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Budd-Chiari syndrome as a primary manifestation of antiphospholipid syndrome: A case report

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Abstract

Antiphospholipid syndrome (APS) is defined to be an acquired, systemic, and immunological disease. Budd-Chiari syndrome (BCS) appearing as a preliminary manifestation of APS is considered to be rare. Here the case of an 18-year-old boy is being reported. The patient had complaints of insidious onset painless abdominal distention for three months and further developed pedal edema. One month later he was found to have a low-grade fever without chills for which he was evaluated in a hospital where he was diagnosed with jaundice, ascites, and liver disease. On further evaluation, he was found to have proteinuria. He was then hospitalized at the gastroenterology specialty of Amrita Institute of Medical Sciences and Research Centre for further evaluation and management. Multi-detector computed tomography abdomen contrast was done and obstruction of all the three hepatic veins and a nodular non-homogenous enhancement of the liver confirmed the diagnosis of BCS. A hepatic venogram showed long segment occlusion with multiple collaterals around it. Hepatic vein angioplasty was done and was started on anticoagulation with warfarin and heparin. This case report gives an insight into the fact that health care professionals must take into account that even though it is not very common, they should not eliminate the probability that BCS can also occur as a primary manifestation of APS.

Key words: Ascites, hepatic vein angioplasty, multi-detector computed tomography, antiphospholipid syndrome, Budd-Chiari syndrome.

Introduction

Antiphospholipid syndrome (APS) is an autoimmune systemic disorder that is considered to be a common cause of hypercoagulability with major presentations like pregnancy morbidities including severe pre-eclampsia, miscarriages, late intrauterine fetal death, and thrombotic events like arterial, venous, or microvascular thrombosis. (1) Budd-Chiari syndrome (BCS) is a rarely observed fateful complication in APS with an incidence of less than one percent of cases. (2) BCS is characterized by the congestion of the hepatic venous outflow initiating from sites at any range from the small hepatic veins to the atriocaval junction, irrespective of the cause of obstruction. In less than 5% of the BCS patients, an inflammatory lesion or a tumor is present in the vicinity of the hepatic venous outflow tract. (3) Inherited and acquired hypercoagulable states are the commonly observed prothrombotic conditions related to BCS. Acquired conditions such as myeloproliferative disorders (MPD) including essential thrombocytosis, myelofibrosis, polycythemia vera, paroxysmal nocturnal hemoglobinuria, inherited hypercoagulable states such as protein C or protein S deficiency, antithrombin III deficiency, factor V Leiden mutations and conditions like Bechet's disease, APS, and oral contraceptives are

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the major causes of BCS. (4) Data available from various studies suggest that BCS occurs in about 1/100,000 of the world population. (5) Patients with BCS have shown clinical manifestations like ascites and abdominal hypertension. (6) BCS presenting as a primary manifestation of APS is a rare case and so by reporting pain and hepatomegaly or may have more complicated symptoms related to the prolonged portal the condition of a boy aged 18 years with insidious onset painless abdominal distension and pedal edema, we would like to depict the fact that Budd-Chiari syndrome is also an inevitable cause of APS.

Case report

A male patient aged 18 years was hospitalized at our unit of medical gastroenterology and hepatology with insidious onset painless abdominal distension for three months and there was no other illness. He then started noticing pedal edema and later he developed low-grade fever without chills for which he was evaluated and found to have jaundice, mild ascites which later progressed to liver cirrhosis with portal hypertension. Child-Pugh scoring was found to belong to Child class B and the model for end-stage liver disease score was found to be 17. He also had complaints of frothy urine and mild proteinuria. Peripheral smear showed normocytic normochromic anemia with thrombocytopenia (hemoglobin 12.2 g/dl, mean corpuscular volume 79.8, platelet count 90,000/ul). Hyperfibrinogenaemia (420 mg/dl) and hypoalbuminemia (2.89 g/dl) were observed. The alkaline phosphatase level was elevated (230.6 IU/l). Elevation in C-reactive protein was found (9.51 mg/l). Anti-cardiolipin antibody immunoglobulin G (IgG) was found to be strongly positive (92.87 IgG phospholipid unit/ml). The total bilirubin level was 2.4 mg/dl and the direct bilirubin level was 0.3 mg/dl. Doppler ultrasound examination indicated hepatomegaly, coarse echotexture of the liver with right hepatic vein not visualized, sluggish flow in middle and left hepatic veins with suspicious narrowing of flow into hepatic inferior vena cava, reversal flow in the portal vein, mild ascites, fibrosis, and gall bladder polyps. Ultrasound sonography correlation showed completely obliterated. Right and middle hepatic veins were faintly seen with the thready flow, the left hepatic vein showed a focal narrowing near its inferior vena cava confluence with the stagnant flow. Gall bladder appeared collapsed. Right mild pleural effusion was noted. Upper gastrointestinal endoscopy showed a snake-skin pattern of mucosa with diffuse erythema in the stomach, early varices, and portal hypertensive gastropathy. Hepatic and inferior vena cava venogram showed caudate lobe hypertrophy causing compression of inferior vena cava with no gradient across the stenosis. The left hepatic venogram showed long segment occlusion with multiple collaterals around it. After discussion with the radiologist and in view of long segment occlusion of the left hepatic vein, he was planned for hepatic vein angioplasty and hepatic vein stenting. Then he was initially started on anticoagulation therapy with warfarin and heparin. During the hospital stay, he developed renal dysfunction for which he was managed with human albumin. After hepatic vein stenting, he showed improvement in ascites. He was started on diuretics and anticoagulation with unfractionated heparin and warfarin. The dose of warfarin was titrated in order to achieve an international normalized ratio (INR) between 2 and 3.

