Extrahepatic Portal Hypertension Following Abdominal Surgery

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ABSTRACT
We present a case of non-cirrhotic extrahepatic portal hypertension in a 31-year-old woman following extensive abdominal laparotomy for the drainage of multiple retroperitoneal and liver abscesses following a perforated appendix. Chronic portal, splenic, and mesenteric vein thrombosis with portal hypertension was caused by a hypercoagulable state due to the abdominal infection and abdominal surgery. Various etiological aspects of chronic extrahepatic venous thrombosis have not been documented due to the low incidence of these events. We discuss these aspects in the context of our patient.

INTRODUCTION
Portal hypertension is a constellation of altered physiology resulting from impaired blood flow through the major vessels of the portal-venous system. It is most frequently associated with cirrhosis of the liver, whereby fibroblastic proliferation in the portal regions of the hepatic parenchyma impede flow through the intrahepatic and portal vessels.

This impedance results in increased pressure in the larger vessels that drain into the liver, i.e., the portal-venous system, causing flow or shunting of blood into other organs and eventually giving rise to a network of collateral vessels (varices). This altered flow results in enlargement and congestion of the spleen, which in turn leads to a decrease in the circulating blood cells and low peripheral blood counts. Additionally, the varices that develop are frequently a source of upper gastrointestinal bleeding, a complication associated with significant morbidity and mortality.

The present case represents an example of portal hypertension that developed in a non-cirrhosis young patient following abdominal surgery complicated by infection. This septic complication is believed to have caused a hypercoagulable state that later led to extensive thrombosis of the portal-venous system, resulting in portal hypertension.

CASE PRESENTATION
A 31-year-old woman presented for further evaluation of thrombocytopenia and splenomegaly. Approximately 7 years prior to presentation, she underwent an appendectomy at her local hospital, which was complicated by a perforated appendix and peritonitis. After hospital discharge, she developed fever, chills, and abdominal pain despite intravenous antibiotic therapy. Four weeks postoperatively, an exploratory laparotomy revealed multiple liver and retroperitoneal abscesses. Three lower ribs were excised for reasons that remain unclear and drains were placed retroperitoneally for external drainage.

Four years following her second operation she was discovered to have a platelet count of 93,000/ml³ (normal 174,000-450,000/ml³). Annual complete blood cell counts revealed the platelet count to be persistently above 50,000/ml³ but below the normal range. One month prior to hematologic consult, her platelet count was 83,000/ml³. Six months prior to her referral for a hematologic consultation for thrombocytopenia, her spleen was palpable 2 cm below the costal margin. One month prior to presentation, the outside institution's ultrasound of the abdomen revealed prominent splenomegaly with thrombus of the portal and splenic veins. Multiple collateral vessels and focal liver masses suggested focal nodular hyperplasia.

On presentation at our institution, she complained of easy bruising and a 2-year history of persistent fatigue, but no history of bleeding. Medications included Motrin taken on an as-needed basis for headache. There was no history of oral contraceptive use. Family history was significant for recurrent deep venous thrombosis. However, the patient was unaware of her father's specific coagulation disorder. Physical ex-
amination revealed a weight of 72 kg, pulse 76 beats per minute, blood pressure 110/80 mmHg and temperature 97.4°F. There were linear scars along the midline, right lower quadrant, and splenomegaly without hepatomegaly. The spleen was palpable 3 cm below the left costal margin. Abdominal tenderness, distension, and ascites were absent. There was no evidence of bleeding, petechiae, or ecchymosis.

Laboratory data for a hypercoagulable workup, which included factor V Leiden, prothrombin gene G20210A, antinuclear antibodies, antithrombin III, protein C and S, homocysteine levels, and lupus anticoagulants, were negative. Liver function tests, white blood cell count, and hemoglobin levels were normal. Platelet count was 74,000/ml³. Computer tomographic scan of the abdomen was requested that showed splenomegaly, esophageal varices with occlusion of the superior mesenteric, main portal vein, and the right and left hepatic veins. Extensive collaterals were also noted on the imaging scans, documenting the portal hypertension. Despite the collaterals, there was no evidence of ascites. There was inhomogeneous opacification of the liver consistent with portal transformation and collateral formation (Figure 1).

DISCUSSION
Portal hypertension is a complex clinical condition caused by increased resistance to blood flow through the portal-venous system. It occurs as a result of a variety of clinical conditions and is most commonly associated with changes occurring within the liver parenchyma affecting intrahepatic blood flow. The etiology of this entity is usually divided into prehepatic, intrahepatic, and posthepatic causes. The most common condition associated with portal hypertension is cirrhosis of the liver, characterized by extensive fibroblastic proliferation in the periportal or perivenular area, resulting in impedance to intrahepatic blood flow. A major cause of prehepatic portal hypertension is thrombosis or narrowing of the portal vein and/or the major veins that make up the portal venous system. Obstruction of the main portal vein may occur insidiously and patients may remain asymptomatic for an extended period of time. However, acute occlusion may result in a serious, sometimes lethal event accompanied by a constellation of clinical signs and symptoms requiring therapeutic intervention. The incidence of thrombosis of the portal-venous system in well-compensated liver cirrhosis is between 0.6% and 16%, but symptoms of portal hypertension will increase rapidly in the decompensated disease state.

