CLINICAL VIGNETTE

Portal Vein Thrombosis: A Harbinger of an Underlying Hypercoagulable State

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Case Description

A 75-year-old man was found to have new onset thrombocytopenia and elevated liver enzymes on routine lab work ordered by his primary care physician. The liver enzyme abnormalities were in a mixed pattern notable for an alanine transaminase of 42 U/L and an alkaline phosphatase of 169 U/L. His past medical history includes hypertension, dyslipidemia, type 2 diabetes, peripheral arterial disease, and localized bladder carcinoma treated with transurethral resection. On examination the patient was not jaundiced and did not have appreciable ascites or organomegaly.

Follow-up hepatitis testing did not indicate viral infection and abdominal ultrasonography showed lack of flow through the main portal vein and venous collateralization indicating portal vein thrombosis. Mild splenomegaly up to 12.7 centimeters was also noted. CT scan of the abdomen with iodinated contrast confirmed total occlusion of the main portal vein at the confluence of the porta hepatis as well as a lobulated, hypodense lesion in the right posterior lobe with associated intrahepatic biliary ductal dilation and necrotic-appearing lymphadenopathy in the retroperitoneum. Hepatology and hematology-oncology were consulted, and the patient was initiated on apixaban for treatment of the acute portal vein thrombosis.

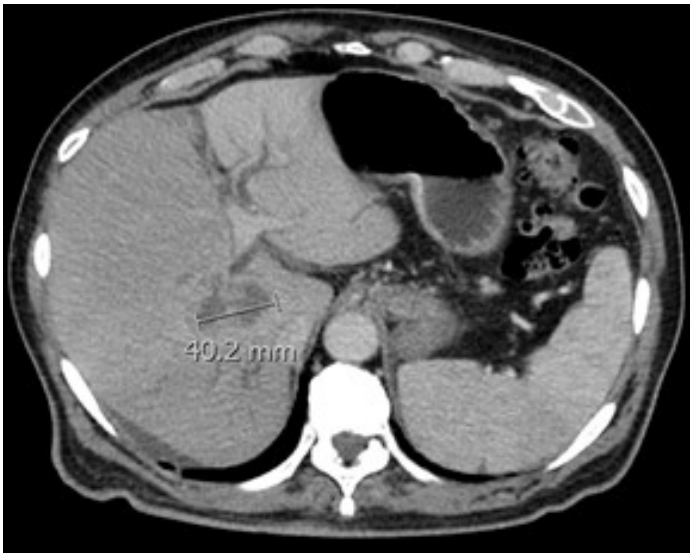

Figure 1 The hypodense, lobulated lesion identified on the initial CT scan which measures up to 4 cm. The intrahepatic biliary duct dilation and portal vein thrombosis were also identified on this scan but not seen on this slice.

Following this evaluation, the patient acknowledged progressive bloating, early satiety, and unintentional weight loss that developed insidiously over the preceding year. Subsequent lab testing found his alkaline phosphatase peaked at 832 U/L. Biopsy of the right hepatic lesion revealed a moderately differentiated adenocarcinoma of pancreaticobiliary origin. The clinical presentation favored a stage IIIb intrahepatic cholangiocarcinoma. Due to the central location of the tumor and extensive lymphadenopathy extending beyond the porta hepatis, the patient was not a surgical candidate and was started on systemic chemotherapy with cisplatin and gemcitabine. The malignancy progressed after two cycles resulting in refractory ascites for which a palliative tunneled peritoneal catheter was placed. He later developed sepsis, severe hemorrhage, and succumbed to multi-organ failure after transitioning to comfort-oriented measures 6 months after the initial abdominal ultrasound.

Discussion

The portal vein arises from the confluence of the splenic and superior mesenteric veins. Portal vein thrombosis (PVT) refers to obstruction of the vein by thrombus most commonly due to underlying portal hypertension and cirrhosis or due to an alternative hypercoagulable state. PVT is relatively common in patients with cirrhosis (about 1 percent of patients with compensated cirrhosis but up to 25 percent of patients awaiting liver transplantation).[1] This case presents a malignancy-related portal vein thrombosis in the absence of cirrhosis or an inherited thrombophilia.

