Case Report

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Internal Medicine Section

Budd-Chiari Syndrome as an Initial Presentation of Antiphospholipid Syndrome in a Male

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ABSTRACT

In Budd-Chiari Syndrome (BCS) there is narrowing and obstruction of the veins of the hepatic veins. Patients have upper quadrant abdominal pain, hepatomegaly and/or ascites. Authors hereby, discuss a case report of a 20-year-old male with history of abdominal pain, progressive distension of abdomen and mild jaundice for two months. He had hepatic vein thrombosis as well as lupus anticoagulant and was positive for anti beta 2-glycoprotein I antibody indicative of antiphospholipid syndrome. The patient was worked up for hypercoagulable states in view of unusual site of venous thrombus. Patient recovered after being treated with prolonged anticoagulation and hepatic vein stenting. The link between antiphospholipid syndrome and BCS is well documented in the literature, but occurrence of BCS due to primary antiphospholipid syndrome is rare. Early identification, treatment of underlying cause can prevent chronic BCS and liver cirrhosis.

Keywords: Anticoagulants, Hepatitis, Hepatic vein stenting, Hepatic vein thrombosis

CASE REPORT

A 20-year-old man visited the Outpatient Department with history of abdominal pain, progressive distension of abdomen and mild jaundice for two months. He consulted a nearby doctor and was prescribed tab. aceclofenac 100 mg twice a day for two weeks. He denied ever receiving blood transfusions, taking ayurvedic medications, or abusing alcohol.

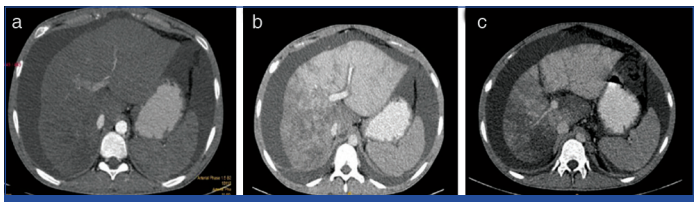
The physical examination revealed icterus. Abdomen veins were distended extending upto the thoracic wall. Liver was palpable 3 cm below right costal margin, and moderate ascites was present. The patient was admitted and further worked up. Blood investigations revealed hyperbilurubinaemia and deranged liver enzymes [Table/Fig-1].

Parameters	Result	Reference values
Haemoglobin (g/dL)	13.5	12.3-15.3
White blood cell count (µL)	5000	4000-10000
Red blood cells×10^6/µL	4.9	4.10-5.10
Packed cell volume (%)	40.7	35.9-44.6
Mean corpuscular volume (fL)	90.6	80-96
Mean corpuscular haemoglobin (pgms)	31.2	27.5-33.2
Mean corpuscular haemoglobin concentration (g/dL)	34.4	33.4-35.5
Platelet count (µL)	2,47,800	1,50,000-4,50,000
Total bilirubin (mg/dL)	3.4	0.10-1.2
Direct bilirubin (mg/dL)	1.5	Upto 0.3
Indirect bilirubin (mg/dL)	1.9	0.1 to 1.0
Aspartate transaminase (U/L)	74	8-48
Alanine transaminase (U/L)	69	7 to 55
Alkaline phosphatase (U/L)	162	40-129
HIV, HBsAg, HCV	Non reactive	Non reactive
Activated partial thromboplastin clotting time (secs)	25.1	19.8-26.2
Prothrombin time and International normalised ratio	1.7	0.85-1.15
Total proteins	7.4	6.4 to 8.2
Serum albumin	3.4	3.4 to 5.0
Serum globulin (g/dL)	4.0	2.3 to 3.5

[Table/Fig-1]: Laboratory investigations on admission to the hospital.
HIV, HBsAg, HCV: Human immunodeficiency virus, Hepatitis B surface antigen, Hepatitis C virus

A diagnostic abdominal paracentesis revealed a straw coloured ascitic fluid containing 3.1 g/dL protein, Serum Ascites Albumin Gradient (SAAG) of 2.8. Ascitic fluid culture revealed no growth and cytology was negative for malignant cells. Adenosine Deaminase (ADA) was 4.3 U/L (normal range was 0-40 U/L).

