Budd Chiari Syndrome in Children


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Abstract

Budd-Chiari syndrome (BCS) is a rare disorder presenting with hepatic venous outflow obstruction from the level of the hepatic veins to the junction of the inferior vena cava (IVC) with the right atrium. It is rare in infants and children so, delay in diagnosis or misdiagnoses are very commonly seen. It results from either primary or secondary cause. Hypercoagulable state can be identified in majority of the cases. The clinical presentations may vary from asymptomatic to fulminant liver failure. A high index of suspicion and imaging findings may help in early diagnosis of this condition. Doppler ultrasonography can be the initial diagnostic investigation of choice. The treatment options include medical therapy along with surgical measures including liver transplantation for end-stage liver disease.

Keywords: Budd-Chiari syndrome, Children, Doppler ultrasonography, Hepatic venous outflow obstruction.

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Introduction

Budd-Chiari Syndrome (BCS) is a heterogenous group of clinical conditions that is associated with hepatic venous outflow obstruction.1 Budd-Chiari syndrome (BCS) was 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 It may have a wide range of presentation from being asymptomatic to acute liver failure.4 Depending on the cause of obstruction, BCS may be primary due to thrombosis/web or secondary when the lesion outside the venous system (tumor, abscess, etc.).5 It can also be classified as (i) acute, develops usually within 1 month or symptomatic for less than 6 month (ii) subacute, insidious onset, it may take as long as 3 months time, usually having minimal/traces or no ascites and (iii) chronic with disease duration of 6 or more months or signs of portal hypertension present.5,9,10 It can be diagnosed by radiological imaging and liver biopsies.6 Appropriate anticoagulation along with regular follow-up may have a good outcome.10

Epidemiology

BCS is a rare condition with varying prevalence geographically. The estimated incidence of BCS in Western countries is 1 in 2.5 million person year.11 Data from outside of the Western world, however, vary significantly. Japan had an estimated incidence of 0.13 per million per year in 1989.12 In Nepal, BCS had an incidence of 2.50 per million per year that accounted for 17% of the patients presenting with chronic liver disease with.13 BCS occurs in 1/100 000 of the general population worldwide.13 Men are affected more in Asia whereas women are commonly affected in Europe.14,15,16

Etiology and Pathogenesis

BCS may be primary due to thrombosis/web or secondary when the lesion is outside the venous system (tumor, abscess).17 The Western countries, thrombosis of hepatic vein is the common cause of primary BCS, whereas in Asians, the cause is idiopathic or related to anatomical anomalies, like membranous obstruction.18

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Irrespective of the cause, hepatic venous outflow tract obstruction results in increased hepatic sinusoidal pressure leading to portal hypertension. The hepatic venous stasis and congestion results in hypoxic damage and ischemic necrosis of adjacent hepatic parenchymal cells.\(^1\) The long term hepatic congestion leads to sinusoidal thrombosis and increased pressure, which ultimately promotes hepatic fibrosis.\(^2\) If no measures are taken to relieve the sinusoidal pressure, then nodular regeneration, fibrosis and ultimately cirrhosis occur.\(^3\)

Several multicenter data showed a combination of several prothrombotic conditions in 25% to 46% of the patients with primary BCS,\(^1,15-22\) which was more than expected in the general population. The prothrombotic conditions found in BCS, in particular the classical type, include: Factor V Leiden mutation, protein C deficiency, protein S deficiency, prothrombin (PT) gene mutation, antithrombin deficiency, antiphospholipid syndrome and paroxysmal nocturnal haemoglobinuria.\(^23\) BCS may also be associated with systemic inflammatory diseases, such as Behçet’s disease, vasculitis, sarcoidosis and other connective tissue diseases.\(^23\)

**Clinical Presentation**

Patients may have a wide range of presentation from being asymptomatic to acute liver failure.\(^4\) One study has shown that about 15% of the patients remain asymptomatic with preservation of some hepatic venous outflow.\(^24\)

Patients of BCS commonly present with abdominal pain (61%), ascites (83%) and hepatomegaly (67%).\(^15\)

Other clinical features include jaundice, splenomegaly, oesophageal bleeding (5%) and hepatic encephalopathy (9%).\(^10,15\)

**Diagnosis**

In most of the cases, Doppler USG can confirm the diagnosis of BCS. One study showed that Doppler USG established the diagnosis of BCS in 95% cases.\(^10\) Asimilarly high diagnostic accuracy (>80%) of Doppler has been shown by others.\(^1,25\) Doppler ultrasonography shows the 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 Budd-Chiari syndrome.\(^26\)

Some other imaging findings for BCS may include hepatic veins without flow signal, and with spider-web appearance, reversed or turbulent flow, collateral hepatic venous circulation. Non-visualization or tortuous hepatic veins are common but these are non-specific sonographic findings of BCS.\(^1\)
Contrast-enhanced CT, MRI scans, Magnetic resonance venogram (MRV) and Hepatics cintigraphy may be useful for determining the presence of any thrombus or detect the site and cause of obstruction. It is seen that thrombosis may be the inciting event for membranous web formation, so all patients should be investigated for the underlying hypercoagulative states. Venography is done when diagnosis is uncertain or to see the anatomy prior to treatment plan.

If imaging fails to show the obstruction then liver biopsy is the other investigation option and it shows congestion, liver cell loss and fibrosis predominantly located in the centrilobular area which can differentiate BCS from veno-occlusive disease.

BCS and some cardiac disorders, like tricuspid regurgitation and constrictive pericarditis may have similar clinical manifestations. So, in such patients, echocardiography is helpful to differentiate from BCS. Other routine tests to see hepatic involvement include- Serum bilirubin, Serum aminotransferase levels, Serum alkaline phosphatase and Serum albumin.

Management
The management options for BCS patients include supportive medical treatment, 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. If patients have a contraindication to warfarin or progressive disease, Rivaroxaban can be a reasonable alternative anticoagulant.

Despite the high efficacy of Rivaroxaban, the risk of bleeding still occurs during its use.

The prognostic indicators are ascites, elevated prothrombin time, encephalopathy, and altered serum levels of sodium, albumin, creatinine, and bilirubin, cirrhosis and the presence of portal hypertension.

Conclusion
BCS is often misdiagnosed as a case of chronic liver disease. Doppler ultrasonography can confirm the diagnosis. A timely diagnosis along with appropriate treatment with oral anticoagulant like-Rivaroxaban may prevent the need of operative procedures of major surgery and liver transplantation.

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References


