomy, and catheter aspiration.^{5,7,11–14} There has been no comparison of different mechanical devices and mostly just case reports exist so far, thus there is no way to know which device performs best.

The Trellis is a hybrid device that uses infusion of a thrombolytic drug (which is trapped between two occlusion balloons at either end of the infusion segment) plus a motor-driven oscillating wire to disperse the lytic drug mechanically throughout the thrombus. It has been used successfully in both peripheral arterial as well as iliofemoral and axillosubclavian venous applications.^{15–19} This appears to be the first report of application of the Trellis device to treat PVT.

In this case, the device worked well at clearing the portal thrombus in a rapid fashion, allowing the entire procedure to be completed in one session instead of

requiring an overnight or multiday lytic infusion. Although the patient did have a hemorrhagic complication, the fact that it occurred 24 hours after the lysis procedure was completed does raise the question if the hemorrhage was truly caused by the thrombolysis. Complications have been reported to occur in 9 to 60% of portal thrombolysis patients and include bleeding requiring transfusion, intraperitoneal bleeding, hemothorax, nosebleeds, hematuria, dyspnea, and type III heart block.^{4,5,14,20} The dose of thrombolytic drug used in our case was in line with reported cases of Trellis-augmented thrombolysis in peripheral vessels,^{5,6,15} however, the optimal thrombolytic dose still needs to be determined.

There are only a few small series with no more than 20 patients in any one series. The overall clinical success rate for PVT lysis cases is 70 to 91%;^{4,5,8} however, not all reports of PVT lysis have been positive. Bilbao et al²¹ described two cases in which they were unable to restore and maintain portal patency despite aggressive therapy with multiple techniques. They postulated that early rethrombosis could be caused by underlying pyelophlebitis, hematological disorder, damaged portal endothelium, a structural abnormality like a portal vein aneurysm, absence of outflow, or thrombosis extending into venules preventing adequate inflow. The first three causes relate to factors that might stimulate clot formation even in the presence of reasonable blood flow. The later three causes are factors that would slow portal blood flow and predispose to rethrombosis because of stasis.

CONCLUSION

Management of PVT requires knowledge of many different techniques. Although we are far from defining what the optimal technique is for treating PVT, this case at least illustrates that newer devices may significantly speed up the thrombolysis process.

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