ACG CASE REPORTS JOURNAL

CASE REPORT | LIVER

Porto-Sinusoidal Vascular Disease in a Patient With Diffuse Aortitis and Massive Ascites

Emily Lin, MD[1], and Brian T. Lee, MD[2]

[1]*Department of Medicine, Loma Linda University Medical Center, Loma Linda, CA*
[2]*Department of Gastroenterology and Transplant Institute, Loma Linda University Health, Loma Linda, CA*

ABSTRACT

A 69-year-old man with no history of liver disease presented with massive ascites. Imaging demonstrated diffuse wall thickening of the entire aorta, renal pelvis, and ureters along with an enlarged main portal vein, portosystemic collaterals, and peritoneal thickening concerning for large vessel vasculitis. Liver biopsy was consistent with obliterative portal venopathy. The patient was started on corticosteroid therapy with improvement in his ascites. This case study reveals a rare association between vasculitis and portal-sinusoidal vascular disease and idiopathic non-cirrhotic portal hypertension, highlighting the heterogenous clinical presentation of this disease entity.

INTRODUCTION

Porto-sinusoidal vascular disease (PSVD) and idiopathic non-cirrhotic portal hypertension (INCPH) have recently been recognized in the spectrum of vascular liver disease. This disease entity can have a heterogeneous presentation of clinical and histologic findings and has been associated with several immunologic and systemic diseases.[1,2] We report the first known case of a patient who developed massive ascites and was found to have PSVD and INCPH in the setting of diffuse aortitis.

CASE REPORT

A 69-year-old man presented for outpatient consultation because of large volume ascites. He first developed ascites after an abdominal hernia repair, requiring large volume paracentesis for fluid removal. The patient was also found to be newly anemic with a 50-pound weight loss over the span of several months; prior endoscopic workup was unremarkable. History was significant for chronic kidney disease stage 3 and left femoral deep venous thrombosis. Otherwise, the patient had no history of liver disease and recent alcohol or substance use, and a review of systems was negative. Physical examination was notable for tense ascites, lower extremity edema, and temporal wasting, but no stigmata of chronic liver disease. Laboratory results revealed white blood cell 15.29 K/μL, hemoglobin 10.1 g/dL, platelet 530 K/μL, creatinine 1.5 mg/dL, aspartate aminotransferase 7 U/L, alanine aminotransferase 12 U/L, alkaline phosphatase 93 U/L, total bilirubin $<$0.2 mg/dL, albumin 2.9 g/dL, total protein 6.8 g/dL, and international normalized ratio 1.5. Immunologic workup resulted in elevated anti-nuclear antibodies 1:160 with a homogeneous pattern, erythrocyte sedimentation rate 72 mm/h, and C-reactive protein 9.3 mg/L. Workup for underlying liver disease, including viral hepatitis serologies, was unrevealing. Ascitic fluid analysis showed a low serum-ascites albumin gradient of 0.9 g/dL (2.3–1.4 g/dL) and a fluid protein of 3.7 g/dL; cytology was negative for malignancy. Echocardiogram was also unremarkable.

Owing to concern for malignancy, evaluation for lymphoproliferative disease was initiated. Chest and abdominal computed tomography imaging demonstrated diffuse wall thickening of the entire aorta (Figure 1), renal pelvis, and ureters along with an enlarged main portal vein, portosystemic collaterals (Figure 1), and peritoneal thickening. Transjugular liver biopsy showed a normal hepatic venous pressure gradient (HVPG) of 3 mm Hg (13–10 mm Hg). Histology revealed several portal vein radicles and herniation of portal vein segments into hepatic parenchyma, consistent with obliterative portal venopathy (OPV) (Figure 2). Trichrome stain did not show significant fibrosis. Evaluation for infectious and immune-mediated causes of aortitis including syphilis, retroperitoneal fibrosis, and immunoglobulin G4-related disease was negative. Biopsy of perinephric tissue was also

ACG Case Rep J 2022;9:e00812. doi:10.14309/crj.0000000000000812. Published online: July 6, 2022

Correspondence: Emily Lin, MD (elin@llu.edu).