Abdominal ultrasound scan showed an enlarged liver with an inhomogeneous echo texture, moderate ascites. Colour doppler showed thrombosis of right and middle hepatic vein with absent flow in left hepatic vein. Triphasic Contrast Enhanced Computed Tomography (CECT) of abdomen and pelvis revealed atrophic right hepatic lobe, hypertrophic left lobe with persistent ill-defined hypodense areas in right hepatic lobe and caudate lobe-likely due to necrosis, non visualisation of right hepatic and middle hepatic vein-likely thrombosed, opacification of left hepatic vein, mild splenomegaly, marked ascites and bilateral pleural effusion suggestive of Budd-Chiari Syndrome (BCS) [Table/Fig-2].



[Table/Fig-2]: Triphasic CECT of abdomen showing atrophic right lobe, hypertrophy of caudate lobe, caudate to right lobe of liver ratio is 0.79 (increased). Right and middle hepatic veins are thrombosed, left hepatic vein shows partial opacification. a): Arterial phase; b): Portal phase; c): Venous phase.

The working diagnosis at this point was acute hepatic venous thrombosis (BCS). As a result, patient was worked up for hypercoagulability and extended thrombophilia profile revealed two out of three tests positive for antiphospholipid syndrome [Table/Fig-3].

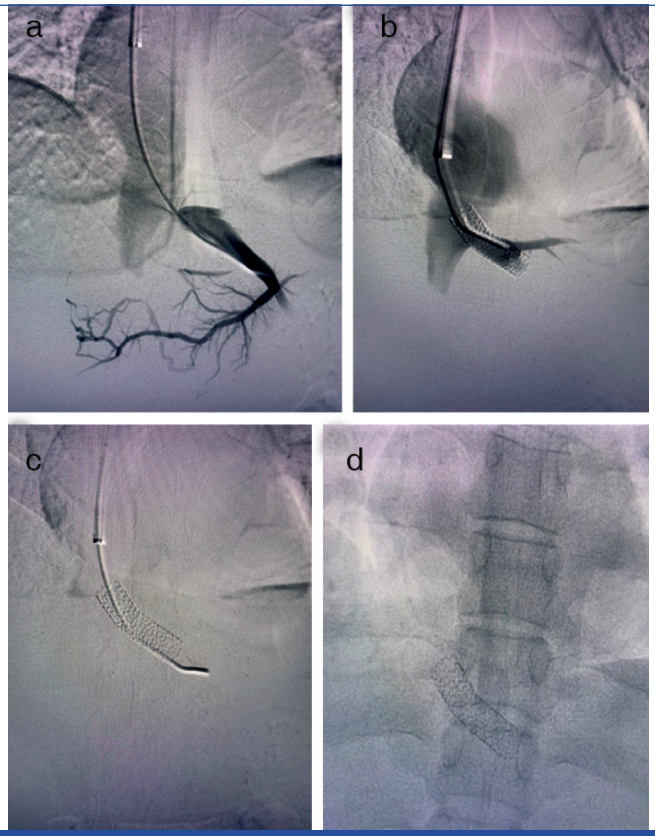
Parameters	Results
Antinuclear Antibody (ANA) profile	Negative
Protein C, S	Negative
Antithrombin III	Negative
Leiden mutation in factor V	Negative
Homocysteine	Negative

Antiphospholipid Profile (APLA)	
Lupus anticoagulant Diluted Russell Viper Venom Time (dRVVT)	Moderately positive
Anticardiolipin antibodies (aCL)	Negative (6.5 U/mL)
Beta-2 glycoprotein 1 IgM	Positive

[Table/Fig-3]: Thrombophilia profile.

