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Review Article

Budd Chiari Syndrome: Review Article

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Abstract

Budd Chiari Syndrome (BCS) includes disorders causing hepatic venous outflow obstruction either at the level of the Hepatic Veins (HV) or at the Inferior Vena Cava (IVC) because of which raised hepatic sinusoidal pressure and portal hypertension occurs. By diagnostic imaging techniques, the nature, location and extension of the obstruction can be found out. The high clinical suspicion of BCS patients may undergo hepatic venography or venacavography directly so that recanalization of the obstructed segment could not be delayed.

Keywords: Liver; Portal vein; Hepatic venous outflow obstruction; Thrombosis; Ascites

Introduction

Budd-Chiari Syndrome (BCS) is a rare entity because of which hepatic venous flow gets obstructed leading to hepatomegaly, Ascites, and abdominal pain. It could be due to either thrombotic or non thrombotic disorders. It was first described by Budd in 1845 and later by Hans Chiari in 1899. If Hepatic outflow obstructed regardless of the cause or level of obstruction then that is primary BCS. The obstruction can be anywhere in the small Hepatic Veins (HV) to the orifice of the Inferior Vena Cava (IVC) into the right atrium. Hepatic venous outflow obstruction due to compression or invasion by extravascular lesions, which can be benign or malignant diseases such as abscesses, carcinoma of kidney and liver, or secondary to cardiac or pericardial diseases is known as secondary BCS. Veno-Occlusive Disease (VOD), also called as Sinusoidal Obstruction Syndrome (SOS), which is due to toxins, nonthrombotic obstruction of prehepatic veins is excluded from the definition of BCS [1-3].

Epidemiology

BCS is extremely rare and its incidence is about 1 case per million populations per year. In Asia predominant cases are of pure IVC or combined IVC/HV block, whereas in western countries pure HV obstruction predominates. No supporting data which suggest that sex affects the predisposition to BCS. Most common age of presentation is in the third or fourth decade of life and it commonly affects young to middle-aged adults, but it may also occur in children or elderly persons [4-7].

Aetiology

The primary BCS is mainly a venous disease (thrombosis or phlebitis) and secondary BCS is related to compression or invasion by a lesion outside the veins like benign or malignant tumors, abscesses, intrahepatic cysts and hematomas [8]. The risk factors which are responsible for BCS are mentioned in Table 1.

Pathophysiology

Venous flow obstruction between hepatic venules and the IVC is the main pathophysiologic event. Silent BCS denotes occlusion of a single hepatic vein whereas overt BCS occludes at least 2 hepatic veins. Hepatomegaly occurs due to obstruction of the hepatic vein which in further leads to venous congestion of the liver. Hepatomegaly stretches the liver capsule because of which abdominal pain occurs. Most common lobe enlarged is caudate lobe because blood is shunted through it directly into the IVC. The hepatic vein or IVC obstruction causes increased hydrostatic pressure in portal capillaries which alters vascular pressure gradients and results in dilation of hepatic sinusoids and fluid leakage into the interstitial space. Hepatic function is affected by the amount of stasis and resultant hypoxia. The increased sinusoidal pressure itself can sometimes causes hepatocellular necrosis [8-10].

The chronic changes that occur after obstruction includes centrilobular fibrosis which can manifest within weeks, and periportal nodular regeneration, progressive fibrosis and cirrhosis which takes months to develop. The literature mentioned that up regulation of specific genes in chronic BCS contributes to liver destruction through the stimulation of extracellular matrix proliferation those results in liver fibrosis. The genes commonly involved in this process are matrix metalloproteinase 7 and superior cervical ganglion 10 (SCG10), which are increased in expression, and thrombospondin-1, which is decreased.

Clinical Presentation

The triad of BCS are abdominal pain, ascites, and hepatomegaly. Right upper quadrant pain is the main symptom in acute onset obstruction. Abdominal distention is because of Ascites. Patients can be asymptomatic for a while or present with few symptoms initially if liver has time to develop collaterals and decompress. Marked dilatation of the subcutaneous vein on the trunk has high specificity but low sensitivity for IVC block. On Physical examination patient presents with icterus, Ascites, hepatosplenomegaly, and ankle edema, dilated and engorged veins. If the BCS progresses further, it can lead to liver failure and portal hypertension. The four main clinical variations are acute disease of the liver, sub acute disease of the liver, fulminant disease of the liver and liver decompensation.

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Table 1: Risk Factors associated with BCS.