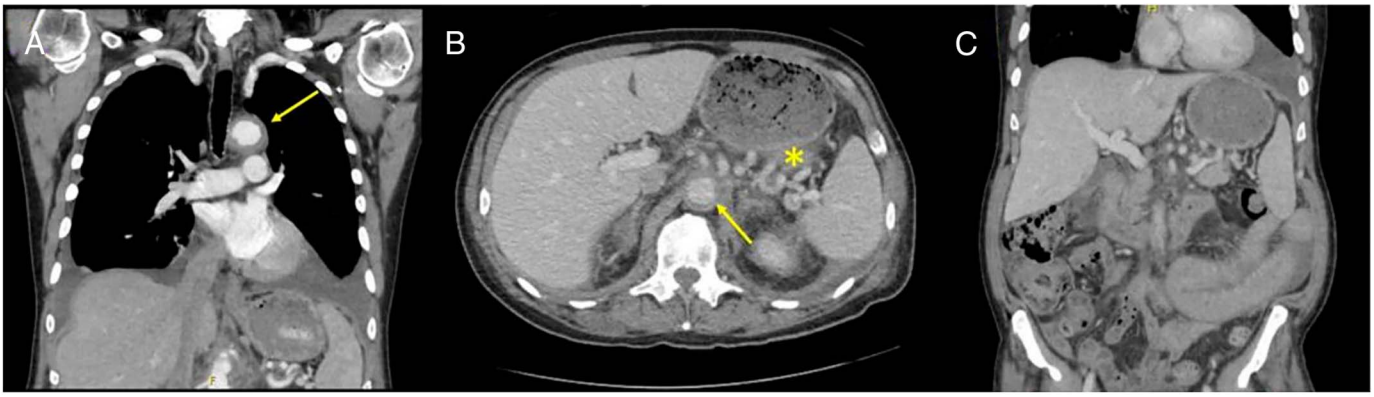

Figure 1. (A) Coronal view of chest computed tomography (CT) showing a thickened aortic arch. (B) Axial view of abdominal CT after paracentesis showing the thickened abdominal aorta (arrow) consistent with vasculitis and portosystemic collaterals (asterisk). (C) Coronal view of abdominal CT showing the patent portal vein and presence of portosystemic collaterals.

performed to evaluate for malignancies and myeloproliferative diseases including angiosarcoma and Erdheim-Chester disease. However, findings were nondiagnostic.

Rheumatology was consulted, and the patient was deemed to have isolated idiopathic large vessel vasculitis because he did not fulfill criteria for classic large vessel vasculitis including giant cell arteritis. The patient was started on intravenous methylprednisolone 80 mg daily before transitioning to a long-term prednisone taper. He had improvement of his ascites over the next few months and was subsequently transitioned to tocilizumab as a steroid-sparing agent.

DISCUSSION

Idiopathic non-cirrhotic portal hypertension is defined by the presence of clinical findings of portal hypertension in the absence of liver disease.[1] Porto-sinusoidal vascular disease is a recently proposed clinical entity characterized by non-cirrhotic portal hypertension and is diagnosed by histopathologic findings on liver biopsy.[3] The 3 histologic findings identified in the spectrum of PSVD are OPV, nodular regenerative hyperplasia, and incomplete septal cirrhosis.[4]

Patients with PSVD and INCPH may present with ascites, variceal bleeding, or encephalopathy, making it difficult to distinguish from cirrhosis without biopsy. Biochemical workup in PSVD typically reveals preserved liver function and aminotransferase levels[5] while demonstrating nonspecific abnormalities such as the presence of anti-nuclear antibodies.[6] HVPG is often normal or only mildly elevated compared with portal venous pressures found in patients with cirrhosis[7,8] based on the following standardized parameters: normal portal venous pressure defined as $\leq$5 mm Hg, mild portal hypertension defined as 6–9 mm Hg, and significant portal hypertension defined as $\geq$10 mm Hg.[9] This is likely because INCPH is typically characterized by presinusoidal changes in liver architecture and thus can be underestimated when measuring the HVPG. Furthermore, studies have shown an association between PSVD and autoimmune diseases and hypercoagulable states.[10–12] Interestingly, our patient exhibited many of these features, including a normal HVPG, positive anti-nuclear antibodies, and a history of deep venous thrombosis.