Antiphospholipid (APLA) profile repeated after 12 weeks were positive for lupus anticoagulant and beta-2 glycoprotein IgG. As a result, primary antiphospholid syndrome was diagnosed as the aetiology of BCS. The patient was treated with diuretics (tab. frusemide 20 mg) twice a day for 10 days which decreased his ascites, and was started on low molecular weight heparin 60 mg subcutaneous twice a day for 5 days and bridged with tab. warfarin 5 mg aiming to an International Normalised Ratio (INR) of about three.

Later patient was posted for intervention therapy on 10th day of anticoagulant therapy. Good flow was noted in right and middle hepatic vein indicating resolution of thrombus. Opacification and stenosis were noted in ostium of left hepatic vein and a balloon mounted stent (9×37 mm) was placed in left hepatic vein [Table/Fig-4a-d]. Postprocedure doppler confirmed good flow in all hepatic veins and patent left hepatic vein stent. Patient was discharged on 5th day of intervention therapy on tab. warfarin 5 mg. Liver function tests repeated after 1 month postdischarge showed normalisation of bilirubin and liver enzymes [Table/Fig-5].

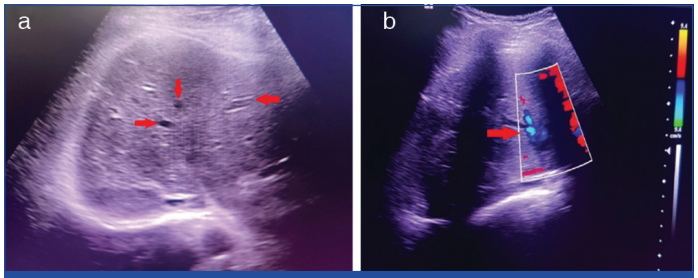


[Table/Fig-4]: a) Angiography showing contrast uptake in right and middle hepatic vein; b) Left hepatic vein ostial stenosis; c) Stenting of left hepatic vein; d) A balloon mounted stent in-situ in left hepatic vein (postprocedure image).

Parameters	Values
Total bilirubin (mg/dL)	0.9
Direct bilirubin (mg/dL)	0.1
Indirect bilirubin (mg/dL)	0.8
Aspartate transaminase (U/L)	24
Alanine transaminase (U/L)	29
Alkaline phosphatase (U/L)	112
Prothrombin time and International normalised ratio	3.2

[Table/Fig-5]: Blood investigations after 1 month of discharge.

The patient was followed-up for one year on outpatient basis. He improved tremendously and remained symptom-free, with no recurrence of his ascites. A repeat colour doppler ultrasound and CT after 1 month of discharge revealed improved hepatic perfusion and venous flow, hepatic vein recanalisation, patent stent [Table/Fig-6a,b]. While on prolonged anticoagulation with tab. warfarin 5 mg, his condition remained under control.



[Table/Fig-6]: a) Ultrasonography of liver showing normal size, echotexture. Right and middle hepatic veins are visualised and a patent stent noted in left hepatic vein; b) Colour doppler showing normal flow in right and middle hepatic veins.

DISCUSSION

The Budd-Chiari Syndrome (BCS) is a condition caused by an obstruction of the major hepatic veins. Budd first mentioned this condition in the mid 1800s, and Chiari provided additional information in the 1890s. The classic triad of BCS of hepatic vein is ascites, hepatomegaly, and abdominal pain [1].

Hypercoagulable states, neoplasms, congenital webs in the inferior vena cava and/or hepatic veins, medications, including oral contraceptives, and have all been linked to the syndrome [2]. According to Espinosa G et al., 32 out of 43 patients had primary APS, eight had APS related to Systemic Lupus Erythematosus (SLE), and three had other types of APS. In 28 patients (65%), BCS was the first symptom of APS, while nine patients (21%) had a history of major venous occlusion. Common symptoms included abdominal pain, ascites, and splenomegaly. Other symptoms included abdominal distension, fever, vomiting, hepatomegaly, and jaundice. Oral contraceptive medication, pregnancy, and major surgery have all been linked to BCS. In 77 cases, the anticoagulant for lupus was positive [3].

