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Case Report

Successful treatment of Budd-Chiari Syndrome with rivaroxaban in a 6-week-old Bangladeshi infant

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Budd-Chiari syndrome (BCS) is the clinical spectrum presenting with hepatic venous outflow obstruction from the hepatic veins to the junction of the inferior vena cava (IVC) and the right atrium. This syndrome is rare in infants and children, which leads to misdiagnoses or delayed diagnoses. Clinical presentations may be non-specific. A high index of suspicion and imaging findings may help in early diagnosis of this condition. We report a rare case of BCS in a 6-week-old male infant who presented with jaundice and gradual abdominal distension. He was successfully treated with rivaroxaban.**[Paediatr Indones. 2022;62:138-42; DOI: 10.14238/pi62.1.2022.138-42**].

Keywords: *abdominal distension; Budd-Chiari syndrome; children; hepatic venous outflow*

Budd-Chiari syndrome is a heterogenous group of clinical conditions associated with hepatic venous outflow obstruction,[1] and first recognized by Budd and Chiari in 1845 and 1899, respectively.[2] It is characterized by a triad of ascites, hepatomegaly, and right upper quadrant pain. It is rare in children and infants.[3] This syndrome may have a non-specific presentation in children. It is considered primary if an endoluminal lesion (thrombosis/web) is the prime cause of obstruction of hepatic venous outflow, and secondary if an obstruction occurs due to the lesion being outside the venous system (tumor, abscess, etc.).[4] It can also be classified as (i) acute, usually developing within 1 month or symptomatic for less than 6 months; (ii) subacute, insidious onset taking as long as 3 months' time to become asymptomatic, usually having minimal/trace or no ascites; and (iii) chronic, with disease duration of 6 or more months or presenting with signs of portal hypertension.[5-7] Budd-Chiari syndrome can be diagnosed by radiological imaging and liver biopsy.[8] Here we report a rare case of BCS in a 6-week-old male infant who presented with gradual abdominal distension and jaundice. Doppler ultrasound was used to confirm the diagnosis of Budd-Chiari syndrome.

The case

A six-week-old male infant presented to the Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University (BSMMU) with a history of gradual abdominal distension and jaundice for 2 weeks. There was no history of fever, passage of pale stool, or dark

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urine. On examination, he was mildly pale, icteric, with normal vitals and normal anthropometry. The liver was palpable 5 cm from right costal margin and splenomegaly (sized 4cm) ascites was noted. Laboratory investigations including radiological imaging are shown in **Table 1**. Complete blood count showed hemoglobin of 12 g/dL (11.5-15 g/dL) and total white blood cell (WBC) count of 4,000 cells/mm^3. The patient had an elevated erythrocyte sedimentation rate (ESR) of 45 mm in 1st hr and thrombocytopenia (platelet 58,000/mm^3). Other routine tests such as renal function and urine examination were normal. However, his liver function test showed prothrombin time (PT) of 23 sec, INR 1.95, and APTT 80 sec. Other lab results were serum ALT 55 U/L as well as serum bilirubin total 12.7 mg/dL and direct 10 mg/dL (direct hyperbilirubinemia).

Table 1. Investigations

Investigations	Results
Liver function tests	
Serum albumin	28g/L
Serum bilirubin	
Total	12.7 mg/dL
Direct	10 mg/dL
Prothrombin time	23 sec
INR	1.95
Serum ALT	55 U/L
Complete blood count	
Hb	12 g/dL
ESR	45 mm in 1st hr
WBC	4,000/mm^3
Differential count	
Neutrophil	21%
Lymphocyte	68%
Macrophag	11%
Platelet	58,000/mm^3
Serum creatinine	0.48 mg/dL
Serum electrolyte	
Na	140 mmol/L
K	4.8 mmol/L
Cl	98mmol/L
TCO_2	22 mmol/L
USG of abdomen	Moderate ascites
Doppler study	
At admission	Hypoechoic thrombus seen at the proximal part (1.5 mm) of IVC, suggestive of BCS, moderate ascites, normal duplex study of portal vein and hepatic vein.
1 week after oral rivaroxaban	Normal
Chest X-ray P/A view	Normal
Echocardiography	Normal cardiac anatomy with good bi-ventricular function

Color Doppler study showed hypoechoic thrombus at the proximal part (1.5 mm) of the IVC along with moderate ascites, suggestive of BCS, whereas Doppler study of the portal vein and hepatic vein was normal. Hence, we diagnosed the patient with BCS due to the presence of thrombus in the IVC. He was treated with an oral anticoagulant (rivaroxaban at 0.8mg/kg/day, single dose for 1 week), fresh frozen plasma (FFP) transfusion, and injectable antibiotics.

