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EDITORIAL

Budd–Chiari syndrome: a focussed and collaborative approach

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Introduction

Budd–Chiari syndrome (BCS) is a rare disorder caused by obstruction of the hepatic venous outflow tract at any level between the small hepatic veins and the right atrium, hence also known as hepatic venous outflow tract obstruction (HVOTO) (Fig. 1a–c). This obstruction leads to venous stasis resulting in congestive hepatopathy [1]. This congestive hepatopathy results in increased sinusoidal pressure with hepatic sinusoidal thrombosis as evidenced by fibrin deposition within sinusoids [2]. This sinusoidal thrombosis in turn causes reduced hepatic perfusion leading to ischemia and necrosis of hepatocytes especially in perivenular zones leading to fibrosis and portal hypertension [1, 2].

BCS may result due to primary venous problem or may be secondary to compression/invasion of venous outflow by a space occupying lesion within or outside the liver [3]. The onset of disease may be fulminant/acute, sub-acute or chronic and accordingly the presenting complaints of the patients [3]. The recognizable causes for BCS include inherited or acquired hypercoagulable state. Other risk factors for the development of BCS include pregnancy, malnutrition, and the use of oral contraceptives. There is a difference in presentation of BCS in developed nations and the developing nations. Acute presentation is more common in the West, whereas sub-acute or chronic form is more often seen in the East [1–4]. Further, while myeloproliferative neoplasms (MPN) account for 35–50% of cases in European countries with JAK-2 mutations seen in about 90% of patients, no major causal factors have been identified in patients from China [4]. The frequency of MPNs is also low in India, Middle East and Mediterranean regions.

Clinical presentation and diagnosis

Clinical presentation may vary from no symptoms to abdominal discomfort or ascites with splenomegaly and signs of portal hypertension in chronic cases. Subacute disease may present with ascites or variceal bleeding. In acute disease, patients present with tender hepatomegaly, ascites and jaundice [1, 3, 4].

The diagnosis of BCS is made by clinical presentation and confirmatory investigations. Deranged liver function tests are a cardinal feature; however, it may remain normal in some patients. Serum aspartate and alanine aminotransferase levels may increase up to more than five times the upper limit of the normal in fulminant and acute BCS [3–5]. Findings suggesting a suspicion for BCS are presented in Table 1. Whenever one or more of these findings are present, then BCS should be ruled out by further investigations. Radiological imaging is the most important tool to confirm the diagnosis and should be carried out even when there is low clinical suspicion [3–5].

BCS may affect any age group but is commonly seen in third to fifth decade [6]. The clinical presentation is different for pediatric and adult patients and same has been reported. However, the disease is frequently seen involving adolescents but the literature remains sparse. In this issue of the Journal, Shukla et al. present data of 43 adolescents with a different presentation for this age group [6]. They found hepatomegaly leading to abdominal discomfort without ascites as the most common presentation as compared to ascites being a common presentation in adults as well as pediatric population in the previous reports. Also, thrombophilic disorders unlike adults were uncommon in these adolescents, as also seen in pediatric age. Outcomes to the treatment were better in adolescents as compared to children and similar to adults [6].

Shukla and colleagues highlight in this article that the disease has a milder form of presentation in adolescents,

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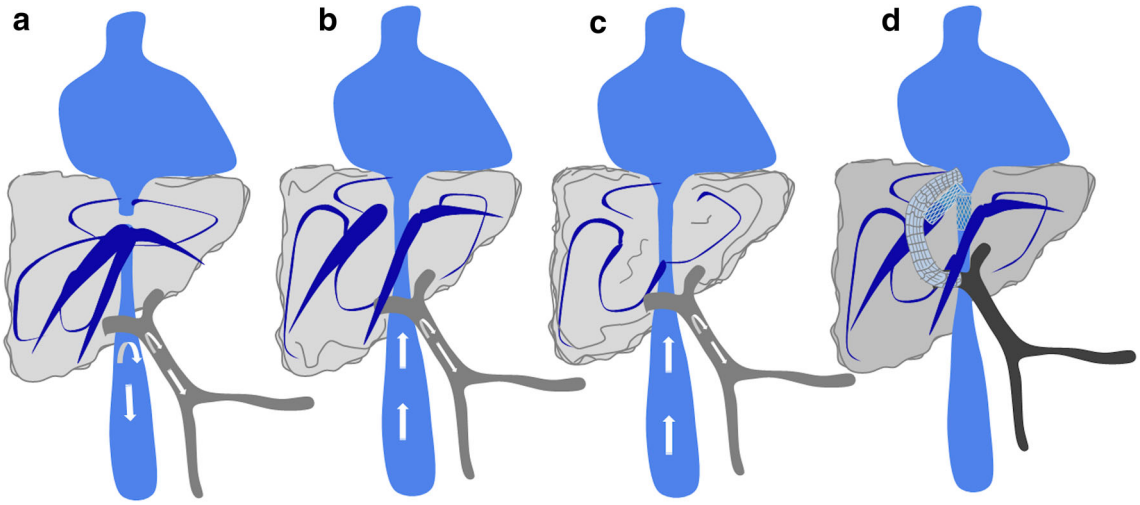