To the best of our knowledge, this is the first reported case of PSVD and INCPH manifesting as OPV and massive ascites in the setting of isolated idiopathic large vessel vasculitis. Hepatic involvement in large vessel vasculitis is historically rare. Typically, these patients may present with elevated liver enzymes as

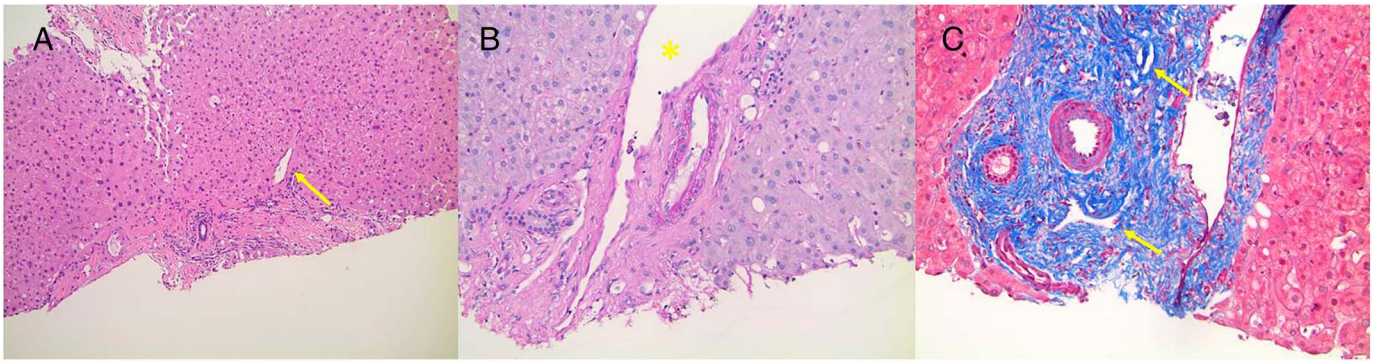

Figure 2. (A, B) Liver histology identifying the herniated portal vein (arrow, asterisk) into hepatic parenchyma (hematoxylin and eosin stain). (C) Increased number of portal vascular channels (arrows) (trichrome stain).

part of an acute phase response or with incidental findings of stenosis in the hepatic vasculature without any overt clinical manifestations.[13] Currently, the relationship between PSVD and immunologic diseases, including vasculitis, remains under investigation. Studies suggest that OPV could be the result of chronic antigenic stimulation of sinusoidal endothelial cells in the setting of systemic immunologic disease.[2,14] Notably, patients with INCPH have greater expression of human leukocyte DR antigens targeting the venous radicles in the portal tract compared with patients with chronic hepatitis or cirrhosis, suggesting that these venous structures are susceptible to immunologic attack.[15]

Massive ascites in patients with immunologic disease such as systemic vasculitis is relatively uncommon, and the precise mechanism for the development of ascites in these disorders is unclear. One hypothesis is that microvascular damage secondary to a chronic inflammatory state leads to obstructed intrahepatic vessels, resulting in increased intrahepatic resistance and accumulation of peritoneal fluid.[14,16] Other studies analyzing lupus patients with ascites have revealed increased immune-complex deposition and complement activation in peritoneal microvessels, which increases permeability of the serous membrane and subsequently causes leakage of fluid and protein into the peritoneal cavity,[17–19] resulting in low-serum-ascites albumin gradient ascites as seen in this case.

Currently, the treatment of patients with INCPH is largely focused on preventing and managing complications of portal hypertension as per guidelines for cirrhosis.[1,11] Case studies have shown that patients with immunologic diseases who present with ascites typically respond well to high-dose steroids followed by a taper,[17,20] which worked well in our patient's case. Ultimately, this case study reveals an uncommon association between large vessel vasculitis and PSVD and INCPH, highlighting the heterogenous clinical presentation of this disease entity. This report adds to an assortment of rare cases which may improve recognition of INCPH and its associated risk factors while simultaneously shedding light on the pathogenesis and management of PSVD.

DISCLOSURES

Author contributions: E. Lin reviewed the literature and wrote the manuscript. BT Lee provided the images, revised the manuscript for intellectual content, and is the article guarantor. All authors edited and approved the final manuscript.

Financial disclosure: None to report.

Previous presentation: This case was presented as a poster presentation at the American College of Gastroenterology Annual Scientific Meeting; October 25, 2021; Las Vegas, Nevada.

Informed consent was obtained for this case report.

