Portal Hypertension and Ascites in Extramedullary Hematopoiesis

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Myeloproliferative diseases (MPD) are clonal stem cell disorders which mainly include polycythemia vera (PV), essential thrombocythemia (ET), and idiopathic myelofibrosis (IMF). They are characterized by leucocytosis, thrombocytosis, erythrocytosis, splenomegaly, and bone marrow hypercellularity. This might also result in extramedullary hematopoiesis. Abdominal manifestation has been recognized as a feature of these disorders. Splenomegaly and hepatomegaly are fairly common as opposed to ascites which is rare. The MPDs mainly affect the hepatic circulatory systems. The common hepatic manifestations are Budd–Chiari syndrome (BCS), portal vein thrombosis (PVT), and nodular regenerative hyperplasia.

A few other features seen in MPDs are caused by extramedullary hematopoiesis, increased hepatic blood flow, and secondary hemosiderosis from multiple blood transfusions. Portal hypertension is found in up to 7% of patients. We report a case of portal hypertension with ascites in a patient with extramedullary hematopoiesis treated with transjugular intrahepatic portocaval shunt (TIPS). (J CLIN EXP HEPATOL 2012;2:188–190)

Myeloproliferative diseases (MPD) are clonal stem cell disorders.¹ The major MPDs include polycythemia vera (PV), essential thrombocythemia (ET), and idiopathic myelofibrosis (IMF).² They are characterized by leukocytosis, thrombocytosis, erythrocytosis, splenomegaly, and bone marrow hypercellularity. This might also result in extramedullary hematopoiesis. Abdominal manifestation has been recognized as a feature of these disorders. Splenomegaly and hepatomegaly are fairly common as opposed to ascites which is rare (prevalence ranging from 2% to 10%).^{3,4} The hepatic manifestations of this group of disorders are similar. The MPDs mainly affect the hepatic circulatory systems. The common hepatic manifestations are Budd–Chiari syndrome (BCS), portal vein thrombosis (PVT), and nodular regenerative hyperplasia.²

A few other features seen in MPDs are caused by extramedullary hematopoiesis, increased hepatic blood flow, and secondary hemosiderosis from multiple blood transfusions. Portal hypertension is found in up to 7% of patients. In latent or atypical MPD, portopulmonary hypertension has also been described. On occasions, MPD can transform into leukemia causing extensive infiltration of the liver

leading to hepatic decompensation. We report a case of portal hypertension with ascites in a patient with extramedullary hematopoiesis treated with transjugular intrahepatic portocaval shunt (TIPS).

Case Report

A 45-year-old lady presented with a history of generalized weakness and abdominal distention for 2 months. She had no history of fever, weight loss, oliguria, or upper gastrointestinal bleed. She was a known case of diabetes for 5 years and had no past history of jaundice or tuberculosis.

Clinical examination revealed gross pallor, massive ascites, splenomegaly, no cervical lymphadenopathy, or edema feet.

Investigations showed hemoglobin of 6.5 g%, total leucocyte count (TLC) 3400, and platelets of 233,300/mm³ and erythrocyte sedimentation rate (ESR) was 100 mm/hr. Liver function tests, renal function tests, and thyroid profile were normal. Viral markers, anti-nuclear antibody (ANA), anti-smooth muscle antibody (ASMA), and protein electrophoresis were normal. Abdominal ultrasound showed coarse liver echo texture and splenomegaly with massive ascites. On color Doppler, hepatic veins, inferior vena cava (IVC), and splenoportal axis were patent.

Ascitic fluid examination showed total protein 3.9 g%, albumin 1.1 g%, serum ascitic fluid albumin gradient (SAAG) 1.8 mg%, sugar 107 mg/dL, cells 1200/mm³ (92% lymphocytes), and adenosine deaminase (ADA) 31 IU/L. Fluid was negative for malignant cells and culture. She was started on anti-tubercular treatment. During 2 months of treatment, she did not show any improvement and required repeated paracentesis. At this stage, the patient was referred to our center. Baseline work-up at our center was

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Abbreviations: BCS: Budd–Chiari syndrome; ET: essential thrombocythemia; IMF: idiopathic myelofibrosis; IVC: inferior vena cava; MPD: myeloproliferative diseases; PV: polycythemia vera; PVT: portal vein thrombosis; SAAG: serum ascitic fluid albumin gradient; TIPS: transjugular intrahepatic portocaval shunt

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Figure 1 Liver histology showing hematopoietic foci within hepatic sinusoids.

similar to her previous work-up except her serum iron profile was normal. Coomb's test was strongly positive. She was evaluated by a hematologist including bone marrow aspiration, biopsy, cytogenetic studies of bone marrow, JAK-2^{V617F} mutation and was diagnosed as IMF with Coomb's positive hemolytic anemia. JAK-2^{V617F} mutation was found to be negative.

