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Report of the Budd-Chiari Syndrome in A 21-Year-Old Boy with JAK-2 V617F: A Case Report and Review of the Literature

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ABSTRACT

Budd-Chiari syndrome (BCS) is considered as a rare disease characterized by thrombotic or non-thrombotic obstruction of the venous outflow from hepatic vein into the inferior vena cava (IVC). A 21-year-old boy was admitted in the hospital with a 4-days history of abdominal pain and vomiting. Colour Doppler evaluation revealed suspicious extrinsic compression, low flow of the inferior vena cava (IVC), and abnormal narrowing of hepatic veins. The patient underwent CT venography, by which caudate lobe hypertrophy, early enhancement of the caudate lobe and central zone of the liver, inhomogeneous mottled liver, flip-flop pattern ensues, and the slit-like narrowing of the hepatic IVC without hepatic veins identification. Furthermore, hepatic venous outflow obstruction suggested the diagnostic features of BCS based on CT imaging findings. Besides, the allele-specific PCR showed Janus kinase 2 (JAK2) V617F mutation.

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INTRODUCTION

Budd-Chiari syndrome (BCS) is considered as thrombotic or non-thrombotic obstruction of the venous outflow from hepatic vein in to the suprahepatic inferior vena cava (IVC), resulted in reduced hepatic perfusion, in turn, leading to ischemic damage, necrosis, and fibrosis as well as portal hypertension [1-6]. Hepatic manifestation of BCS has been defined to be associated with multiple underlying prothrombotic risk factors, such as myeloproliferative disorder. Janus kinase 2 (JAK2) V617F mutation has been reported to be the first step for diagnosis of a myeloproliferative neoplasia underlying a BCS, contributing to a more severe form of BCS, but manageable by current therapies [7]. A portion of MPNs didn't show the JAK2 V617F mutation, but different mutations have been attracted attentions in patients with MPN. This case report highlights the presence of the BCS in a patient with JAK2 mutation.

Case Presentation

A 21-year-old boy was admitted to the emergency room in Baqiyatallah Hospital with a 4-days history of abdominal pain, vomiting, and fatigue. He described persistent generalized abdominal pain along with nausea. Our patient showed little improvement by exertion, but it was not pain-free. He felt his abdomen larger and had experienced shortness of breath in the past few days, which worsened over time, especially during sleep. The patient visited a local clinic with non-bloody diarrhea before admission to hospital. The patient's urine was pale and had decreased volume but no burning or recurrence. The patient had no history of a specific illness and had no problem except occasional headaches, while vital signs were stable. There was no discoloration or lesion on the skin. Except for mild abdominal swelling and mild noise reduction in both lung and shifting dullness, there was no other finding. The neurological evaluation showed no abnormal findings.

The liver function tests showed a slight increase in liver enzyme levels (Wbc: 8.2; Hb: 16.5; Plt: 430; AST: 139; ALT: 60; Total bilirubin: 3.5; Direct bilirubin: 1.5; international normalized ratio [INR]: 1.1), where the aspartate aminotransferases (AST/ALT) showed their increased levels. An initial Grey scale Ultrasonogram of the abdomen at emergency ward reported abnormal ascites with mild hepatomegaly and splenomegaly. A diagnostic and therapeutic tap was performed for ascites fluid, which contained high SAAG and high protein. Accordingly, continued evaluation of the laboratory for possible causes was initially unhelpful. Viral, metabolic, and infectious causes were finally found to be negative.

Regarding to ascites, suspicion of thrombotic etiology remained. An ultrasonogram of the abdomen revealed abnormal ascites with mild hepatomegaly and splenomegaly. Colour Doppler examination appeared suspicious extrinsic compression, and low flow of IVC with abnormal narrowing of hepatic veins which were not seen well with their entire course. In addition, portal vein was slightly dilated (15 mm) with slow hepatopetal flow by a mean velocity of 12 cm/s and loss of respiratory phasicity. Therefore CT venography showed a broad spectrum of changes, where hepatomegaly was observed with mottled liver parenchyma (nutmeg liver), followed by caudate lobe hypertrophy and splenomegaly with a large volume of ascites, hyperattenuating structure, and early enhancement of the caudate lobe and central zone of the liver, hypo attenuation of the peripheral zone of the liver (flip-flop appearance), and the intracavitary pressures to the inferior vena cava (IVC) with severe narrowing as well as the slit-like appearance of IVC without hepatic veins identification (**Figure 1**).

