Acute Thrombosis of Left Portal Vein during Right Portal Vein Embolization Extended to Segment 4

Colette M. Shaw, M.D.,¹ and David C. Madoff, M.D.¹

ABSTRACT

Portal vein thrombosis (PVT) is an uncommon, but potentially devastating complication of portal vein embolization (PVE). Its occurrence relates to both local and systemic risk factors. In the setting of PVE, precipitating factors include injury to the vessel wall and reduced portal flow. Contributory factors include portal hypertension, hypercoagulopathy, inflammatory processes, malignancy, pregnancy, oral contraceptive use, and asplenia. The goal of therapy is to prevent thrombus progression and lyse existing clot. Hepatectomy is impossible if adequate recanalization has not occurred and/or overt portal hypertension develops. The mechanisms for thrombus development, its diagnosis, management, and prognosis are discussed.

KEYWORDS: Portal vein embolization, liver resection, liver hypertrophy, thrombosis

CASE REPORT

A 64-year-old woman underwent Whipple pancreaticoduodenectomy, en bloc resection of the inferior vena cava with primary reconstruction, and a hepatic wedge resection from the left lateral segments for the treatment of a metastatic islet cell tumor arising in the pancreatic head. Follow-up computed tomography (CT) of the abdomen performed 2 years after surgical resection revealed multiple right hepatic metastases (Fig. 1). Given the close proximity of the largest lesion to the middle hepatic vein, the surgical plan was to perform an extended right hepatectomy. CT volumetric analysis revealed an insufficient future liver remnant (FLR) volume of 15% of the total liver volume. The patient was referred to interventional radiology for right portal vein embolization (PVE) extended to segment 4 in an

attempt to hypertrophy the left lateral liver prior to surgery.

The procedure was initially performed with conscious sedation administered by a dedicated nurse under medical supervision. There was continuous monitoring of oxygen saturation and heart rate, and intermittent monitoring of blood pressure during the procedure. Medications given were intravenous midazolam and fentanyl. The right portal vein anatomy was assessed with ultrasound in advance. Using sonographic guidance, access to a right anterior portal vein was achieved using a 22-gauge (22G) Chiba needle (Cook, Inc, Bloomington, IN) via an intercostal approach. Venography confirmed intraluminal position and access was secured with a 6F sheath. Portal venography was performed from the portal vein trunk using a 5-French (5F)

¹Division of Diagnostic Imaging, Interventional Radiology Section, The University of Texas M. D. Anderson Cancer Center, Houston, Texas.

Address for correspondence and reprint requests: David C. Madoff, M.D., Division of Interventional Radiology, Department of Radiology, New York-Presbyterian Hospital/Weill Cornell Medical Center, 525 East 68th Street, New York, NY 10065 (e-mail: dcm9006@med.cornell.edu).

Complications in Interventional Oncology; Guest Editor, Robert J. Lewandowski, M.D.

Semin Intervent Radiol 2011;28:156–161. Copyright © 2011 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662.

DOI: <http://dx.doi.org/10.1055/s-0031-1280655>.

ISSN 0739-9529.

Figure 1 Computed tomography of the abdomen—portal venous phase. Two enhancing mass lesions are identified in the right lobe. The largest measures 6 cm in diameter and abuts the middle hepatic vein (arrow). The pretreatment future liver remnant volume measured 15.1% of the total liver volume.

Omniflush[®] catheter (Angiodynamics, Inc., Queensbury, NY) (Fig. 2A). This demonstrated hepatopetal flow with no evidence of portal hypertension. A selective left portal venogram was performed with a 5F Kumpe catheter (Cook) (Fig. 2B). Using a 3F microcatheter system, three segment 4 veins were selected and 100–300 μ m Contour SE polyvinyl alcohol (PVA; Boston Scientific, Natick, MA) particles were infused until near stasis was achieved. Embolization was completed with placement of microcoils in the proximal aspect of the portal veins. Attempts to catheterize the remaining segment 4 branches were halted due to patient retching and vomiting. At this time, the patient was intubated and sedation was administered by an anesthesiologist. The 5F Kumpe catheter (Cook) was exchanged out over a 035" Bentson wire (Cook) for a 5F SOS II catheter (Angiodynamics). Attention was then turned to the

right portal vein branches. These vessels were selected and embolization performed using 100–300 μ m and 300–500 μ m Contour SE PVA (Boston Scientific) particles followed by macrocoils. A follow-up portogram was performed from the portal vein trunk using the 5F Omni Flush catheter (Angiodynamics). Heterogeneous parenchymal enhancement in the left lateral segment raised the possibility of nontarget embolization (NTE) and/or acute left portal vein thrombosis (PVT) (Fig. 3A). A selective left portal venogram showed filling defects in the left portal vein and multiple branch vessels consistent with acute thrombosis (Fig. 3B). A 6 cm infusion wire was then advanced through the 5F Kumpe catheter and placed across the left portal vein (Fig. 3C). The side holes of the infusion wire that were within the right portal vein were covered over by the Kumpe catheter so that all of the thrombolytic agent (tissue

Figure 2 (A) Portal venogram anteroposterior (AP) projection performed from the portal vein trunk. Normal portal venogram with hepatopetal flow and no evidence of portal hypertension. (B) Selective left portal venogram AP projection. Normal parenchymal perfusion of the left lobe of liver including segment 4.

