

ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

Section Editor: Eugene R. Schiff, MD

Management of Portal Vein Thrombosis

Thomas D. Boyer, MD
Professor of Medicine
Director, Liver Research Institute
University Medical Center
University of Arizona

G&H Can you describe the various manifestations of portal vein thrombosis?

TB Portal vein thrombosis (PVT) is exactly what its name implies: thrombosis of the portal vein and/or its tributaries, which include the splenic vein and the superior and inferior mesenteric veins. The thrombosis can occur within the main portal vein, or it can occur in the branches of the portal vein within the liver itself. It can be an occluding thrombus or nonoccluding, with a clot present but continued blood flow through the vessel. The sequela of a long-standing PVT is cavernous formation of the portal vein, which represents bridging collaterals around the occlusion.

Isolated splenic vein thrombosis can develop in tandem with a patent portal vein. However, it is unusual to have thrombosis of the inferior/superior mesenteric veins without involvement of the portal vein itself. Finally, there is the possibility of mesenteric venous thrombosis, where every vessel in the abdomen is thrombosed.

G&H Do the different manifestations of PVT have distinct etiologies?

TB My approach is to treat all PVTs as the same process but with different causes. In patients with isolated splenic vein thrombosis, primary pancreatic disease or pancreatic malignancy may be the underlying cause. If the patient has thrombosed their entire portal venous system, they most likely have a prothrombotic disorder.

The other important factor that puts these events in context is the establishment of whether the patient has

cirrhosis. The cause of PVT in cirrhotic patients is not the same as that in noncirrhotics and that distinction makes a big difference in how these patients are managed.

G&H What are the symptoms of PVT that differentiate it from portal hypertension?

TB Cirrhotic patients with PVT will most likely have all of the standard manifestations of portal hypertension (ascites, varices, hepatic encephalopathy) because they have cirrhosis. When PVT occurs in a noncirrhotic, they can develop some symptoms of portal hypertension, but it is important to note that these patients, in general, will develop varices but no ascites. It has been shown in animal models that if the portal vein is tied off, the animals develop varices but no ascites because the liver is not involved. When ascites occur in patients with PVT, they may have underlying cirrhosis. In patients with PVT but no liver disease, the main manifestation of portal hypertension is either esophageal or gastric varices, which can potentially bleed. Lastly, noncirrhotic patients with PVT can develop bowel ischemia, whereas this rarely occurs in cirrhotics with PVT.

G&H How do noncirrhotic patients with PVT typically present?

TB These patients usually will present with abdominal pain due to bowel ischemia from congestion. They might initially be seen by a general practitioner, a surgeon, or a gastroenterologist. Because of the abdominal pain, they generally undergo an imaging study and thrombosis of the vessels is detected. Most noncirrhotic patients will ultimately be diagnosed with a prothrombotic disorder like factor 5 leiden mutation, lupus anticoagulant, Protein C/Protein S deficiency, underlying myeloproliferative disorders, or mutations in the thrombin gene.

G&H What are the initial steps to treating these patients?

TB At the time of diagnosis, if the patient has symptoms of bowel ischemia, then they are anticoagulated with heparin. Because the majority of them will ultimately

be diagnosed with a prothrombotic disorder, blood work must be drawn before they are anticoagulated, as anticoagulation therapy interferes with some of the blood tests used to diagnose clotting disorders. Once the patient has stabilized, they can be switched to warfarin sodium (Coumadin, Bristol-Myers Squibb). Those with a prothrombotic disorder will require lifelong anticoagulation therapy.

If no defined disorder is detected, it is more uncertain how to proceed, in terms of long-term anticoagulation. My philosophy is to leave patients on maintenance anticoagulation if I am not sure of the cause of their venous thrombosis. New prothrombotic disorders are described on a regular basis, and patients may be experiencing one that has not yet been detected.

G&H What other factors must be considered in deciding when and how to anticoagulate these patients?

TB Noncirrhotic patients who present with an acute illness require immediate anticoagulation as described above. If a patient presents with bleeding varices and imaging reveals cavernous transformation of their portal vein, denoting long-standing disease, management becomes more complex. The rationale for giving anticoagulant therapy is not as clear in these patients, and the use of anticoagulation in a patient who has bled from varices is not advisable.

Most patients fall between these two extremes. Patients with nonbleeding varices and PVT should be anticoagulated in the hope of recanalization of the portal vein. If the patient is imaged and a partial thrombosis of the portal vein is found, I would anticoagulate to avoid completion of the process and the onset of symptoms. In extremely rare cases, these patients, if left untreated, could develop bowel ischemia and, ultimately, a bowel infarction. If anticoagulant therapy is prescribed in stable, asymptomatic patients, heparin is not necessary. If the PVT is found incidentally, patients can be maintained on warfarin, especially if a prothrombotic disorder is present.

G&H How are symptoms of PVT differentiated from portal hypertension in cirrhotic patients?

TB Symptoms in the cirrhotic patient with and without PVT are similar, and most patients are undiagnosed until they undergo imaging. Cirrhotic patients undergo imaging at relatively regular intervals, mainly to look for cancer or during evaluation for liver transplant, and are frequently found to have PVT (10–20%). It appears

that this high incidence is due largely to the stasis that develops as portal hypertension worsens. The velocity of blood flow in the portal vein lessens, and flow can actually reverse. This stasis leads to clotting and thrombosis just as it would in any other venous system.

G&H What is the approach to treatment in cirrhotic patients?

TB Cirrhotic patients have an endogenous risk for bleeding and should not receive anticoagulant therapy for PVT. There is no evidence that anticoagulants are of any benefit because, in these patients, the condition is most likely long-standing. I look at PVT in cirrhotics as an incidental finding, which could make portal hypertension worse but has no simple therapeutic options. The only therapy would be to remove the clot either during a transjugular intrahepatic portal system shunt or a surgical procedure. Most clinicians will not recommend this unless they cannot manage the variceal bleeding endoscopically and have an available interventional radiologist who is confident that they can enter the portal vein and remove the thrombus.

One other caveat in cirrhotic patients is that if PVT is detected, hepatocellular carcinoma (HCC) must be ruled out as the cause. HCC can grow into the portal vein and cause PVT. Sophisticated sonography is required in at-risk patients in order to visualize the vessels and see possible neovascularization in the thrombus in the portal vein, which indicates a malignancy, as opposed to a bland thrombus.

At the time of transplant, PVT is also a potential issue in cirrhotics because the portal vein cannot be connected to the new liver. If the transplant patient has a patent inferior mesenteric vein, it can be used in place of the portal vein, but if the entire portal venous system is thrombosed, transplant is not an option. Fortunately, in cirrhotic patients, thrombosis of the mesenteric vascular system is very uncommon.

Suggested Reading

Acosta S, Alhadad A, Svensson P, Ekberg O. Epidemiology, risk and prognostic factors in mesenteric venous thrombosis. *Br J Surg*. 2008;95:1245-1251.

Agarwal AK, Raj Kumar K, Agarwal S, Singh S. Significance of splenic vein thrombosis in chronic pancreatitis. *Am J Surg*. 2008;196:149-154.

Ertugrul I, Koklu S, Basar O, et al. Thrombosis of the portal venous system: a prospective study. *J Clin Gastroenterol*. 2008;42:835-838.

Condat B, Valla D. Nonmalignant portal vein thrombosis in adults. *Nat Clin Pract Gastroenterol Hepatol*. 2006;3:505-515.

Condat B, Pessione F, Hillaire S, et al. Current outcome of portal vein thrombosis in adults: risk and benefit of anticoagulant therapy. *Gastroenterology*. 2001;120:490-497.