ACG CASE REPORTS JOURNAL

CASE REPORT | LIVER

Hereditary Hemorrhagic Telangiectasia and Refractory Ascites

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ABSTRACT

Hereditary hemorrhagic telangiectasia is a rare autosomal dominant disease that can involve the liver. The presence of arteriohepatic venous shunts can lead to high output cardiac failure and biliary ischemia, whereas arterioportal venous shunts can result in portal hypertension. Cirrhosis and nodular regenerative hyperplasia are also reported in these patients. Management of these patients in the setting of symptomatic liver disease is challenging. Transarterial embolization and hepatic artery ligation are usually considered palliative options. In selected cases, orthotopic liver transplantation can cure both liver disease and heart failure.

INTRODUCTION

Evaluation of refractory ascites can sometimes be challenging. Hereditary hemorrhagic telangiectasia (HHT) is a rare condition that can involve the liver, occasionally causing liver-related symptoms. The presence of arterioportal venous shunts can result in clinically significant portal hypertension. These patients may also have varying degrees of liver fibrosis and occasionally cirrhosis. We report a rare case where a patient presented with refractory ascites resulting from hepatic disease due to HHT.

CASE REPORT

A 66-year-old-woman was referred to our center for the evaluation for orthotopic liver transplantation (OLT) with a presumptive diagnosis of nonalcoholic fatty liver disease–related decompensated cirrhosis. She had complaints of abdominal distention and swelling of feet for the past 18 months and had diuretic refractory ascites requiring repeated abdominal paracentesis for the past 1 year. She had no other history suggestive of chronic liver disease. She did not have metabolic risk factors for nonalcoholic fatty liver disease. The etiological workup for liver disease including viral profile, autoimmune workup, and metabolic liver disease profile were negative. Her laboratory test results revealed a normal platelet count of 3.23×10^5 per microliter and an international normalized ratio of 1.1. The liver function tests showed normal bilirubin, alanine transaminase of 35 IU/L, aspartate transaminase of 23 IU/L, alkaline phosphatase of 449 IU/L, and serum albumin of 3.2 g/dL. Serum sodium was 129 mEq/L, and renal function was normal. Her abdominal computed tomography revealed a normal sized liver with nodular margins and ascites. Upper gastrointestinal endoscopy revealed a few small arteriovenous malformations (AVMs) in the body of the stomach.

Ascitic fluid protein was 3.2 g/dL, and serum ascites albumin gradient was 1.4. Given the patient's high protein ascites, a cardiac etiology was suspected. Her echocardiogram revealed normal left ventricular systolic function with ejection fraction of 65%–70% and moderate tricuspid regurgitation with right ventricular systolic pressure of 60 mm Hg. Coronary angiogram and right heart catheterization were normal. Bubble echocardiogram revealed few bubbles in left atrium, 10–12 beats after appearance in right atrium, suggestive of intrapulmonary shunts. For further evaluation of her liver disease, she underwent a transjugular liver biopsy, and the hepatic venous portal gradient measured was 35 mm Hg. Hepatic angiogram showed markedly dilated common and

ACG Case Rep J 2020;7:e00458. doi:10.14309/crj.0000000000000458. Published online: October 14, 2020

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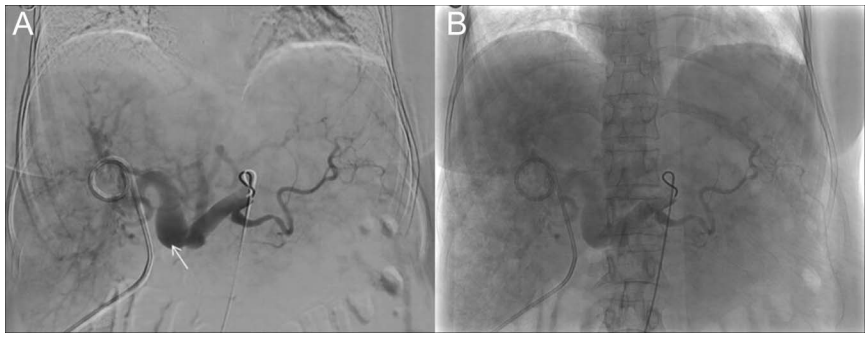

Figure 1. Hepatic angiogram showing (A) dilated common and proper hepatic artery (white arrow) and diffusely abnormal corkscrew arteries in the right lobe and (B) early filling of the portal vein with retrograde flow into the inferior mesenteric vein.

proper hepatic artery and diffusely abnormal corkscrew arteries in the right lobe with early filling of portal vein with retrograde flow into the inferior mesenteric vein (Figure 1). Liver biopsy revealed unpaired hepatic arteries with thickened walls, sinusoidal dilatation, and features suggestive of vascular malformation with advanced fibrosis (Figure 2). She was diagnosed to have HHT with portal hypertension due to hepatic arterioportal vein shunting.