Acquired hypercoagulable conditions (Table 1) are the most common cause of thrombosis of the portal-venous system in non-cirrhotic patients. This predisposition to venous thromboembolism can occur as a result of an acute or chronic inflammatory and infectious disease, post-intra-abdominal surgical procedure, intra-abdominal malignancies (primary or metastatic), myeloproliferative diseases, pregnancy, postpartum state, use of oral contraceptives, and trauma.

Additionally, genetically inherited hypercoagulable states or coagulopathies (Table 1) may also predispose to thrombosis of the portal-venous system resulting in portal hypertension. These include, among others, factor V Leiden, prothrombin gene G20210A mutation, protein C, protein S and antithrombin III deficiencies, and hyperhomocystinemia. Oral contraceptives are associated with hypercoagulability and account for about 9%-18% of mesenteric thrombosis in young adults. Myeloproliferative disorders are a leading cause of portal vein thrombosis with a prevalence of 30%-40% particularly in younger patients. Studies have shown that consequences of portal and hepatic vein thrombosis may be the first symptom of a myeloproliferative disease.

The increased blood flow shunted through the spleen causes splenomegaly resulting in anemia, thrombocytopenia, and leukopenia, a condition called hypersplenism. Bleeding secondary to thrombocytopenia is rare, as the overall platelet survival is relatively normal. However, the development of esophageal varices often leads to upper gastrointestinal bleeding, a major
complication of portal hypertension that is associated with high mortality. The prognosis for variceal bleeding secondary to non-cirrhotic obstruction of the portal system is significantly better than cirrhotic patients with comparable levels of liver function impairment and severity of the portal hypertension.\textsuperscript{26} Mortality is usually related to concurrent conditions leading to thrombosis and not to the complications of portal hypertension.\textsuperscript{9,26}

Treatment is symptomatic with the aim of controlling variceal bleeding using beta-blockers, such as propranolol.\textsuperscript{2,27,28} There is a limited role of prophylactic esophageal variceal ligation for patients with high grade varices\textsuperscript{2,29,30} and endoscopy is used to control active bleeding and prevent recurrent bleeding.\textsuperscript{31} If the bleeding is extensive and cannot be controlled by conservative measures, patients should be considered for a surgical porto-systemic shunt procedure by an experienced surgeon.\textsuperscript{2} Anticoagulation is beneficial in acute thrombosis,\textsuperscript{4,32} but in chronic thrombosis it is recommended only for people with a known prothrombotic state\textsuperscript{1,4,33} and recurrent thrombus formation.\textsuperscript{20}

Our patient underwent an appendectomy followed by additional surgery to drain the abscesses at another institution. The inflammatory state that existed subsequently due to the appendicitis and the postoperative abscesses may have contributed to a hypercoagulable state, resulting in thrombosis of her portal-venous system. This postulation is supported by reports of acute septic thrombophlebitis of the portal and mesenteric veins following appendicitis and diverticulitis.\textsuperscript{34-36} However, the chronicity of our patient’s presentations led to the conclusion that the pathogenesis of the extensive splanchnic thrombosis was the chronic inflammatory and septic process that ensued after surgery resulting in a hypercoagulable state. The family history of a coagulation disorder raised the suspicion of a genetic hypercoagulable state but the negative hypercoagulation workup ruled out that possibility. Additionally, there were no antecedent aspects in our patient’s past medical history suspicious for her having had a hypercoagulable state prior to her surgery.

Data regarding intra-abdominal surgery causing chronic thrombosis are limited and studies have concentrated on acute and subacute thrombosis. Surgical interventions such as hepatobiliary surgery, splenectomy, liver transplantation, jejunal resection, colectomy, and abdominal surgeries in general have been associated with thrombosis during the postoperative period.\textsuperscript{2,22,27,37-41} Reports of portal venous thrombosis occurring 3-4 years after surgery suggest there may be a persistent hypercoagulable state following any surgery.\textsuperscript{38-42}

**CONCLUSION**

Our patient’s thrombocytopenia was thought to arise from complications of her previous surgery. The abdominal infection in combination with the appendectomy and exploratory laparotomy led to a hypercoagulable state followed by fibrosis, which resulted in portal hypertension and splenomegaly. The splenomegaly resulted in thrombocytopenia. No intervention was indicated as she did not exhibit any symptoms related to thrombocytopenia or hypertension and was started on primary prophylaxis with propranolol. Her condition is, however, progressive, and intervention will be reconsidered should she have symptoms.

Various etiological aspects of chronic portal, splenic, and mesenteric venous thrombosis are unclear because of the low incidence of these events. Further investigations using randomized trials will aid in understanding the pathogenesis and guide treatment. Conducting these trials will be a very tenuous task and will warrant assessment of the risk-benefit ratio.

**Acknowledgments:** The authors thank Marshfield Clinic Research Foundation for its support through the assistance of Linda Weis and Alice Stargardt in the preparation of this manuscript.

**Funding/Support:** None declared.

**Financial Disclosures:** None declared.

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