

# Extrahepatic Portal Hypertension Following Abdominal Surgery

*Ajit Singh Ahluwalia, MD, MHA; Joseph J. Mazza, MD, MACP; Steven H. Yale, MD*

## 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/ml<sup>3</sup> (normal 174,000-450,000/ml<sup>3</sup>). Annual complete blood cell counts revealed the platelet count to be persistently above 50,000/ml<sup>3</sup> but below the normal range. One month prior to hematologic consult, her platelet count was 83,000/ml<sup>3</sup>. Six months prior to her referral for a hematology 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 bruisability 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-

**Author Affiliations:** Marshfield Clinic, Marshfield, Wis (Ahluwalia, Mazza, Yale); Clinical Research Center, Marshfield Clinic Research Foundation, Marshfield, Wis (Yale).

**Corresponding Author:** Steven H. Yale, MD, Clinical Research Center, Marshfield Clinic Research Foundation, 1000 N Oak Ave, Marshfield, WI 54449; phone 715.387.9110; fax 715.389.3808; e-mail yale.steven@mcrf.mfldclin.edu.

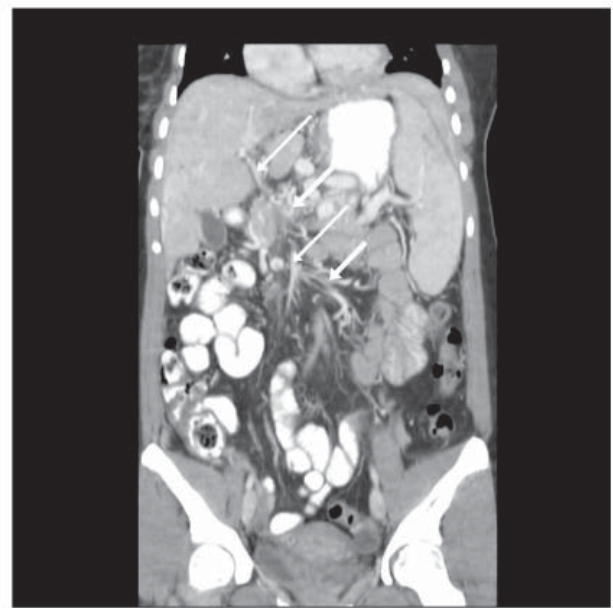
amination revealed a weight of 72 kg, pulse 76 beats per minute, blood pressure 110/80 mmHg and temperature 97.4°F. There were linear scars along the midline, right lower quadrant, and splenomegaly without hepatomegaly. The spleen was palpable 3 cm below the left costal margin. Abdominal tenderness, 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/ml<sup>3</sup>. 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,<sup>1</sup> 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.<sup>2-4</sup> 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.<sup>5-7</sup>

Acquired hypercoagulable conditions (Table 1) are the most common cause of thrombosis of the portal-



**Figure 1.** Extensive collateral formation (thick arrows) throughout the abdomen with portal, splenic and superior mesenteric vein thrombosis (thin arrows).

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.<sup>2,8-12</sup> 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.<sup>2-5,8-21</sup> Oral contraceptives are associated with hypercoagulability and account for about 9%-18% of mesenteric thrombosis in young adults.<sup>3,10,11</sup> Myeloproliferative disorders are a leading cause of portal vein thrombosis with a prevalence of 30%,<sup>8,12</sup> particularly in younger patients.<sup>22</sup> Studies have shown that consequences of portal and hepatic vein thrombosis may be the first symptom of a myeloproliferative disease.<sup>23</sup>

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.<sup>2,4,24,25</sup> However, the development of esophagogastric varices often leads to upper gastrointestinal bleeding, a major

**Table 1.** Etiology of Portal Vein Thrombosis in Non-Cirrhotic Patients

Acquired Causes
Acute and chronic inflammatory states
Acute and chronic infectious states
Post-intra-abdominal surgical procedure
Intra-abdominal malignancies (primary or metastatic)
Myeloproliferative diseases
Pregnancy
Postpartum state
Use of oral contraceptives
Trauma
Genetic Causes
Prothrombotic states
• Factor V Leiden
• Prothrombin gene G20210A mutation
• Protein C and protein S deficiencies
• Antithrombin III deficiencies
• Hyperhomocystinemia

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.<sup>26</sup> Mortality is usually related to concurrent conditions leading to thrombosis and not to the complications of portal hypertension.<sup>9,26</sup>

Treatment is symptomatic with the aim of controlling variceal bleeding using beta-blockers, such as propranolol.<sup>2,27,28</sup> There is a limited role of prophylactic esophageal variceal ligation for patients with high grade varices<sup>2,29,30</sup> and endoscopy is used to control active bleeding and prevent recurrent bleeding.<sup>31</sup> 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.<sup>2</sup> Anticoagulation is beneficial in acute thrombosis,<sup>4,32</sup> but in chronic thrombosis it is recommended only for people with a known prothrombotic state<sup>1,4,33</sup> and recurrent thrombus formation.<sup>20</sup>

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.<sup>34-36</sup> 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.<sup>2,20,27,37-41</sup> Reports of portal venous thrombosis occurring 3-4 years after surgery suggest there may be a persistent hypercoagulable state following any surgery.<sup>38-40</sup>

## 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.

## REFERENCES

1. Guyton AC, Hall JE. The liver as an organ. In Guyton AC, Hall JE (eds.) *Textbook of Medical Physiology*. 11th ed. New York, NY: Saunders; 2005.
2. Kumar S, Sarr MG, Kamath PS. Mesenteric venous thrombosis. *N Engl J Med*. 2001;345:1683-1688.
3. Harward TR, Green D, Bergan JJ, Rizzo RJ, Yao JS.