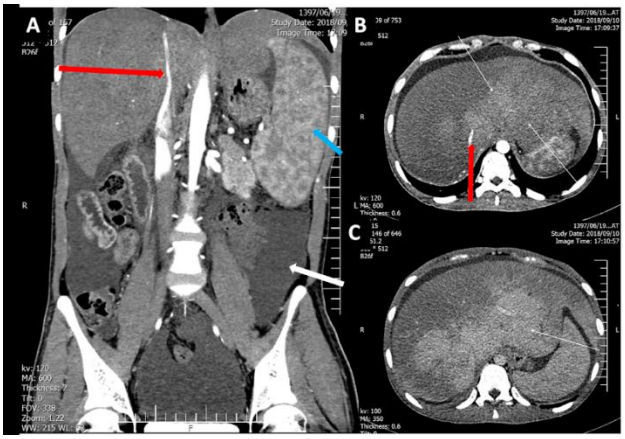

Fig 1: Coronal (A) and axial (B&C) CT scan with contrast show classic imaging finding of the BCS: 1- Splenomegaly (blue arrow) with a large volume of ascites (solid white arrow); 2-hepatomegaly and caudate lobe enlargement with inhomogeneous mottled liver parenchyma (nutmeg liver); 3-Hyperattenuation and early enhancement at the caudate lobe and central zone of the liver (thin white arrows), lack of enhancement and hypo attenuation of the peripheral zone of the liver (flip-flop appearance); 4-Severe narrowing and slit-like appearance of IVC (red arrow) with an inability to identify hepatic veins.

The present evidence suggests a diagnosis of BCS for the patient based on findings on CT scans.

Our patient underwent endoscopy and evaluation of varicose veins, where was labeled grade 1. Subsequently, in addition to the initiation of an anti-coagulant, cardiac consultation was requested for the possibility of reopening the vascular path with thrombolysis or other methods such as vascular stenting or angioplasty, which were not possible for the patient. A baseline evaluation was initiated for determining the underlying cause of BCS, which included inflammatory, immunologic, and thrombotic causes. Finally, a JAK-2 V617F mutation was reported for our patients using allele-specific polymerase chain reaction. Treatment for this patient included prevention of thrombosis by the administration of heparin followed by enoxaparin, leading to the improvement of liver functions. Decrease abdominal ascites and abdominal pain and elevated serum albumin levels in subsequent visits indicate success in the improvement of liver functions. The evaluation was not performed for normal indocyanine green clearance but ALT and serum bilirubin levels along with INR remained normal and no ascites recurrence demonstrated control of liver injury in the acute phase.

DISCUSSION

BCS occurs due to obstruction of hepatic venous outflow, resulted in congestion and portal hypertension, consequently, leading to liver damage. BCS can occur as acute onset in 20% of cases, while 5% of cases exhibit acute liver failure [8-10]. Several reports described the clinical manifestation and pathological condition of BCS.

The presentation of BCS is described to be linked to hepatic venous outflow obstruction and collateral venous ducts, leading to classifications of disease into multiple groups (i.e., fulminant, acute, subacute, and/or chronic), [3]. Due to the heterogeneous clinical manifestation of BCS, all causes of acute hepatitis, acute liver failure, and chronic liver disease should be considered; however, validation of the prognostic value of the mentioned classification needs confirmation [11].

BCS has been contributed to increased serum levels of bilirubin and alkaline phosphatase, as well as increased serum transferase levels, while serum albumin level has been indicated to show a moderate decrease [5,10]. In the present study, a slight increase in liver enzyme levels was found. Laboratory tests such as PT or INR, bilirubin, creatinine, Albumin, and ALT are considered as prognostic indicators for BCS. It is noteworthy that laboratory tests (e.g., INR, albumin, blood chemistry tests, and renal function assessment) can be helpfully applied in the prediction of the severity, and monitoring of therapeutic response, as well as the possibility of mortality [12].

A definitive CT scan evidence of a hepatic venous outflow obstruction shows the diagnostic features of BCS in our patient.

The diagnostic imaging (e.g., Doppler ultrasonography, computed tomography [CT] and magnetic resonance imaging [MRI] could be the starting point in the diagnosis of BCS. Gray-scale sonography in combination with Color and pulsed Doppler sonography has been previously described as the first-choice approach in the diagnosis of Budd-Chiari syndrome. Doppler ultrasound offers a sensitivity of >75%. CT scan and MRI modalities are capable of demonstrating hepatic parenchyma with high spatial resolution, and extrahepatic collateral network, thereby providing the related PVT, and scheduling a treatment strategy. It is worth noting that a CT scan is better able to demonstrate regions with reduced perfusion or necrosis in the liver parenchyma [13-16], and are able to show clearance of contrast from the caudate lobe and patchy enhancement

associated with portal perfusion, therefore a multidisciplinary strategy can be considered for the diagnosis when suspected clinical diagnosis is obvious [16]. In the present study, Gray-scale sonography of the abdomen revealed abnormal ascites with mild hepatomegaly and splenomegaly. Colour Doppler examination highlighted suspicious extrinsic compression, and low flow of IVC with abnormal narrowing of hepatic veins. In addition, portal vein was slightly dilated (15 mm) with slow hepatopetal flow.

Half of the patients with primary BCS have been estimated to have a myeloproliferative disorder, so evaluation of the Janus kinase 2 (JAK2) V617F mutation in peripheral granulocytes can be very helpful in recognition of this disease [6]. Our case showed the occurrence of BCS, as well as JAK2 V617F mutation.

CONCLUSION

In summary, our case report demonstrated unique properties of BCS, which were associated with the degree of obstruction, as well as the occurrence of JAK2 V617F mutation.

CONFLICT OF INTEREST

None

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