Upper gastrointestinal endoscopy revealed grade 1 varices. She underwent hepatic venous pressure gradient measurement and transjugular liver biopsy. Free and wedged hepatic venous pressures were 12 mmHg and 36 mmHg, respectively. Inferior vena cava pressure was 6 mm and right atrial pressure was 2 mmHg. Wedged hepatic venous pressure gradient was 24 mmHg. Transjugular liver biopsy showed extensive extramedullary hematopoiesis. Hepatic sinusoids were packed with hemopoietic cells (Figure 1). She was subjected to triphasic helical computed tomography (CT) scan with CT angiograph. Computed tomography scan suggested nodules in the mesentery suggestive of extramedullary hematopoiesis and patent hepatic veins IVC and splenoportal axis (Figure 2). Diagnostic laparoscopy was performed which revealed coarse liver with multiple nodules over the liver and mesentery (Figure 3). Work-up for chronic liver disease including viral and autoimmune markers, iron studies, and laparoscopic appearance of liver with histology have excluded liver cirrhosis conclusively.

Figure 2 Computed tomography scan showing nodules in hepatic parenchyma, omentum, ascites, and splenomegaly.

Figure 3 Laparoscopy showing whitish nodules on the liver, falciparum ligament, and omentum.

Biopsy from the nodules showed evidence of extramedullary hematopoiesis. Bone marrow biopsy was also done. It showed hypercellular marrow. On liver histology, normal hemopoietic cells (myeloid and erythroid) were seen within sinusoids along with occasional megakaryocytes, suggestive of extramedullary hematopoiesis. Hepatocytes were unremarkable. There was no evidence of malignancy. Alfa-fetoprotein (AFP) and CA-125 were within normal limits. The patient was subjected to TIPS and follow-up after 1 week showed patent shunt with complete disappearance of ascites. She was put on oral anticoagulant Warfarin to maintain international normalized ratio

(INR) between 2.5 and 3.5. The patient was followed up with a hematologist for her Coomb's positive hemolytic anemia and myeloproliferative disorders. The patient was treated with steroids for Coomb's positive hemolytic anemia. For myelofibrosis, no treatment was given. At the end of 4 months of follow-up on anticoagulation treatment, she remained free of ascites and TIPS stent was patent.

DISCUSSION

Ascites can be classified on the basis of SAAG. A SAAG >1.1 is suggestive of portal hypertension.⁵ Patients with SAAG >1.1 and ascitic fluid total protein levels >2.5 are suggestive of cardiac causes or BCS. This patient had normal cardiac evaluation and patent hepatic veins and IVC which ruled out both these causes of ascites. The patient was presumably treated with diagnosis of tubercular peritonitis without any benefit. High-wedge hepatic venous pressure and transjugular liver biopsy gave us a conclusive diagnosis of portal hypertension due to extramedullary hematopoiesis. Computed tomography scan of the abdomen showed characteristic nodular appearances of omentum and the liver surface. Diagnostic laparoscopy helped us to reconfirm the diagnosis and exclude the other causes like tuberculosis and malignancy.

Patients with MPD can develop portal hypertension and ascites due to splanchnic venous thrombosis or extramedullary hematopoiesis in the liver omentum and peritoneum.²

Our patient had no evidence of splenic venous thrombosis and ascites and portal hypertension were due to extramedullary hematopoiesis in the liver, omentum, and peritoneum.

Patients with ascites due to portal hypertension which are refractory to diuretic treatment are treated with recurrent paracentesis with albumin infusion.⁶ Transjugular

intrahepatic portocaval shunt is a very good alternative for the treatment of refractory ascites especially with preserved liver function.⁷ There have been a few case reports of TIPS for the treatment of portal hypertension and ascites in patients with extramedullary hematopoiesis.⁸

Our patient responded very well to TIPS but long-term prognosis of the patient will depend on the behavior of MPD.

CONFLICTS OF INTEREST

All authors have none to declare.

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