Received October 27, 2021; Accepted April 4, 2022

REFERENCES

1. Aggarwal S, Fiel MI, Schiano TD. Obliterative portal venopathy: A clinical and histopathological review. *Dig Dis Sci*. 2013;58(10):2767–76.
2. Tsuneyama K, Harada K, Katayanagi K, et al. Overlap of idiopathic portal hypertension and scleroderma: Report of two autopsy cases and a review of literature. *J Gastroenterol Hepatol*. 2002;17(2):217–23.
3. De Gottardi A, Rautou PE, Schouten J, et al. Porto-sinusoidal vascular disease: Proposal and description of a novel entity. *Lancet Gastroenterol Hepatol*. 2019;4(5):399–411.
4. Kmeid M, Liu X, Ballentine S, Lee H. Idiopathic non-cirrhotic portal hypertension and porto-sinusoidal vascular disease: Review of current data. *Gastroenterology Res*. 2021;14(2):49–65.
5. Dhiman RK, Chawla Y, Vasishta RK, et al. Non-cirrhotic portal fibrosis (idiopathic portal hypertension): Experience with 151 patients and a review of the literature. *J Gastroenterol Hepatol*. 2002;17(1):6–16.
6. Nakanuma Y, Saito K, Obata Y. National survey of autoimmune phenomena in idiopathic portal hypertension in Japan. In *Annual Report of Japanese Study Group on Abnormal Portal Hemodynamics*. Japanese Welfare Ministry: Tokyo, 1991, pp 78–80.
7. Bosch J, Mastai R, Kravetz D, Navasa M, Rodés J. Hemodynamic evaluation of the patient with portal hypertension. *Semin Liver Dis*. 1986;6(4):309–17.
8. Sarin SK. Non-cirrhotic portal fibrosis. *J Gastroenterol Hepatol*. 2002;17(-Suppl 3):S214–23.
9. Suk KT. Hepatic venous pressure gradient: Clinical use in chronic liver disease. *Clin Mol Hepatol*. 2014;20(1):6–14.
10. Imabayashi K, Nakano K, Iwata S, Tanaka Y. A case of systemic lupus erythematosus with marked ascites due to idiopathic non-cirrhotic portal hypertension. *Mod Rheumatol Case Rep*. 2021;5(2):285–91.
11. Saito K, Nakanuma Y, Takegoshi K, et al. Non-specific immunological abnormalities and association of autoimmune diseases in idiopathic portal hypertension. A study by questionnaire. *Hepatogastroenterology*. 1993;40(2):163–6.
12. Schouten JN, Garcia-Pagan JC, Valla DC, Janssen HL. Idiopathic non-cirrhotic portal hypertension. *Hepatology*. 2011;54(3):1071–81.
13. Cid M. Diagnosis of gastrointestinal vasculitis [abstract]. *Ann Rheum Dis*. 2019;78:21–22.
14. Ziol M, Poirel H, Kountchou GN, et al. Intrasinusoidal cytotoxic CD8+ T cells in nodular regenerative hyperplasia of the liver. *Hum Pathol*. 2004;35(10):1241–51.
15. Terada T, Nakanuma Y, Hoso M, Obata H. Expression of HLA-DR antigen on hepatic vascular endothelial cells in idiopathic portal hypertension. *Clin Exp Immunol*. 1991;84(2):303–7.
16. Sweeney EC. Non-cirrhotic portal hypertension in Felty's syndrome. *Ir J Med Sci*. 1975;144(4):172–4.
17. Ishiguro N, Tomino Y, Fujito K, Nakayama S, Koide H. A case of massive ascites due to lupus peritonitis with a dramatic response to steroid pulse therapy. *Jpn J Med*. 1989;28(5):608–11.
18. Nolph KD, Stoltz ML, Maher JF. Altered peritoneal permeability in patients with systemic vasculitis. *Ann Intern Med*. 1971;75(5):753–5.
19. Weinstein PJ, Noyer CM. Rapid onset of massive ascites as the initial presentation of systemic lupus erythematosus. *Am J Gastroenterol*. 2000;95(1):302–3.
20. Geraldino-Pardilla L, Gartshteyn Y, Mendoza F. Massive serositis as the initial presentation of systemic lupus erythe-matosus: A report of two cases and review of the literature. *J Rheum Dis Treat*. 2015;1:028.