Patients with PVT who do not have cirrhosis or portal hypertension should be evaluated for other predisposing conditions based on family history and patient characteristics. Alternative causes of hypercoagulable states include malignancy (hematologic or GI-related), heritable thrombophilic conditions (Factor V Leiden), autoimmune/inflammatory disorders (inflammatory bowel disease, infection), certain hormonal states (pregnancy, contraception), or surgery/trauma.[2]

The most common abdominal malignancy associated with acute PVT is hepatocellular carcinoma though pancreaticobiliary tumors are also common culprits given proximity to the portal vein increasing risk of direct compression of the vasculature, inducing a local inflammatory milieu.[2,3] In these circumstances, the initial imaging diagnostic of the thrombosis may suggest an

underlying local malignancy as in this case. If cirrhosis or obvious malignancy are absent, a secondary broader hypercoagulable evaluation may be warranted.

Patients with acute PVT can present variably with fevers, abdominal pain, GI bleeding due infarction, or may be asymptomatic. Lab testing generally reveals normal liver function tests although a transient increase in serum transaminases can occur. When bowel ischemia is present, labs may show a leukocytosis, acid-base derangements, or renal injury.[4]

Patients with suspected acute PVT should undergo contrast-enhanced CT imaging for diagnosis and to characterize the extent of thrombosis and collateralization formation. An ultrasound with Doppler is a reasonable first approach in patients for whom there is a lower index of suspicion but should be followed by a CT if the ultrasound suggests PVT. As in this patient, the imaging diagnostic of the PVT also characterized the nature and extent of the malignancy which contributed to the final diagnosis and treatment plan.

When thrombosis is thought to be acute, anticoagulation is recommended for 3 to 6 months and may be extended indefinitely if a persistent or non-reversible risk factor is identified. The length of anticoagulation must be balanced by the patient's individualized bleeding risk. Untreated PVT can lead to portal hypertension resulting in ascites and formation of varices. If the thrombus extends to the mesenteric veins, there is increased risk of intestinal ischemia and infarction which can be catastrophic due risk of hemorrhage and sepsis (commonly due to *Bacteroides fragilis* or *Escherichia coli).*[2] Chronic PVT would be suggested by the lack of acute symptoms or lab abnormalities. The benefits of treatment with anticoagulation are less clear in this scenario and treatment strategies should be individualized. Several case reports have documented the use of catheter-administered lytic therapies although with risks of serious bleeding complications. The efficacy of anticoagulation is high with up to 60 to 90 percent of patients achieving patent portal venous flow within the first few weeks of anticoagulation, with 2% mortality at one year.[5,6] However, the prognosis will vary depending on presence of certain underlying condition predisposing to PVT and is typically guarded with malignancy as in this patient.

This case illustrates how routine but diligent evaluation of new liver enzyme abnormalities with appropriate labs and imaging led to the diagnosis of portal vein thrombosis and the underlying predisposing condition – advanced cholangiocarcinoma. This case also exemplifies the typically insidious nature of cholangiocarcinoma which rarely becomes symptomatic until advanced stages of the disease. By pursuing additional testing rather than assuming the presence of now ubiquitous non-alcoholic fatty liver disease, this patient received an earlier diagnosis and appropriate therapies.

Conclusion

Acute portal vein thrombosis results in obstruction of flow through the hepatic portal venous system and is commonly associated with cirrhosis or other acquired or inherited hypercoagulable states. In addition to searching for an underlying pathology based on a patient's individual characteristics, acute PVT is treated with anticoagulation with the goal of re-canalizing the portal vein and preventing portal hypertension and complications including ascites, hemorrhage, and infection. Maintaining a broad differential and pursuing targeted diagnostics is critical to arriving at the correct diagnosis and treatment strategy in any patient presenting with new liver injury.

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