A. Primary BCS
1. Hematological disorders: Polycythaemia Rubra Vera, Antiphospholipid antibody syndrome myeloproliferative disorder.
2. Inherited thrombotic diathesis: Hyperhomocysteinemia.
3. Coagulopathies: Protein C and S deficiency, AT-III deficiency, Factor V Leiden deficiency.
4. Others: Paroxysmal nocturnal hemoglobinuria, Behchet disease, Hypereosinophilic syndrome, granulomatous venulitis and ulcerative colitis, oral contraceptive use, Pregnancy.
B. Secondary BCS
1. Tumors: Hepatocellular carcinoma, renal cell carcinoma, Leiomyosarcoma, Adrenal carcinoma, Wilms tumor, Right atrial myxoma.
2. Alveolar Hydatid Cyst.
3. Parasitic & Non-Parasitic Cysts and Abscess.
4. Abdominal Trauma.

- **Acute and subacute forms:** This is characterised by sudden occurence of icterus, abdominal pain, ascites, hepatomegaly, and renal failure.
- **Chronic form:** It is most common form of BCS presents with increasing Ascites, renal impairment (50% cases) and absent jaundice.
- **Fulminant form:** It is an uncommon presentation in which patient present with icterus, Ascites, painful hepatomegaly, and renal failure [11].

In certain situation, as mentioned below, we have to consider the BCS.

1. Sudden onset of Ascites with tender hepatomegaly
2. Massive Ascites with relatively normal liver function
3. liver biopsy showing sinusoidal dilation after ruling out of cardiac disease
4. Severe hepatic failure associated with enlarged liver and Ascites
5. Chronic liver disease with unknown causes.
6. Coagulatioin abnormality with underlying liver disease [12,13].

The complications of BCS may include the hepatic encephalopathy, gastrointestinal bleeding, hepato-renal syndrome and complications secondary to hypercoagulable state. BCS is diagnosed on the basis of history, clinical features, hepatic function tests and imaging studies.

Laboratory evaluation

Liver function tests consist of aspartate, alanine aminotransferases and alkaline phosphatase which can be normal or elevated. Serum albumin, bilirubin and prothrombin level can be normal or increased. Ascitic fluid evaluation reveals clues to the diagnosis, including raised protein concentrations (>3 g/dL) and serum Ascites-albumin concentration gradient (>1.1 g/dl) are suggestive of Budd Chiari syndrome. Increased serum creatinine level is due to prerenal dysfunction.

Imaging studies

Early identification and evaluation of the disease requires detailed imaging of hepato biliary system which is also useful to determine the precise level and degree of obstruction.

Doppler ultrasonography: Specific findings on Doppler ultrasonography for HV obstruction includes a) large Hepatic vein with absent flow signal or reversal of flow, b) collaterals developed will connect hepatic vein or intercostal vein with their continuous flow, c) a spider web appearance in the vicinity of HV ostia, d) absent or flattening of hepatic vein waveform without fluttering. Also, the nonspecific findings include heterogeneous hepatic parenchyma, intrahepatic collateral veins, splenomegaly, caudate lobe hypertrophy, Ascites and collateral veins [14,15].

Computed tomography (CT) scanning: In acute forms CT scan will show patches with increased enhancement in the central portion of the liver and decreased enhancement in the peripheral region due to portal backflow whereas subacute and chronic forms characterized by liver atrophy with an enlarged caudate lobe and multiple intrahepatic and extra hepatic collateral veins seen. Chronic forms also show many regenerative hypervascular nodules of various sizes [16,17].

Magnetic resonance imaging (MRI): MRIs of acute and subacute forms show peripheral areas with low intensity signals on T1 and high intensity signals on T2. But there were no such differences noted in peripheral and central zones with either of the signals. A regenerative nodule appears as isointense or hypointense on T2 weighted scans and they are hyperintense on T1 images. MRI provides adequate and appropriate information regarding the path of the IVC and hepatic veins and it's also useful for assessing the extent of obstructions in hepato- biliary system [18,19].

Hepatic venography, CT venography and magnetic resonance venography (MRV): Hepatic venography depicts the changes as follows: complete narrowing of hepatic vein, may or may not be associated with a stenosis of the intrahepatic IVC, intrahepatic collateral veins and spider web appearance. Inferior cavography demonstrates stenosis or occlusion of the IVC. Gold standard for evaluation of the IVC and hepatic veins is Digital Subtraction Angiography (DSA) which further allows the evaluation of level of obstruction, the presence of an occlusive membrane, and it also explains differentiation between a thrombus and a tumor. It also allows visualization of collateral veins that developed intra and extra hepatically. Therapeutic interventions can be considered at the same time, like including balloon angioplasty, localized thrombolysis, and stent placement.

Liver biopsy

Percutaneous liver biopsy useful in assessing prognosis if liver transplantation is planned. It is mainly useful to know the degree of hepatocellular damage and presence of fibrosis. Findings after Pathologic evaluation are (1) high-grade venous congestion and centrilobular liver cell atrophy, (2) thrombi located in the terminal hepatic venules.