Discussion

Budd-Chiari syndrome is a clinical condition characterized by hepatic venous outflow obstruction at any level from the small hepatic veins to the atriocaval junction.[2] It is rare in children and infants. One study of 177 patients showed that children comprised only 5% of those affected.[7] In the largest pediatric study of 9 South African cases, membranous obstruction of the IVC was seen.[9] Likewise, our patient had obstruction in the IVC.

The BCS is categorized as primary or secondary on the basis of etiology and site of venous outflow obstruction. Primary BCS arises from within the lumen of the veins or venules and occurs due to thrombi, webs, or endophlebitis. Secondary BCS results when lesions such as a tumor, abscess or cyst, cause extrinsic compression of the hepatic venous outflow tract.[2] Children symptomatic for less than 6 months are considered to have acute BCS, whereas those with disease duration of 6 or more months or signs of portal hypertension (PHT) are termed as chronic BCS.[7] Our case had primary BCS with chronic presentation, as the cause was thrombus in the IVC and despite presentation at 1 month of age, he had signs of portal hypertension (splenomegaly and ascites).

A previous study reported that male children are more commonly affected with BCS than females, presenting with ascites, hepatomegaly, jaundice, splenomegaly, encephalopathy, or GI bleeding.[10] Our male patient presented with ascites, jaundice, hepatomegaly, and splenomegaly. Doppler USG is helpful for the diagnosis of BCS, reportedly establishing the diagnosis of BCS in 95% of cases.10 Similarly high diagnostic accuracy (>80%) using Doppler was shown by others.[7,11] Doppler ultrasonography can reveal