Discussion

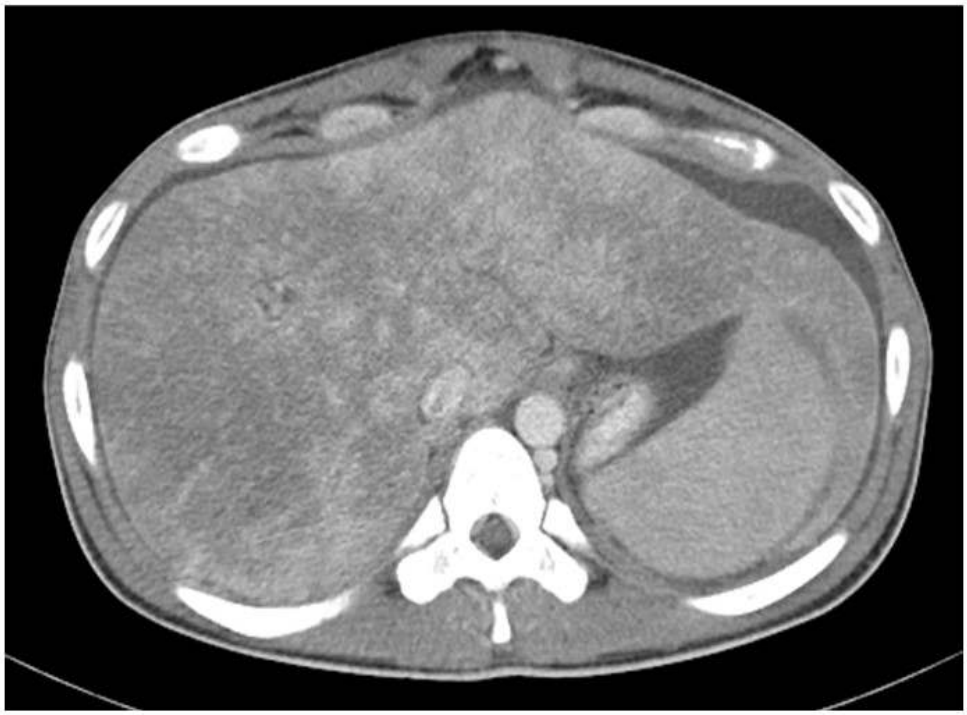
BCS as an initial presentation of APS occurs rarely. The characteristic feature of BCS in the majority of patients include fluid build-up in the abdomen, hepatomegaly, abdominal pain, varicose vein on the lower legs, and collateral vessels present at the wall of the abdomen which occurs as the result of obstruction of the hepatic vein or the inferior vena cava. According to Langlet's recent clinicopathological classification, BCS can be divided into three classes. Type 1 involves acute injury with the onset of obstruction in the hepatic outflow, type 2 involves chronic lesions corresponding to the sequential pattern of hepatic outflow obstruction, and type 3 is presented with acute injury superimposed on chronic lesions. (7) In this case, the patient was observed with a patchy nodular nonhomogeneous enhancement of the liver with volume redistribution and complete obliteration of right hepatic vein and thready flow in middle hepatic vein, which was suggestive of BCS type 2. The classical representation of APS is featured by thrombosis occurring in the veins and arteries, fetal losses as well as reduced platelet count along with antiphospholipid antibodies, anti-beta-2-glycoprotein I, lupus anticoagulant, and anticardiolipin antibody. (8) The involvement of the liver is considered to be the mainstream APS abdominal manifestations such as BCS, hepatic infarction or cirrhosis, portal hypertension, autoimmune hepatitis, biliary cirrhosis, and liver transplantation. **Figure 1** shows the abdominal computerized tomography (CT) image of the patient where the liver involvement of the disease was depicted. These manifestations are then followed by several thrombotic events, which involve many branches of the intestinal vasculature. (9) In **Figure 2**, occlusion of the hepatic veins as well as intrahepatic venous

