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Case Report

Rapid Onset Ascites: A Rare Case Report of Budd-Chiari Syndrome

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Abstract

Budd-Chiari Syndrome is an uncommon condition characterized by clinical features related to hepatic venous outflow obstruction resulting either from thrombotic or non-thrombotic causes. Presentations may vary from asymptomatic to acute fulminant hepatic failure. A meticulous history, examination and imaging studies are invaluable for a prompt diagnosis and initiation of time-sensitive treatment. This report presents a case of a young female with rapid onset ascites due to prothrombotic state of unknown cause with occlusion of all hepatic veins on doppler ultrasonography, without liver impairment.

Key words: Budd- Chiari Syndrome (BCS), hepatic vein occlusion, portal hypertension, Doppler ultrasound

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Introduction

Budd- Chiari Syndrome (BCS) is an uncommon clinical condition defined by hepatic venous outflow obstuction, at any level from the hepatic veins to the union of IVC into the right atrium, and may involve solely the hepatic veins, the IVC or both. The definition excludes cardiac, pericardial and sinusoidal obstruction syndromes. It was first coined in 1845 by British internist George Budd who described 3 cases of hepatic vein thrombosis due to abscess-induced phlebitis and in 1899 by Austrian pathologist Hans Chiari, who reported the primary pathological description of a liver with "obliterating endophlebitis of the hepatic veins". It has been described to occur in 1 in 100000 in the general population.

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Primary BCS presents with endoluminal obstruction within the vein either due to thrombus, webs or stenosis. Secondary BCS is caused by extrinsic compression upon the veins by tumors of the liver or kidneys, polycystic kidneys, abscesses and cysts, large nodules of focal nodular hyperplasia[1] and may even occur due to compression of hepatic veins following hepatic resection[2], blunt abdominal trauma or liver herniation.[3] Studies have associated the presence of an underlying prothrombotic disorder in primary BCS where at least one hereditary or acquired hypercoagulable condition was identified in 75% of patients, with more than one etiological factor in 25% cases,[4] with myeloproliferative diseases among the most common causes. Clinical presentations of abdominal pain, ascites, hepatomegaly, variceal and gastrointestinal hemorrhage or encephalopathy, depending on the degree of obstruction. Occlusion of 2 or more hepatic veins compromises venous outflow resulting in increased sinusoidal and portal pressures with reduced sinusoidal flow, hepatic congestion, interstitial fluid filtration with development of ascites and post-sinusoidal portal hypertension. Hypoxic hepatocyte damage eventually leads to the histological findings of non-inflammatory centrilobular necrosis in 70% cases with progressive fibrosis, nodular regenerative hyperplasia and cirrhosis.[5] Initial abdominal ultrasonography with Doppler study is vital; to show the extent of venous abnormalities and

liver morphology. Other relevant investigations for further assessment of possible etiologies may be needed if no apparent cause is found. Treatment depends on the clinical presentation, cause and anatomic location of the occlusion. Medical management involves control of portal hypertension, ascites and anticoagulation. If medical management is insufficient, most patients will require either surgical or endovascular interventions.

Case Report

A 22 year old unmarried female of Bangladeshi origin presented with abdominal distension for 8 days, initially mild and rapidly increased over the first 3 days. It was associated with anorexia, vomiting and a constant dull upper abdominal pain with postprandial fullness, worsened by taking heavy meals with no relieving factors. She also complained of feverish feeling with occasional shortness of breath on lying down without cough or chest pain. She had no history of leg edema, calf muscle pains, changes in urine volume or colour, frothy urine, weight loss, joint pain, rashes, yellow discoloration of skin or eyes with no previous altered bowel habits, melena or hematemesis. She denied any episodes of spontaneous lactation or nipple discharge. She reported a 6-month history of irregular menstruation in the form of oligomenorrhea and menorrhagia. She was prescribed oral Norethisterone 5mg three times a day and Domperidone, 11 days back, taking them for 2days and discontinued after experiencing side-effects of abdominal distension. She gave a childhood history of jaundice with no previous hospitalization, surgery, blood transfusion or donation, intravenous drug use or sexual exposure. Personal history revealed a normal level of physical activity but with reluctance to drink adequate amounts of fluids despite the ongoing hot, humid climate. She received a 2nd dose of COVID-19 vaccination (Pfizer) 1 ½ months back. Her family members are well with no significant medical conditions or similar illnesses. On examination, she was found to be ill-looking, mildly anaemic, non-icteric and mildly dehydrated, blood pressure 110/80mmHg, pulse 90bpm with regular rhythm, respiratory rate 20 breaths/min with some shortness of breath, SpO_2 97% in room air, axillary temperature of 101°F. She had normal facial features, normal JVP, absence of clubbing, leukonychia, skin rash, palpable lymph nodes or thyroid gland and an admission weight of 49 Kg. Abdomen was moderately distended with an abdominal girth of 86cm with no visible masses or peristalsis, engorged vessels, scars marks or spider nevi. Moderate ascites was present with tenderness in the right hypochondriac and epigastric region with no palpable masses and no organomegaly. Bowel sounds were present with no hepatic and renal bruits or venous hum. No other stigmata suggestive of chronic liver disease or features of hepatic encephalopathy was present. There was mild left sided pleural effusion with normal precordial examination with no murmurs. She had normal breast size with normal axillary and pubic hair distribution. Higher psychic functions, nervous system, fundoscopic and slit lamp examinations were normal.

