JAK2 Basics: Advanced Budd-Chiari Syndrome from a Primary Myeloproliferative Disorder

Case Presentation:
A 32-year-old male with past medical history of multiple small bowel obstructions requiring resection and management of enterocutaneous fistula, as well as essential thrombocytosis with JAK2 mutation confirmed via bone marrow biopsy, complicated by recurrent venous thromboembolism, separate inferior vena cava (IVC) and portal vein thromboses with associated portal hypertension and cirrhosis treated with thrombectomy, presented to our medical center as a transfer from an outside hospital. He was brought to the outside facility for altered mental status, deemed hepatic encephalopathy due to ammonia level > 100. At that facility, he required intubation for imaging purposes as well as vasopressor support. Imaging revealed subacute to chronic occlusion of the IVC and portal vein, most compatible with advanced Budd-Chiari syndrome (BCS). Also seen was compression of the IVC by an enlarged left hepatic lobe. Notably, he had been adherent to apixaban. He was started on heparin and subsequently transferred to UMC for hepatology evaluation. Interventional radiology determined patient was not a candidate for TIPS. He initially improved and was able to extubated and transferred out of the intensive care unit (ICU). However, 24 hours after his transfer, he had multiple episodes of large volume hematemesis requiring reintubation and transfer back to the ICU. Esophagogastroduodenoscopy (EGD) revealed several large varices with stigmata of recent bleeding, and banding was performed. Also seen on EGD was erosive gastropathy with active bleeding, requiring treatment with clipping and hemostatic powder. He was not deemed a candidate for any further invasive measures. Unfortunately, he continued to decompensate despite multiple pressor agents, progressing to extensive multiorgan failure and eventually death.

Discussion:
BCS is defined as hepatic venous outflow obstruction at any level from the small hepatic veins to the junction of the IVC and right atrium, excluding veno-occlusive disease and cardiac disorders. A hypercoagulable state can be identified in about 75% of patients, and primary myeloproliferative disorders are a leading cause of disease. Hepatic congestion leads to the hypoxic damage of hepatocytes, which further leads to necrosis and atrophy. Progressive fibrosis and eventually cirrhosis can develop. Resulting portal hypertension produces the associated manifestations of ascites, hepatic encephalopathy, and esophageal varices. The caudate lobe, which directly drains into the IVC, can undergo compensatory hypertrophy in about half of cases, compressing the IVC and further contributing to outflow obstruction. Diagnostic workup should always begin by using ultrasound with Doppler imaging. When the exam is technically difficult or when diagnostic features cannot be demonstrated, computed tomography (CT) or magnetic resonance imaging (MRI) should be obtained, with MRI being the preferred of the two. Venography may be considered and has added benefits of hemodynamic evaluation and tissue biopsy, while it often exposes an individual to higher doses of iodinated contrast. Determination of etiology should always include a thorough evaluation for a thrombogenic condition, although a combined etiology is present in 25% of patients. Therefore, a single identified cause should not mean foregoing investigation of other potential factors. All patients with BCS should undergo long-term anticoagulation, even in the absence of an identified prothrombotic condition. Evidence suggests that direct oral anticoagulants may be equivalent to low-molecular-weight heparin and vitamin K antagonists. Anticoagulation is to be done along with management of complications of portal hypertension, i.e., diuretics for ascites, banding for varices. More interventional modalities include angioplasty and stenting, transjugular intrahepatic portosystemic shunt (TIPS), and orthotopic liver transplantation as a final option. Most algorithms list these techniques in a stepwise fashion, barring any contraindications. However, interventions must be tailored to the patient, and endpoints for treatment success are not well established. Our patient's severe hepatic encephalopathy served as a contraindication to TIPS, and his extensive clot burden precluded the use of angioplasty. His anticoagulation status was also complicated by active gastric bleeding. Substantial gaps exist in our knowledge of this disease and treatment selection. Prognostication can be difficult, and progression of myeloproliferative disease may alter this.