collaterals are illustrated. As per the revised Sapporo criteria for the classification of APS (also called the Sydney criteria), it is indicated by pregnancy complications, thrombosis, or both in patients having persistent antiphospholipid antibody including anti-beta-2-glycoprotein I (GPI) antibodies, anticardiolipin antibodies, or lupus anticoagulant. Other relevant presentations of the APS that do not belong to this criteria include hematologic complications like thrombocytopenia and hemolytic anemia, renal complications including acute thrombotic microangiopathy and chronic vaso-occlusive lesions, cardiac manifestations like valve vegetations or thickening, dermatologic, and neurologic manifestations. (10) Patients presenting with typical clinical manifestations are evaluated for diagnosis which is more closely associated with the moderate-high titer anticardiolipin antibody and anti-beta-2-GPI, or positive lupus anticoagulant tests. (11) APS in our patient was defined by the hepatic involvement, thrombocytopenia, anemia, and strongly positive anticardiolipin antibody IgG. At present anticoagulation therapy is considered as the cornerstone in the management of thrombotic episodes and prevention of APS. Heparin is commonly used for the management of acute thrombosis. Warfarin with an INR target of 2-3 is the standard choice for secondary prevention of arteriovenous thrombosis, along with this additional low dose aspirin or high-intensity anticoagulation is given for arterial thrombosis. (12) The determination of the factors involved in inducing thrombosis in these classes of patients is essential for the effective management of the disease as well as the prevention of further complications.

Conclusion

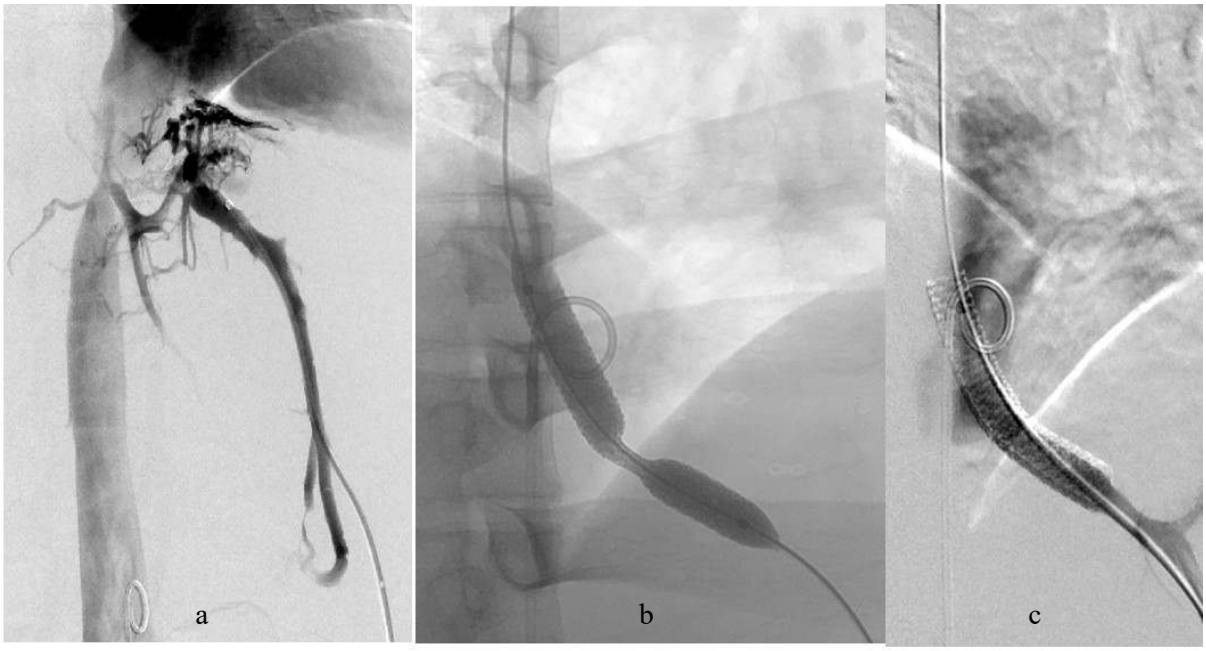
When young patients are presented with hepatic vein occlusion, APS should be considered as one of the differential diagnoses. APS can cause arterial or venous thrombosis, but APS affects the hepatic vein as the initial presentation is rare. Early identification of APS can prevent further complications.

Figure 1. Contrast-enhanced abdominal CT image



Legend: CT=computerized tomography. Contrast-enhanced abdominal CT images obtained in an 18-year-old boy showed patchy enhancement of the liver parenchyma, hypertrophy of the left hepatic lobe and caudate lobe. All three hepatic veins are not visualized. Ascites is also evident.

Figure 2. Occlusion of the hepatic veins as well as intrahepatic venous collaterals



Legend: IVC=inferior vena cava.
a. Initial left hepatic venogram obtained shows occlusion of the distal left hepatic vein and spiderweb-like intrahepatic venous collaterals. Right and middle hepatic veins were completely thrombosed on ultrasound. IVC venogram done at the same time shows normal caliber.
b. The occlusion was crossed and a 8 mm x 55 mm balloon-expandable stent was deployed across the thrombosed segment.
c. Post stenting free flow of contrast is noted into the IVC with the disappearance of the waist intrahepatic venous collaterals.

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