Fig. 1 **a–d** Diagrammatic representation **a** showing interrupted suprahepatic IVC leading to formation of small intrahepatic veno-venous collaterals trying to drain into right atrium with reversal of flow in IVC and portal vein (treatment in this case would be IVC recanalization), **b** shows patent IVC with occlusion hepatic veins at the osteum and treatment in this case would be recanalization of the best hepatic vein. **c** shows patent IVC and complete occlusion of all three native hepatic vein with very small intrahepatic veno-venous collaterals. The treatment in this case would be creation of portosystemic shunt (TIPS/DIPS). **d** shows the treatment option available in all three varieties of outflow occlusion consisting of IVC/Hepatic vein recanalization or creation of TIPS/DIPS

Table 1 Guide for suspecting HVOTO

When to suspect HVOTO?
1. Visible abdominal/back wall veins
2. Portal hypertension in the absence of
Hepatitis B virus infection
Hepatitis C virus infection
Chronic alcohol use
3. Unexplained chronic liver disease in children and adolescents
4. Liver decompensation in post-partum female or female using oral contraceptives
5. Sudden Liver decompensation in young male with history of steroid use
6. Disproportionately high fibroscan in comparison to the clinical presentation

which could be due to better angiogenesis and collateral formation, secondary to hormonal changes in this age group and hence, the response to medical management is better as compared to pediatric and adult patients [6]. This hypothesis is based on a study demonstrating better collateral formation in young rabbits due to high VEGF levels in young subjects. However, authors did not study the expression of VEGF in the study population, hence, leaving this hypothesis open for discussion and further study. This finding suggests that severe form of disease seen in adults may probably be the result of delayed diagnosis. This may open up a debate whether patients diagnosed with BCS with minimal or no symptoms should be offered treatment to decongest the liver to prevent progression of disease or the treatment to decongest the liver should be offered only if patients become symptomatic for the disease while patients being only on medical management.

Liver stiffness measurements (LSM) using Fibroscan can be a promising tool to decide regarding the time of intervention. In asymptomatic patients, serial LSM may be used to assess the changes in liver congestion with medical management and in case of rising LSM, the patient may be offered endovascular treatments for liver decongestion [7]. LSM can also be used as a non-invasive tool to assess hepatic congestion before and after venous outflow restoration [8]. It is an indirect method to assess the outcome and therapeutic benefits of interventions aimed at decongesting the liver [8].

The management of patients with BCS remains complex mostly due to a plethora of clinical presentations, resulting from venous flow, potential of collateral development, vascular compliance, endothelial integrity and pro-coagulant status of an individual. These local factors in addition to causing venous occlusion, also lead to development of hepatic parenchymal injury by ischemia and compression. These could result in hepatic fibrosis which if progressive could mimic cirrhosis of the liver. Liver biopsy, though challenging, is an important guide to detect the level of fibrosis/necrosis and to plan treatment in BCS. For fulminant disease, the jury is clear and mandates liver transplantation; whereas there is no specified guideline available for the management of BCS with or without cirrhosis.

There is, therefore, a need for a comprehensive algorithm taking into consideration both the venous occlusion and the stage of liver disease while deciding treatment for BCS. The BCS may be subcategorized into three subgroups