Her blood count showed haemoglobin 9.3gm/dl, ESR 22mm in 1st hour, total count of WBC 10500/cu mm, neutrophil 74%, lymphocytes 22% Hct 31.2% Total RBC 4.03 million/cu mm, Platelet count 180000/cu mm, MCV 77.4fL, MCH 23.1pg, RDW 20.7%, Microcytic hypochromic anaemia on PBF, serum creatinine 1.11mg/dl, serum albumin 3.39gm/dL, serum ALT 42 U/L, prothrombin time 16 seconds, INR 1.42, Na^+133 mmol/l, K^+3.8mmol/l, CRP 6.1mg/L, Normal Urine R/E with 24 hour UTP 0.07gm/24hrs , serum bilirubin 0.9 mg/dL, HBsAg and Anti-HCV antibody negative, serum TSH 3.29uIU/mL, FSH 0.25mIU/ml, LH 0.22mIU/ml with elevated Prolactin > 70.41ng/ml. Abdominal ultrasound showed mild to moderate ascites with left sided minimal pleural effusion, ascitic fluid study revealed protein 2.07g/dl and albumin 1.06g/dl (SAAG: 2.3g/dL), Total cell 03/cu mm, lymphocytes and mesothelial cells, no malignant cells, normal ADA 3.478 U/L, GeneXpert for MTB negative with negative MT test. Second line investigations revealed elevated LDH (510 U/L) and D-dimer (4.59 ugFEU/ml), serum ferritin 18.4ng/ml, serum iron 31 ug/dL. Elevated ANA-55.21AU/ML, AntidsDNA negative, elevated CA-125 190 U/ml, negative Anti-smooth muscle antibody and Antiphospholipid antibodies. ECG

showed sinus tachycardia with a normal Echocardiography 2D, M-mode and Colour Doppler. Upper GI Endoscopy showing multiple small-sized oesophageal varices in lower part, gastritis and duodenal polyps. Stool for H. Pylori antigen was negative. Multiple axial non-contrast and contrast Abdominal CT showed coarse hepatic parenchyma with prominent caudate lobe and ascites. Fibroscan revealed a liver stiffness median of 75kPa. Doppler ultrasound (Fig. 1) showed complete occlusion of all hepatic veins replaced by echogenic cord-like structure with no vascular flow, portal vein and inferior vena cava was not dilated, with no thrombus or flow reversal seen. She was diagnosed a case of Budd- Chiari Syndrome with liver cirrhosis with portal hypertension. Following an initial paracentes is, there was rapid reaccumulation of ascites within 24 hours. Subcutaneous low molecular weight heparin (Enoxaparin) was initiated of 40mg 12 hourly with oral Furosemide and Spironolactone with repeat paracentesis.

She was closely monitored and treated for dehydration and hypotensive episodes with daily body weight and abdominal girth measurements which showed gradual reduction in both (45kg and 81cm respectively). Gastroenterology specialist consultation was taken and after 6 days of Enoxaparin, she was discharged after both clinical and biochemical improvements of serum ALT (36 U/L) and D-Dimer (1.44ugFEU/ml). Oral Rivaroxaban 10 mg once daily, Furosemide 40mg once daily and Spironolactone 150mg daily in divided doses was prescribed. Referral consultation to an Interventional Hepatology specialist was advised with a plan for liver biopsy. However, she presented back after 11 days, with a two-day history of vomiting, lower abdominal pain and fever, moderately dehydrated, BP 90/60mmHg, axillary temperature 101°F, lower abdominal tenderness with mild hepatomegaly. Investigations revealed haemoglobin 10.3gm/dl, ESR 31mm in 1st hour, total count of WBC 13100/cmm, neutrophil 84%, CRP 7.5mg/L, elevated D-Dimer 6.56ugFEU/ml, serum ALT 27U/L. Management was done with intravenous fluids and re-initiated subcutaneous low molecular weight heparin (Enoxaparin) 40mg 12 hourly. On the 5th day, repeat D-Dimer was 0.67ugFEU/ml, prothrombin time 20 seconds, INR 1.87. A review Doppler ultrasound revealed a partial occlusion of the middle hepatic vein near confluence with no vascular flow, with normal flow signal in right and left hepatic veins. Subsequent endoscopic variceal band ligation was performed which was followed by transfemoral Inferior Venocavogram (Fig 1) that revealed a long segment narrowing of the hepatic and suprahepatic portions of inferior vena cava extending from D-11 (IVCP 15mmHg) to D-8 (IVCP 4mmHg). Treatment was continued with subcutaneous LMWH (Enoxaparin) 20 mg OD and diuretics and advised for further follow up visits.