- Mesenteric venous thrombosis. *J Vasc Surg.* 1989;9:328-333.
4. Webster GJ, Burroughs AK, Riordan SM. Review article: portal vein thrombosis—new insights into aetiology and management. *Aliment Pharmacol Ther.* 2005;21:1-9.
  5. Janssen HL, Meinardi JR, Vleggaar FP, et al. Factor V Leiden mutation, prothrombin gene mutation, and deficiencies in coagulation inhibitors associated with Budd-Chiari syndrome and portal vein thrombosis: results of a case-control study. *Blood.* 2000;96:2364-2368.
  6. Amitrano L, Guardascione MA, Brancaccio V, et al. Risk factors and clinical presentation of portal vein thrombosis in patients with liver cirrhosis. *J Hepatol.* 2004;40:736-741.
  7. Nonami T, Yokoyama I, Iwatsuki S, Starzl TE. The incidence of portal vein thrombosis at liver transplantation. *Hepatology.* 1992;16:1195-1198.
  8. Denninger MH, Chait Y, Casadevall N, et al. Cause of portal or hepatic venous thrombosis in adults: the role of multiple concurrent factors. *Hepatology.* 2000;31:587-591.
  9. Janssen HL, Wijnhoud A, Haagsma EB, et al. Extrahepatic portal vein thrombosis: aetiology and determinants of survival. *Gut.* 2001;49:720-724.
  10. Abdu RA, Zakhour BJ, Dallis DJ. Mesenteric venous thrombosis—1911 to 1984. *Surgery.* 1987;101:383-388.
  11. Hassan HA. Oral contraceptive-induced mesenteric venous thrombosis with resultant intestinal ischemia. *J Clin Gastroenterol.* 1999;29:90-95.
  12. Valla D, Casadevall N, Huisse MG, et al. Etiology of portal vein thrombosis in adults. a prospective evaluation of primary myeloproliferative disorders. *Gastroenterology.* 1988;94:1063-1069.
  13. Poort SR, Rosendaal FR, Reitsma PH, Bertina RM. A common genetic variation in the 3'-untranslated region of the prothrombin gene is associated with elevated plasma prothrombin levels and an increase in venous thrombosis. *Blood.* 1996;88:3698-3703.
  14. Chamouard P, Pencreach E, Maloisel F, et al. Frequent factor II G20210A mutation in idiopathic portal vein thrombosis. *Gastroenterology.* 1999;116:144-148.
  15. Silingardi M, Ghirarduzzi A, Galimberti D, Iorio A, Iori I. Mesenteric-portal vein thrombosis in a patient with hyperhomocysteinemia and heterozygous for 20210A prothrombin allele. *Thromb Haemost.* 2000;84:358-359.
  16. Marie I, Levesque H, Le Cam-Duchez V, Borg JY, Ducrotte P, Philippe C. Mesenteric venous thrombosis revealing both factor II G20212A mutation and hyperhomocysteinemia related to pernicious anemia. *Gastroenterology.* 2000;118:237-238.
  17. Buchel O, Roskams T, Van Damme B, Nevens F, Pirenne J, Fevery J. Nodular regenerative hyperplasia, portal vein thrombosis, and avascular hip necrosis due to hyperhomocysteinemia. *Gut.* 2005;54:1021-1023.
  18. Lopez Serrano P, Martin Scapa MA, Aleman Villanueva S, Vazquez M, Cid Gomez L. Extrahepatic portal hypertension: spleno-portal thrombosis secondary to protein C deficiency. *Ann Med Int.* 2003;20:473-476.
  19. Egesel T, Buyukasik Y, Dundar SV, Gurgey A, Kirazli S, Bayraktar Y. The role of natural anticoagulant deficiencies and factor V Leiden in the development of idiopathic portal vein thrombosis. *J Clin Gastroenterol.* 2000;30:66-71.
  20. Valla DC, Condat B. Portal vein thrombosis in adults: pathophysiology, pathogenesis and management. *J Hepatol.* 2000;32:865-871.
  21. Mazza JJ. Hypercoagulability and venous thromboembolism: a review. *WMJ.* 2004;103:41-49.
  22. Teofili L, De Stefano V, Leone G, et al. Hematological causes of venous thrombosis in young people: high incidence of myeloproliferative disorder as underlying disease in patients with splanchnic venous thrombosis. *Thromb Haemost.* 1992;67:297-301.
  23. McNamara C, Juneja S, Wolf M, Grigg A. Portal or hepatic vein thrombosis as the first presentation of a myeloproliferative disorder in patients with normal peripheral blood counts. *Clin Lab Haematol.* 2002;24:239-242.
  24. Lacey JV, Penner JA. Management of idiopathic thrombocytopenic purpura in the adult. *Semin Thromb Hemost.* 1977;3:160-174.