Figure 3 (A) Nonselective portal venogram anteroposterior (AP) projection. Inhomogeneous parenchymal perfusion of the left lateral segments. (B) Left portal venogram AP projection. Filling defects consistent with acute thrombus in the branches of the left portal vein (arrowhead). (C) Fluoroscopic image AP projection: Infusion wire in the left portal vein.

plasminogen activator was infused at 0.5 mg/h overnight) would be infused only into the left portal vein for maximum effect. The patient was then monitored in the intensive care unit with fibrinogen levels acquired every 4 hours. The following morning the patient returned to the interventional radiology suite. Follow-up venography through the indwelling Kumpe catheter showed resolution of the thrombus with normal parenchymal perfusion of segments 2 and 3 (Fig. 4). The patient was commenced on a prophylactic dose of subcutaneous heparin and discharged within 24 hours of the procedure.

A restaging CT of the abdomen and pelvis with liver volumetry was performed 4 weeks after PVE. The left lateral segment demonstrated normal contrast enhancement and measured 25% of the total liver volume

(Fig. 5). The metastases in the right lobe had progressed in the intervening period. The patient underwent an extended right hepatectomy shortly thereafter. The postoperative course was complicated by an infected biloma necessitating percutaneous drainage. The patient was discharged home on postoperative day 15. The patient survived for over 2 years after liver resection before succumbing to her disease.

DISCUSSION

PVE is a safe and effective procedure with an overall complication rate reported between 9% and 12%.¹ Acute PVT is an uncommon, but potentially major complication of PVE. Using Virchow's triad, the factors contributing to thrombosis include endothelial injury or

Figure 4 Left portal venogram anteroposterior projection. Postthrombolysis, there is normal parenchymal perfusion in the left lateral segments with no evidence of residual thrombus.

dysfunction, hypercoagulability, and hemodynamic changes.²

Etiology

If the thrombotic event occurs during the embolization procedure, as in the case presented here, the precipitating factor usually relates to technique (i.e., access approach, embolic agent, etc.). Although right PVE performed via a contralateral transhepatic approach is considered straight forward, the risk of injury to the future liver remnant including its portal vein is increased. In this setting, thrombosis of the left portal veins can be due to formation or propagation of thrombus along the catheter shaft or from venous occlusion by the catheter itself. In a review of 188 patients who underwent PVE from a contralateral approach, Di Stefano et al reported one case of complete PVT.³ This was attributed to catheter manipulation in a stenotic left portal vein

Figure 5 Computed tomography (CT) of the abdomen—portal venous phase. Posttreatment liver CT shows coils within segment 4 and the right liver. Posttreatment future liver remnant volume is 25% of the total liver volume, an increase of 10%.

branch feeding segments 2 and 3. The right anterior portal vein arose from the left portal vein resulting in complete thrombosis. Hepatectomy was abandoned and the patient subsequently underwent transplantation. Kodama et al reported a single episode of PVT following 45 technically successful PVEs.⁴ The thrombus was identified in the lateral portal vein in segment 2 following a contralateral transhepatic approach. No further intervention was required and the patient underwent right hepatectomy 17 days later. For this reason, and the fact that complications are more common in the punctured lobe, an ipsilateral approach is now recommended by many investigators.

Nontarget embolization can predispose to thrombosis if the flow is sufficiently slowed. In most instances, the event goes unnoticed. However, nontarget embolization is only apparent during the procedure or on follow-up imaging if radiopaque embolic agents such as *n*-butyl cyanoacrylate (NBCA) or metallic coils are used. Di Stefano et al reported 2 major complications related to nontarget embolization that occurred during embolization of the right portal vein branches using NBCA via contralateral approach. Both events occurred at the end of the procedure when flow in the right portal vein branches were near stasis and were attributed to dislodgement of NBCA by the catheter and migration into the vein draining the future liver remnant. Recanalization was achieved with immediate portal vein angioplasty. One patient underwent uneventful hepatectomy; the other required a portoportal graft intraoperatively due to recurrent thrombosis. Although concern for nontarget embolization has also been raised when advancing catheters through previously embolized portal veins with an ipsilateral transhepatic approach, this has not occurred in the nearly 400 cases of PVE procedures performed at our institution.