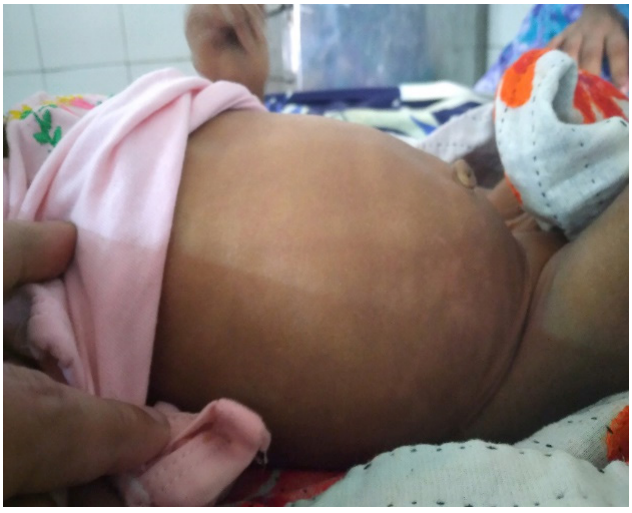

Figure 1. The patient's abdomen at admission

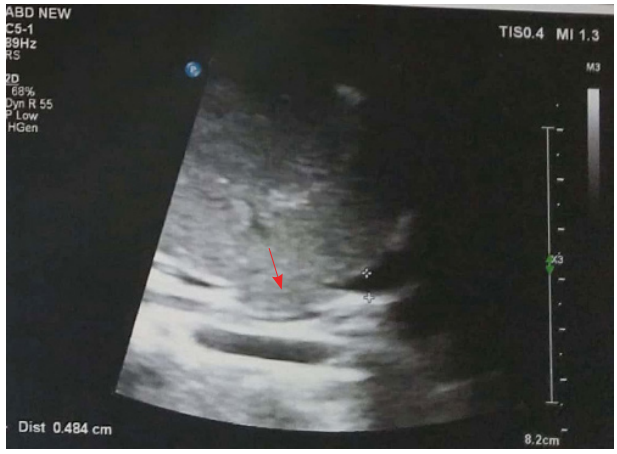

Figure 2. Doppler USG showing thrombus in proximal IVC (red arrow) at admission

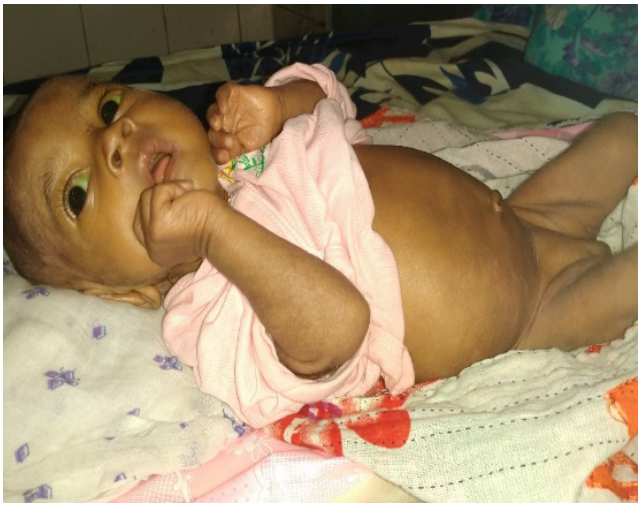

Figure 3. The patient after rivaroxaban

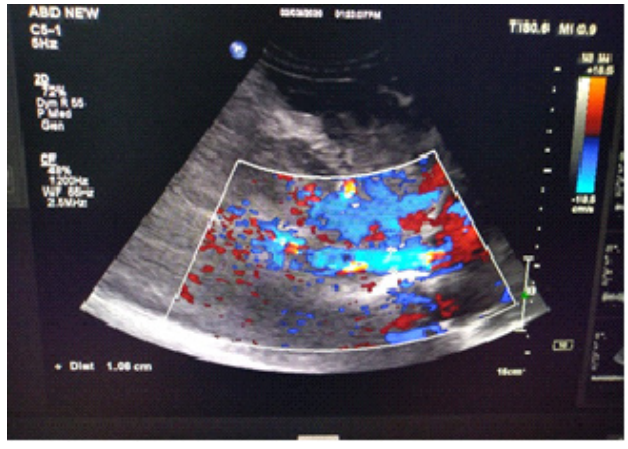

Figure 4. Doppler USG (no thrombus after rivaroxaban)

specific findings in the hepatic or caval veins, such as stenosis, thrombosis, fibrotic cord, or insufficient recanalization of the vessel, along with caudate lobe hypertrophy which are highly specific for BCS.[12] In our patient, the diagnosis of BCS was confirmed by Doppler USG of the portal vein, IVC, and hepatic vein, revealing a thrombus in the proximal part of the IVC.

Other imaging findings for BCS may include hepatic veins without flow signal and with a spider-web appearance, reversed or turbulent flow, as well as collateral hepatic venous circulation. Non-visualization or tortuous hepatic veins are common, but these are non-specific sonographic findings of BCS.[1] No such findings were seen in our case.

Contrast-enhanced CT, MRI scans, magnetic resonance venogram (MRV), and hepatic scintigraphy may be useful to determine the presence of any thrombus or to detect the site and cause of obstruction.3 Thrombosis may be the inciting event for membranous web formation, so all patients should be evaluated for underlying hypercoagulative states.[2] We could not perform other such investigations, due to financial constraints of our patient's family. Moreover, the Doppler study had already confirmed the diagnosis of BCS in our patient.

To assess hepatic involvement, serum bilirubin, aminotransferase levels, alkaline phosphatase, and albumin should be evaluated. Liver biopsy can reveal

congestion, liver cell loss, and fibrosis predominantly located in the centrilobular area, which can differentiate BCS from veno-occlusive disease.[13] Our patient was icteric but other liver function tests were normal, so we did not perform a liver biopsy.

The BCS and some cardiac disorders, such as tricuspid regurgitation and constrictive pericarditis, may have similar clinical manifestations. In such patients, echocardiography is helpful to differentiate from BCS.[1] Echocardiography showed normal findings in our patient.

Different therapeutic options for BCS management include supportive medical treatment and anticoagulation therapy, whereas surgical measures include balloon angioplasty, decompressive porto-systemic shunt procedures, transjugular intrahepatic portosystemic shunt (TIPS), and liver transplantation for end-stage liver disease.[14,15] If patients have a contraindication to warfarin or progressive disease, rivaroxaban can be a reasonable alternative anticoagulant.[16] Our patient had coagulopathy, so rivaroxaban (at 0.8mg/kgBW/day, single dose) was given for a week. The repeat Doppler showed no thrombus, so the drug was discontinued, and patient's attendant was advised for routine follow up. Despite the high efficacy of rivaroxaban, there is still a risk of bleeding during its use.[17] There was no complication of bleeding seen in our patient.

The prognostic indicators of BCS are ascites, elevated prothrombin time, encephalopathy, and altered serum levels of sodium, albumin, creatinine, as well as bilirubin, cirrhosis and the presence of portal hypertension.[18] Our patient had features of portal hypertension, but he responded to oral rivaroxaban clinically and biochemically, as his ascites and jaundice improved after treatment. Hence, the prognosis of our patient was good.

In conclusion, BCS is rare in children and infants. Children may have variable presentation, but ascites, hepatomegaly, fulminant hepatic failure, despite relatively normal liver function tests. Doppler ultrasonography can confirm the diagnosis. A timely diagnosis along with appropriate treatment with an oral anticoagulant like rivaroxaban may prevent the need for operative procedures and liver transplantation.

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