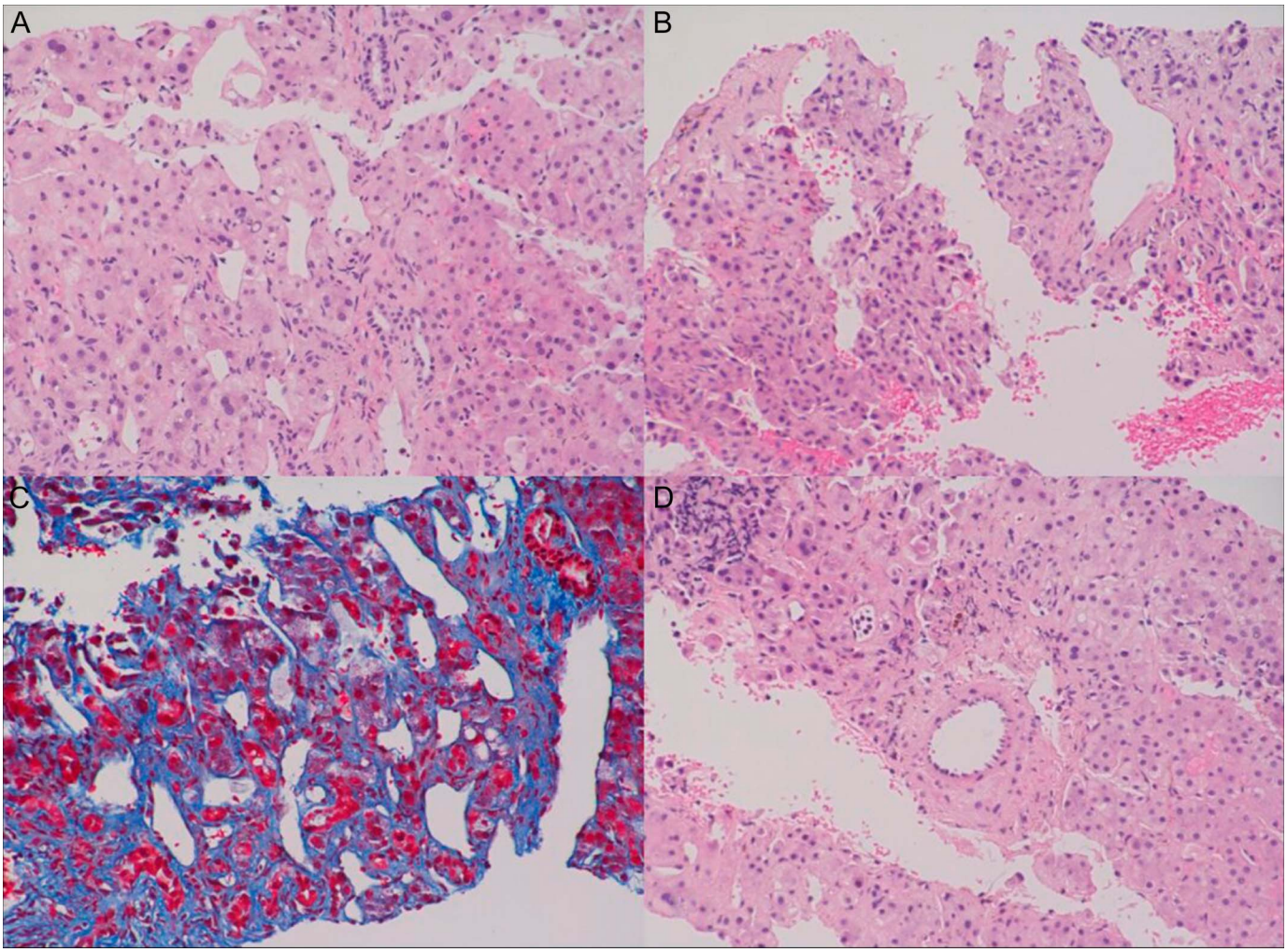

Figure 2. Liver biopsy showing (A and B) hepatic parenchyma with unpaired hepatic arterioles (hematoxylin and eosin stain, 40× magnification), (C) showing bridging fibrosis (trichrome stain, 40× magnification), and (D) sinusoidal dilatation (hematoxylin and eosin stain, 40× magnification).