Meticulous catheter technique is required if nontarget embolization is to be reduced. As mentioned above, catheter manipulation through or near recently embolized vessels should be minimized. For this reason, embolization of segment 4 branches, when required, should be performed first. The use of a guide catheter or sheath, and thorough flushing of the delivery catheter in the target vessel may help reduce shedding of embolic material from the catheter as it is withdrawn or reintroduced. Inexperience with NBCA may also increase the risk of nontarget embolization when the vessels are near stasis. A switch to particulate embolic material at this stage may help reduce reflux.

In the case presented, the 5F catheter was within the left portal vein while the microcatheter was being advanced into the remaining segment 4 branches. During this time, the patient began retching and vomiting. These events most likely led to endothelial injury of the left portal vein and subsequent thrombus formation. Because of the urgent need for anesthesia support, the

complication was not immediately apparent (i.e., left portography was not performed before right PVE was initiated). The thrombotic event was only identified at the end of the procedure from the final portal venogram. Initially, the etiology of the thrombosis was unclear. However, given that the left portal vein and branches to the FLR were successfully recanalized with only chemical thrombolysis, it is very unlikely that the thrombosis was the result of nontarget embolization of the embolic material. Rather, the patient's retching and vomiting most likely led to endothelial injury of the left portal vein and subsequent thrombus formation.

If thrombosis is identified in the days or weeks after PVE, other risk factors for PVT should be considered. Although PVE-induced endothelial injury and altered hemodynamics are the most likely initiating events for thrombosis, the relative contribution from other systemic or local factors may be significant. PVE complications, including PVT, occur with greater frequency in patients with chronic liver disease. The mechanism most likely relates to slow flow. Because major hepatic resection can be performed safely in patients with cirrhosis who have preserved liver function (Child-Pugh Class A) and normal ICGR₁₅ (<10%), clinically occult portal hypertension may go unnoticed if portal pressures are not acquired. At the University of Texas MD Anderson Cancer Center, the mean portal pressure is measured from the portal vein trunk prior to PVE in patients with chronic liver disease. A pressure greater than 20 mmHg, is a contraindication to embolization. The relationship between pre-PVE portal pressure and PVE outcomes, and between the portal pressure gradient and PVE outcomes is unclear, however, an absolute portal pressure of 20 mmHg correlates with a portosystemic gradient of ~13–18 mmHg, namely significant portal hypertension. A dilemma arises when portosystemic collaterals are identified. If present on the initial portal venogram, their presence, though indicative of portal hypertension, may reduce the portal pressure sufficiently to enable PVE to proceed. Given that PVE is usually associated with a 2–3 mmHg rise in portal pressure, some shunts may only become apparent on the final study. In any case, their presence serves to divert flow from the intrahepatic portal venous system increasing the risk for PVT. At our institution, efforts are made to occlude these vessels via coil embolization prior to or following PVE.

A case report described massive portal and mesenteric venous thrombosis 14 days after an uneventful PVE in a patient with gallbladder carcinoma; Doppler ultrasound performed 3 days after PVE showed the portal vein of the future liver remnant to be widely patent.⁵ The patient was asymptomatic, and thus was treated with anticoagulation and systemic thrombolysis. A thrombophilia screen revealed deficient levels of protein S. Patients with protein S deficiency have a

50% chance of developing recurrent thrombosis before age 45 with such events often associated with other precipitating factors.⁶

Diagnosis and Management

In the setting of PVE, the diagnosis is made during the embolization procedure or by follow-up imaging. If significant thrombosis occurs, the patient may present with pain, fever, or symptoms and signs of portal hypertension. Treatment is directed at alleviating the patient's symptoms, restoring portal flow in the future liver remnant, and preventing the development of portal hypertension. For those who have undergone PVE, recanalization is critical if they are to have a long-term chance of cure.

The standard treatment for PVT is systemic thrombolysis with anticoagulants, and local thrombolysis via the superior mesenteric artery (SMA), a transjugular or a transhepatic catheter-directed approach.⁷ Transarterial thrombolysis via the SMA involves placement of a catheter into the SMA via the femoral artery, but requires large doses of thrombolytics and may be ineffective in patients with large portosystemic shunts.⁸ The transjugular approach involves creation of a portosystemic shunt to divert portal flow.^{9,10} With the transhepatic percutaneous approach, the operator can directly access the thrombus, infuse high concentrations of thrombolytic locally, and reduce the risks of systemic fibrinolysis.^{11,12} Intraabdominal bleeding may be averted by embolizing the tract with coils or gelatin sponge after removal of the catheter. To prevent recurrent PVT, the flow through coexisting portosystemic shunts needs to be occluded.