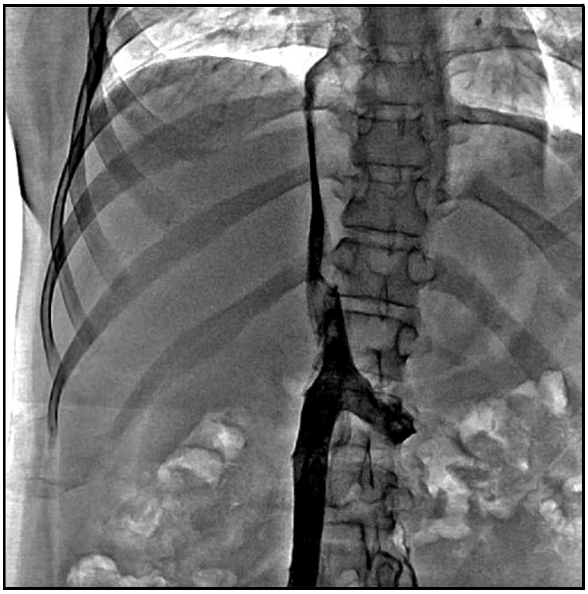

Fig 1: Inferior Venocavogram showing long segment narrowing of Hepatic and Suprahepatic portions of the IVC, extending from D-12 to D-8

Discussion

A diagnosis of Budd- Chiari Syndrome in clinically suspected patients is usually made with presence of one of the following; (1) abrupt onset of ascites and painful hepatomegaly, (2) Massive ascites with relatively preserved liver function, (3) Sinusoidal dilation in liver biopsy without heart disease, (4)Fulminant hepatic failure with abrupt onset of ascites and hepatomegaly, (5) Unexplained chronic liver disease and (6) Liver disease with an associated thrombogenic disorder.[5]

The index case presented with abrupt onset ascites with moderately preserved liver function, proceeding with a differential of BCS alongside assessment for the common causes of chronic liver disease and ascites in the region was necessary. A thorough history helped to identify any underlying conditions of thrombophilia, antiphospholipid syndrome and autoimmune conditions.

Data suggested a varying prevalence among countries; in Nepal it appeared to be the leading cause of liver diseases, however was found to be rare in Japan and France. The location of obstruction also differed as some studies showed predominant inferior vena cava or combined hepatic vein and inferior vena caval involvement in Asia; whereas pure hepatic vein obstruction is common in Western countries. There is a slight predominance in males with median age of 45 years in Asia, whereas in the West, a female preponderance with median age of 35 years is reported.[6, 7, 8,9]