Management

Clinical and anatomical characteristics of patients will denote the modality of treatment to be choose. Different types of treatment

available are medical, surgical and radiological. The choice of therapy depends on the clinical and anatomical characteristics of individuals.

Medical therapy

For patients who do not have symptoms and normal liver enzymes medical therapy alone is recommended. It's also useful in patients whose hepatic tissue is not necrosed.

Anticoagulant therapy: If the cause of BCS is hematologic disorder anticoagulation is very useful. Immediate initiation of anticoagulation with low molecular weight heparin followed by vitamin K antagonists is the first measure to be taken to maintain an International Normalized Ratio (INR) of 2 to 3. Warfarin interferes with hepatic synthesis of vitamin K- dependent coagulation factors, used for the prophylaxis and treatment of venous thrombosis and thromboembolic disorders.

Thrombolytic therapy: Thrombolytic therapy has limited evidences and is inconclusive. Medications used for thrombolysis are streptokinase, urokinase, recombinant tissues plasminogen activator (rt-PA).

Radiological intervention

Local thrombolysis performed by an interventional radiologist is preferable over systemic thrombolysis as the risk associated with systemic thrombolysis is higher. Other radiologic procedures include balloon angioplasty, stent placement or a Transjugular Intrahepatic Portacaval Shunt (TIPS).

Balloon angioplasty and stenting: For patients having only small length stenoses percutaneous recanalization by angioplasty or stent of the HV or the IVC is considered, and it serves as an adjunct to medical treatment. Recanalization restores hepatic blood flow and it decompresses the liver without compromising the blood flow to it.

Transjugular intrahepatic portosystemic shunt (TIPS): When other techniques mentioned previously fails for any clinical or technical reasons, TIPS is preferred. This technique is having high efficiency in splanchnic decompression hence it is widely used. TIPS serves as a bridge to transplantation for patients with severe hepatic failure as it causes improvement of liver functions very rapidly.

Surgical procedures

Portosystemic shunts: Various shunts which gave good results are portocavale, mesocavale and mesoatriale shunts. To decompress the liver in the scenario of decreased hepatic venous outflow, portal venous system serves as outflow tract via Portosystemic shunting.

Liver transplantation: Patients not responding to radiological and surgical decompression procedures liver transplantation is considered as best choice of treatment. It is also indicated in patients with decompensate cirrhosis or fulminant acute liver failure [20-26].

Prognosis

The natural history of BCS is not well known. Early presentation, low Child-Pugh score, no Ascites or easily treatable Ascites and low serum creatinine are associated with good prognosis. After liver transplantation 5-year survival rate is 70%. The prognosis is bad for patients who remain untreated, death occur due to liver failure within 3 months to 3 years from the time of diagnosis.

In conclusion, BCS is a rare clinical entity characterised by hepatic venous outflow obstruction. Due to recent advances in interventional techniques, radiological intervention is currently considered the primary treatment for this disorder. These interventional procedures consist of recanalization, balloon dilatation, stent placement and creation of a porto-systemic shunt. BCS is associated with high mortality in the paediatric age group. Survival is poor in patients with decompensate liver disease and those with an acute clinical presentation.