In the case described, the patient developed acute left PVT following deliberate occlusion of >80% of the intrahepatic portal system.¹³ Treatment options included expectant management, systemic anticoagulation, catheter-directed bolus or overnight infusion of a thrombolytic agent into the left portal vein, or a combination of mechanical and pharmacological thrombolysis. Urgent recanalization was required if the patient was to remain a candidate for hepatectomy and if significant PVT-related morbidity was to be avoided. More importantly, without emergent thrombolysis, acute thrombosis of the entire portal system may have occurred which could have resulted in acute liver failure and possible death. Given the small size of some of the thrombosed vessels, mechanical thrombectomy was unlikely to have been effective and may have resulted in further injury to the portal veins supplying the FLR. Therefore, an overnight catheter-directed infusion of tissue plasminogen activator (tPA) into the left portal vein was chosen. The technique used in this case (i.e., covering the infusion wire with the 5F Kumpe catheter within the right portal vein) was used to avoid bleeding at

the puncture site and to maximize the tPA administered to the left portal vein branches. Fortunately, this technique resulted in successful lysis of the entire clot burden. To maintain patency of the segment 2 and 3 portal veins, prophylactic anticoagulation was commenced.

Prognosis

Thrombosis in a minor vessel can be an incidental and often inconsequential finding. Following significant PVT, if attempts to recanalize the portal vein are unsuccessful, the patient at the very least is no longer a suitable candidate for hepatectomy. As described in the case above, the consequences of acute PVT (i.e., thrombosis of the entire portal system) during PVE could be devastating and emergent attempts at thrombolysis are required. In select circumstances, transplant may be an option. Massive PVT can lead to bowel ischemia and venous infarction. In the long-term, portal hypertension may develop leading to ascites, varices, and ultimately liver decompensation.

REFERENCES

1. Makuuchi M, Thai BL, Takayasu K, et al. Preoperative portal embolization to increase safety of major hepatectomy for hilar bile duct carcinoma: a preliminary report. *Surgery* 1990;107(5):521–527
2. Virchow R. Neuer fall von todlicher emboli der lungenartene. *Arch Pathol Anat* 1856;10:225–228
3. Di Stefano DR, de Baere T, Denys A, et al. Preoperative percutaneous portal vein embolization: evaluation of adverse events in 188 patients. *Radiology* 2005;234(2):625–630
4. Kodama Y, Shimizu T, Endo H, Miyamoto N, Miyasaka K. Complications of percutaneous transhepatic portal vein embolization. *J Vasc Interv Radiol* 2002;13(12):1233–1237
5. Ohkubo M, Nagino M, Kamiya J, Arai T, Nishio H, Nimura Y. Portal and mesenteric vein thrombosis after portal vein embolization in a patient with protein S deficiency. *J Hepatobiliary Pancreat Surg* 2004;11(5):338–341
6. Borgel D, Gandrille S, Aiach M. Protein S deficiency. *Thromb Haemost* 1997;78(1):351–356
7. Hidajat N, Stobbe H, Griesshaber V, Schroder RJ, Felix R. Portal vein thrombosis: etiology, diagnostic strategy, therapy and management. *Vasa* 2005;34(2):81–92
8. Henao EA, Bohannon WT, Silva MB Jr. Treatment of portal venous thrombosis with selective superior mesenteric artery infusion of recombinant tissue plasminogen activator. *J Vasc Surg* 2003;38(6):1411–1415
9. Aytekin C, Boyvat F, Kurt A, Yologlu Z, Coskun M. Catheter-directed thrombolysis with transjugular access in portal vein thrombosis secondary to pancreatitis. *Eur J Radiol* 2001;39(2):80–82
10. Brown RS Jr, Lake JR. Transjugular intrahepatic portosystemic shunt as a form of treatment for portal hypertension: indications and contraindications. *Adv Intern Med* 1997;42:485–504
11. Miyazaki Y, Shinomura Y, Kitamura S, et al. Portal vein thrombosis associated with active ulcerative colitis: percutaneous transhepatic recanalization. *Am J Gastroenterol* 1995;90(9):1533–1534
12. Hollingshead M, Burke CT, Mauro MA, Weeks SM, Dixon RG, Jaques PF. Transcatheter thrombolytic therapy for acute mesenteric and portal vein thrombosis. *J Vasc Interv Radiol* 2005;16(5):651–661
13. Madoff DC, Abdalla EK, Gupta S, et al. Transhepatic ipsilateral right portal vein embolization extended to segment IV: improving hypertrophy and resection outcomes with spherical particles and coils. *J Vasc Interv Radiol* 2005;16(2 Pt 1):215–225