  25. Aster RH. Pooling of platelets in the spleen: role in the pathogenesis of "hypersplenic" thrombocytopenia. *J Clin Invest.* 1966;45:645-657.
  26. Merkel C, Bolognesi M, Bellon S, et al. Long-term follow-up study of adult patients with non-cirrhotic obstruction of the portal system: comparison with cirrhotic patients. *J Hepatol.* 1992;15:299-303.
  27. Bendtsen F, Henriksen JH, Sorensen TI. Long-term effects of oral propranolol on splanchnic and systemic haemodynamics in patients with cirrhosis and oesophageal varices. *Scand J Gastroenterol.* 1991;26:933-939.
  28. D'Amico G, Pagliaro L, Bosch J. Pharmacological treatment of portal hypertension: an evidence-based approach. *Semin Liver Dis.* 1999;19:475-505.
  29. Imperiale TF, Chalasani N. A meta-analysis of endoscopic variceal ligation for primary prophylaxis of esophageal variceal bleeding. *Hepatology.* 2001;33:802-807.
  30. Khuroo MS, Khuroo NS, Farahat KL, Khuroo YS, Sofi AA, Dahab ST. Meta-analysis: endoscopic variceal ligation for primary prophylaxis of oesophageal variceal bleeding. *Aliment Pharmacol Ther.* 2005;21:347-361.
  31. Norton ID, Andrews JC, Kamath PS. Management of ectopic varices. *Hepatology.* 1998;28:1154-1158.
  32. Plemmons RM, Dooley DP, Longfield RN. Septic thrombophlebitis of the portal vein (pyelephlebitis): diagnosis and management in the modern era. *Clin Infect Dis.* 1995;21:1114-1120.
  33. 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.
  34. Nishimori H, Ezoe E, Ura H, et al. Septic thrombophlebitis of the portal and superior mesenteric veins as a complication of appendicitis: report of a case. *Surg Today.* 2004;34:173-176.
  35. Germain MA, Soukhni N, Bouzard D. Mesenteric venous thrombosis complicating acute appendicitis. *Ann Chir.* 2002;127:381-384.
  36. Sywak M, Romano C, Raber E, Pasiaka JL. Septic thrombophlebitis of the inferior mesenteric vein from sigmoid diverticulitis. *J Am Coll Surg.* 2003;196:326-327.
  37. Wang MC, Li S, Zhu JY, Leng XS, Du RY. The reason and treatment of portal vein thrombosis in patients with portal hypertension postoperation. *Zhonghua Wai Ke Za Zhi.* 2004;42:269-271.
  38. Ellison EC, Fabri PJ. Complications of splenectomy. etiology, prevention, and management. *Surg Clin North Am.* 1983;63:1313-1330.
  39. Ikeda M, Sekimoto M, Takiguchi S, et al. High incidence of thrombosis of the portal venous system after laparoscopic splenectomy: a prospective study with contrast-enhanced CT scan. *Ann Surg.* 2005;241:208-216.
  40. Brown KM, Kaplan MM, Donowitz M. Extrahepatic portal venous thrombosis: frequent recognition of associated diseases. *J Clin Gastroenterol.* 1985;7:153-159.
  41. Baixauli J, Delaney CP, Senagore AJ, Remzi FH, Fazio VW. Portal vein thrombosis after laparoscopic sigmoid colectomy for diverticulitis: report of a case. *Dis Colon Rectum.* 2003;46:550-553.

# Wisconsin Medical Journal

The mission of the *Wisconsin Medical Journal* is to provide a vehicle for professional communication and continuing education of Wisconsin physicians.

The *Wisconsin Medical Journal* (ISSN 1098-1861) is the official publication of the Wisconsin Medical Society and is devoted to the interests of the medical profession and health care in Wisconsin. The managing editor is responsible for overseeing the production, business operation and contents of the *Wisconsin Medical Journal*. The editorial board, chaired by the medical editor, solicits and peer reviews all scientific articles; it does not screen public health, socioeconomic or organizational articles. Although letters to the editor are reviewed by the medical editor, all signed expressions of opinion belong to the author(s) for which neither the *Wisconsin Medical Journal* nor the Society take responsibility. The *Wisconsin Medical Journal* is indexed in Index Medicus, Hospital Literature Index and Cambridge Scientific Abstracts.

For reprints of this article, contact the *Wisconsin Medical Journal* at 866.442.3800 or e-mail [wmj@wismed.org](mailto:wmj@wismed.org).

© 2007 Wisconsin Medical Society