Clinical presentations include asymptomatic cases (15-20%) with single hepatic vein thrombosis with venous hepatic collaterals; fulminant hepatic failure (5%) developed over a few days with massive hepatomegaly, ascites, elevated liver enzymes, hyperbilirubinemia, encephalopathy, renal failure and coagulopathy. Acute BCS (20%) develops within one month, usually with intractable ascites and abdominal pain. Chronic BCS (60%) presents with congestive cirrhosis with portal hypertension, progressive ascites, splenomegaly, esophageal bleeding in 5-15% cases, renal failure in 50% cases with normal liver function tests.[10, 11,12] Potential environmental risk factors for thrombosis in our patient includes the recent use of oral contraceptive pills combined with inadequate fluid intake and significant dehydration. Oral contraceptive pills, particularly high estrogen- containing pills, predisposes a higher risk of hepatic vein thrombosis (relative risk 2.37) similar to risks of myocardial infarction, stroke and venous thromboembolism.[13] An underlying thrombophilia is usually associated with oral contraceptive use or pregnancy in BCS patients. The recent vaccination for COVID-19 is also a potential precipitating factor for vaccine-induced thrombosis as reported in some cases, however in our case; it could not be confirmed as a vaccine-related complication. Acquired hypercoagulable states, particularly primary myeloproliferative diseases (MPD) have been found to be the leading cause of hepatic vein thrombosis in 20% cases [14] with a prevalence of polycythemia vera in 10-40% of cases. A majority of BCS patients have MPD which is not apparent at the time of presentation. Inherited hypercoagulable states such as Factor V Leiden was found to be present in 25% of BCS patients in Western countries.[14] Other predisposing conditions such as antiphospholipid syndrome was found in about 25% of cases[15] and malnutrition has been described as a risk factor in low income populations. As this patient did not have suggestive history and our investigations did not reveal characteristic results related to MPD or thrombophilia, with no significant family history, these conditions were not evaluated further. The cause of her menstrual irregularity with altered gonadotropin and prolactin levels could not be identified and it may signify an underlying pathology, possibly related to her elevated levels of CA-125 and ANA antibodies. Further evaluations for autoimmune conditions and occult malignancy were needed.

A diagnostic workup of liver function tests including mildly elevated S. ALT and prothrombin time with moderate low S. albumin indicated mild functional impairment with elevated D-Dimer suggesting hypercoagulability. Ascitic fluid protein of < 2.5g/dl (2.07g/dl) with a serum-ascites albumin gradient of 2.3g/dL (≥ 1.11) indicated presence of portal hypertension. Initial abdominal ultrasound is indicated to show expected findings of hepatosplenomegaly, caudate lobe enlargement, inhomogeneous hepatic parenchyma, lack of visualization of hepatic veins, compressed IVC and ascites. Doppler ultrasound is the imaging technique of choice with sensitivity and specificity of 85%[16] with findings of hepatic veins devoid of flow signal, stagnant, reversed or turbulent flow, spider web appearance of hepatic veins, intrahepatic collaterals or a fibrous hyperechoic cord replacing a hepatic vein are all indicative of BCS.[17] The caudate lobe has direct venous drainage into the IVC, often undergoing

compensatory hypertrophy as seen in this patient. MRI may be performed to show hepatic vein thrombosis and evaluate IVC patency however it is not as effective as sonography. The diagnosis of BCS is confirmed by a 'spider-web pattern' on hepatic venography and inferior cavography for the evaluation of hepatic veins, extent of thrombus, caval pressures and IVC occlusion. These may be required when considering surgical shunts and endovascular interventions. Access and availability of such imaging studies guided by experts, have yet to be established in most centers, as was experienced in this case. Treatment should be centered on symptom control with treatment of any identified underlying condition. Early initiation of anticoagulation is recommended in all patients to prevent further extension of the venous thrombus, with low molecular weight heparin initially, followed by warfarin for long term anticoagulation with a target INR 2.0-2.5. Endovascular management will depend on the type of venous abnormality, techniques such as percutaneous transluminal angioplasty (with or without stenting), catheter-directed thrombolysis and endovascular portosystemic shunt creation (transjugular intrahepatic portosystemic shunt procedure/TIPS).

Liver transplantation may be indicated in cases of fulminant hepatic insufficiency and end-stage chronic liver disease with 5-year survival rate of 70%.[18] Prognosis remains poor in untreated patients, with death resulting from progressive liver failure in 3 months to 3 years from the time of diagnosis.[19]

In Bangladesh, the prevalence of BCS remains largely unknown, although a few case studies have been documented with different ages, presenting features and etiologies.[20,21,22,23,] This may be due to constraints in most clinical settings with limited diagnostic resources coupled with therapeutic challenges. In our patient, administration of subcutaneous LMWH appeared to improve her hypercoagulable state as evidenced by the comparatively lessened extent of the hepatic vein occlusions on subsequent Doppler ultrasound, however due to the presence of long segment IVC narrowing; further management could not be pursued due to the limited availability of such advanced interventions. Patient education plays a vital role from initiation, whether regarding diagnostic procedures, management of symptoms, understanding and avoiding the precipitating risk factors and allowing for a good quality of life with the need for appropriate life-long follow up.

Conclusions

Budd Chiari Syndrome is an uncommon condition of hepatic outflow obstruction and may have a varied presentation. Physicians should have knowledge of such conditions particularly in the assessment of patients with rapidly accumulating ascites and abdominal pain with no identifiable cause. A thorough history and examination is essential for diagnosis. Non-invasive Doppler ultrasonography is an invaluable investigation, without which such cases would go undiagnosed or misdiagnosed.

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