References

1. Janssen HL, Garcia-Pagan JC, Elias E, Mentha G, Hadengue A, Valla DC, et al. Budd-Chiari syndrome: a review by an expert panel. J Hepatol. 2003;38(3):364-71.
2. DeLeve LD, Valla DC, Garcia-Tsao G. Vascular disorders of the liver. Hepatology. 2009;49(5):1729-64.
3. Shin N, Kim YH, Xu H, Shi HB, Zhang QQ, Colon Pons JP, et al. Redefining Budd-Chiari syndrome: A systematic review. World J Hepatol. 2016;8(16):691-702.
4. Plessier A, Valla D. Budd-Chiari Syndrome. Semin Liver Dis. 2008;28(3):259-69.
5. Valla D. The diagnosis and management of the Budd-Chiari syndrome: consensus and controversies. Hepatology. 2003;38(4):793-803.
6. Shrestha S, Okuda K, Uchida T, Maharjan K, Shrestha S, Joshi B, et al. Endemicity and clinical picture of liver disease due to obstruction of the hepatic portion of the inferior vena cava in Nepal. J Gastroenterol Hepatol. 1996;11(2):170-9.
7. Valla D. Hepatic venous outflow tract obstruction etipatho- genesis: Asia versus the West. J Gastroenterol Hepatol. 2004;19(s7):S204-11.
8. Boutachali S, Arrivé L. Budd-Chiari syndrome secondary to hepatocellular carcinoma. Clin Res Hepatol Gastroenterol. 2011;35(11):693-4.
9. Bittencourt Mde J, Dias CM, Lage TL, Barros RS, Paz OA, Vieira Wde B. Behçet disease in association with Budd- Chiari syndrome and multiple thrombosis-Case report. An Bras Dermatol. 2013;88(3):448-51.
10. Carvalho D, Oikawa F, Matsuda NM, Yamada AT. Budd- Chiari syndrome in association with Behçet's disease: review of the literature. Sao Paulo Med J. 2011;129(2):107-9.
11. Kyriakidis AV, Vezygiannis I, Pyrgioti M. Budd Chiari Syndrome. Ann of Gastroenterology. 2008;21(4):223-8.
12. Darwish M, Plessier A, Hernández-Guerra M, Fabris F, Eapen CE, Bahr MJ, et al. Etiology, Management, and Outcome of the Budd-Chiari Syndrome. Ann Intern Med. 2009;151(3):167-75.
13. Aydinli M, Bayraktar Y. Budd-Chiari syndrome: Etiology, pathogenesis and diagnosis. World J Gastroenterol. 2007;13(19):2693-6.
14. Boozari B, Bahr MJ, Kubicka S, Klempnauer J, Manns MP, Gebel M. Ultrasonography in patients with Budd-Chiari syndrome: diagnostic signs and prognostic implications. J Hepatol. 2008;49(4):572-80.
15. Sakugawa H, Higashionna A, Oyakawa T, Kadena K, Kinjo F, Saito A. Ultrasound study in the diagnosis of primary Budd-Chiari syndrome (obstruction of the inferior vena cava). Gastroenterol Jpn. 1992;27(1):69-77.
16. Patil P, Deshmukh H, Popat B, Rathod K. Spectrum of imaging in Budd Chiari syndrome. J Med Imaging Radiat Oncol. 2012;56(1):75-83.
17. Maetani Y, Itoh K, Egawa H, Haga H, Sakurai T, Nishida N, et. al. Benign hepatic nodules in Budd-Chiari syn- drome: radiologic-pathologic correlation with emphasis on the central scar. AJR Am J Roentgenol. 2002;178(4):869-75.
18. Virmani V, Khandelwal N, Kang M, Gulati M, Chawla Y. MDCT venography in the evaluation of inferior vena cava in Budd-Chiari syndrome. Indian J Gastroenterol. 2009;28(1):17-23.
19. Lu X, Xu K, Zhang QQ, Yang C, Li SD, Li JS, et al. Study on between magnetic resonance venography and digital subtraction angiography on the inferior vena cava obstructive interface morphology of Budd-Chiari syndrome. Zhonghua Gan Zang Bing Za Zhi. 2011;19(12):923-6.

20. Min A, Atillasoy E, Schwartz M, Thiim M, Miller C, Bodenheimer H. Reassessing the role of medical therapy in the management of hepatic vein thrombosis. Liver Transpl Surg. 1997;3(4):423-9.

21. Darwish S, Valla D, de Groen P, Zeitoun G, Hopmans J, Haagsma E, et al. Determinants of survival and the effect of portosystemic shunting in patients with Budd-Chiari syndrome. Hepatology. 2004;39(2):500-8.

22. Li T, Zhai S, Pang Z, Ma X, Cao H, Bai W, et al. Feasibility and midterm outcomes of percutaneous transhepatic balloon angioplasty for symptomatic Budd-Chiari syndrome secondary to hepatic venous obstruction. J Vasc Surg. 2009;50(5):1079-84.

23. Casado M, Bosch J, García J, Bru C, Bañares R, Bandi J, et al. Clinical events after transjugular intrahepatic por- tosystemic shunt: correlation with hemodynamic findings. Gastroenterol. 1998;114(6):1296-303.

24. Watanabe H, Shinzawa H, Saito T, Ishibashi M, Shirahata N, Miyano S, et al. Successful emergency treatment with a transjugular intrahepatic portosystemic shunt for life-threa- tening Budd-Chiari syndrome with portal thrombotic obs- truction. Hepatogastroenterol. 2000;47(33):839-41.

25. Attwell A, Ludkowski M, Nash R, Kugelmas M. Treatment of Budd-Chiari syndrome in a liver transplant unit, the role of transjugular intrahepatic porto-systemic shunt and liver trans- plantation. Aliment Pharmacol Ther. 2004;20(8):867-73.

26. Gaviria SC, Ramírez AC, Espinoza Herrera YP, Gutiérrez JCR. A review of Budd chiari Syndrome. Rev Col Gastroenterol. 2016:31(3):241-50.