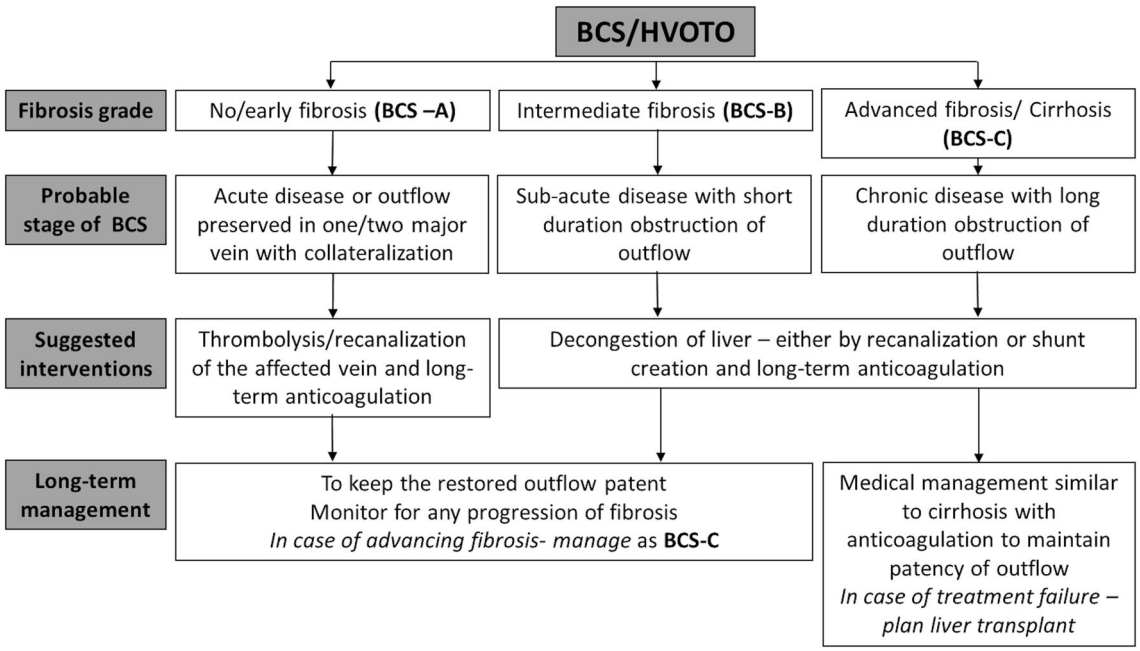

Fig. 2 Algorithm for the management of BCS/HVOTO

(BCS-A–C) depending upon severity of hepatic fibrosis and accordingly treatment may be offered and follow-up may be designed. A simplified algorithm is proposed (Fig. 2).

Management options for BCS include medical, endovascular interventions and surgical, including liver transplantation.

Medical management focuses on control of portal hypertension and ascites with systemic anticoagulation. Medical management is effective in cases with good venous collateralization and is effective in about a quarter of the patients [4, 6]. Anticoagulation remains the most important aspect in the management in all situations (a) whether a prothrombotic disorder is identified or not, (b) whether a patient is only on medical management or requires an endovascular/surgical interventions. As, most patients will require endovascular or surgical intervention, a long-term anticoagulation for maintaining the patency of the collateral or recanalized vein, transjugular intrahepatic porto-systemic shunt (TIPS)/surgical shunt is mandatory [4, 5].

The goal of endovascular treatment is to relieve hepatic congestion resulting in restoration of hepatocyte perfusion and relieving portal hypertension as well as its symptoms thereby halting further deterioration of hepatic function (Fig. 1) [9]. Whenever possible, early recanalization of the obstructed hepatic venous outflow should be the first line of treatment in BCS, because these patients with recanalizable hepatic vein/inferior vena cava (IVC) generally have mild fibrosis with good post intervention outcome [7]. For the patients reported by Shukla et al., whether such an approach should be undertaken remains a debatable question, due to the adolescent age.

Surgical management is considered if endovascular treatments are not feasible and includes membrane resection with/without IVC reconstruction, portosystemic/mesoatrial/portoatrial shunts, and liver transplant [4, 5]. Liver transplant remains the preferred treatment for patients with fulminant BCS [4, 5, 7]. Most authors agree that not all patients with BCS should undergo liver transplant and that this therapeutic option should probably be used exclusively in patients with fulminant BCS or in patients with chronic cirrhosis [5, 9].

Outcome and prognosis

Several scores have been available and evaluated in BCS, such as, the Child–Pugh, MELD, Clichy PI, Rotterdam score, New Clichy PI and BCS-TIPS and may be used to predict the outcomes and prognosis of the disease [6]. The prognosis is better if disease is identified early and treatment is started [7]. Whether these approaches are feasible and provide long-term benefit in the pediatric and adolescent patients remains to be seen. The young BCS provides a unique opportunity to study the natural history and long-term outcome of interventions, to the hepatology and radiology community; one more reason for collaborative work!

Compliance with ethical standards

Conflict of interest Amar Mukund and Shiv Kumar Sarin declare there are no potential conflicts of interest.

Research involving human participants and/or animals This research does not involve human participants and/or animals.

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