DISCUSSION

HHT or Rendu-Osler-Weber disease is a rare, autosomal dominant disease with an incidence of 1–2 per 100,000.[1] Most common mutations are in HHT1 and HHT2 genes. HHT1 mutations are usually associated with pulmonary and cerebral AVMs and HHT2 mutations with liver AVMs and late-onset presentation.[2] Liver involvement is classically reported in up to 31% of patients. With advanced imaging techniques liver involvement is described in in up to 73%.[3] Only 5%–15% of HHT patients are symptomatic. In HHT, there could be 2 types of liver shunts: type-1—between hepatic artery and hepatic vein, which results in biliary ischemia and high-output cardiac failure (HOCF)—and type-2—between hepatic artery and portal vein, resulting in portal hypertension.[4] Martini et al classified hepatic disease in HHT into 3 types based on histological features: patients with hepatic AVMs and fibrosis/cirrhosis, those with only fibrosis/cirrhosis, and those with only AVMs.[5] The second group usually has post-transfusion hepatitis unrelated to HHT.[5] Garcia-Tsao et al, in their study of 19 patients with HHT and symptomatic liver involvement reported liver biopsy findings in 7 patients, abnormal ectatic vessels were seen in all, biliary abnormalities were seen in those with biliary disease, and sinusoidal fibrosis in those with portal hypertension. Nodularity was present in all biopsies, 6 had features suggestive of nodular regenerative hyperplasia, and 5 of the 6 had thick fibrous bands along ectatic vessels (regeneration with fibrosis gave the appearance of cirrhosis in 2 cases). One patient was reported to have true cirrhosis in this study.[4] HOCF usually results in passive congestion and pseudocirrhosis. Liver biopsy is contraindicated in known cases of HHT with liver involvement because of the risk of bleeding.[4,5]

Doppler ultrasound is used to identify and grade hepatic AVMs, with higher grades 3 and 4 usually associated with symptoms and requiring cardiac evaluation.[6] In selected patients with HOCF, recurrent biliary sepsis and portal hypertension, and/or decompensated cirrhosis, OLT is considered. OLT improves HOCF in most cases.[7,8] Low Model For End-Stage Liver Disease-Sodium score could restrict OLT in deceased donor transplant programs. In the United States, additional priority for OLT is assigned by regional review boards on a case-by-case basis.[7] Transjugular intrahepatic portosystemic shunt is not feasible in patients with cardiac failure and/or extensive hepatic AVMs.[6,7] In the largest series of OLT for HHT (40 patients), the overall survival rate was 82.5% with a median follow-up of 69 months.[8] Most patients (58%) transplanted had the heart failure related clinical presentation, either alone or in combination with liver disease; liver explant revealed cirrhosis in 20.5%. Survival was best when they presented with isolated heart failure (93%) rather than portal hypertension (67%). Transarterial embolization or surgical hepatic artery ligation has been attempted for management of HOCF, portal hypertension, and mesenteric steal syndrome but can be complicated by biliary ischemia and necrosis. Hence, these interventions are usually recommended only as palliative options.[8] There are reports of the antiangiogenic agent bevacizumab improving cardiac hemodynamics in patients with HHT, and in some cases, resulting in optimization of HOCF before OLT.[9]

Our patient likely had HHT with type-2 shunts (arterioportal venous shunts) and severe portal hypertension leading to refractory ascites. Her frailty and sarcopenia precluded use of an antiangiogenic agent or transarterial embolization of hepatic artery. She was listed for OLT, but her Model For End-Stage Liver Disease-Sodium score remained low, and she did not have any liver donors. She succumbed to a severe bout of sepsis shortly after listing.

DISCLOSURES

Author contributions: All authors contributed equally to this manuscript. R. Thandassery is the article guarantor.

Financial disclosure: None to report.

Informed consent could not be obtained from the family of the died patient despite several attempts. All identifying information has been removed from this case report to protect patient privacy.

Received April 27, 2020; Accepted July 9, 2020

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