BCS is often categorised by disease duration and severity [4]:

1. Acute: Clinical manifestations develop rapidly over a few weeks, with intractable ascites and hepatic necrosis. Venous collaterals are not seen.
2. Subacute: Has insidious onset, with patients taking up to three months to develop symptoms. Venous collaterals develop, leading to minimal ascites and hepatic necrosis.
3. Chronic: Patients present with complications of cirrhosis. Venous collaterals are present.

The index patient had symptoms lasting for 2 months with SAAG of 2.8. Ultrasonography, colour doppler and CT scan showed thrombi in hepatic veins.

Until recently, BCS was assumed to be idiopathic in a large proportion of cases, antiphospholipid syndrome can cause an increase in thromboxane A2 and act as a type III Plasminogen Activator-Inhibitor (PAI) [5]. It has also been linked to lower levels of prostacyclin, Antithrombin III, protein C, protein S, and factor XII, all of which are thrombogenic [6]. Harris EN et al., classified the APS based on the type of antiphospholipid antibody (lupus anticoagulant and/or anticardiolipin antibodies), arterial or venous thrombosis, and recurrent foetal loss in 1987 [7]. The APS has been related to SLE and other connective tissue diseases, malignant tumours, and long-term drug treatment. However, APS is considered in the absence of all of these conditions ("primary" syndrome) [8]. It was recently demonstrated that patients with antiphospholipid antibodies have thrombosis associated with antiphospholipid antibodies [9].

In SLE, abnormal platelet aggregation, decreased endothelial cell prostacyclin production, inhibition of protein C possibly by eliminating the enhancing effect of phospholipids on thrombomodulin, and decreased fibrinolysis by unopposed tissue PAI, or prekallikrein, as well as the presence of antiphospholipid antibodies, have all been clearly demonstrated [10]. Thrombosis was found in the hepatic veins in the index patient. In a patient with BCS, the presence of a space-occupying lesion on CT or MRI does not always indicate the presence of a tumour. According to Shapiro RS et al., it could be an area of haemorrhagic necrosis [11]. During thrombotic episodes, antiphospholipid antibody titres may be low or fluctuate, and may fall below the detection limit [3,12]. For these reasons, it may be necessary to repeat antiphospholipid antibody tests after the acute episode has passed. Usually, APS antibodies are repeated 12 weeks apart. The diagnostic tools are tabulated in [Table/Fig-7].

Tools	Details
Diagnostic paracentesis	The Serum Ascites-Albumin Gradient (SAAG) is usually <1.1 g/dL in chronic form, whereas in acute form it is >1.1 g/dL.
Biochemical abnormalities	Non specific except for mild elevation in serum aminotransferases (AST/ALT) and alkaline phosphatase level in 25-50% of patients.
Radiological evaluation	Ultrasonography with colour doppler can visualise the thrombi with a sensitivity and specificity of 85-90%. Triphasic contrast CT is helpful in confirming and to rule out mechanical obstruction. Venography can accurately show the site and severity of obstruction, but the invasive nature limits the usefulness of the test.

[Table/Fig-7]: Diagnostic tools in Budd-Chiari Syndrome (BCS) [4].

Patients with high antiphospholipid levels and a history of major thrombosis need to take warfarin for a long time, possibly permanently and high INR to be maintained. From the available data, the clinical course after hepatic vein thrombosis cannot be accurately predicted. In patients with APS, a high risk of recurrent thrombotic events has been reported after warfarin withdrawal. Antiplatelet agents' efficacy hasn't been proven conclusively [3].

CONCLUSION(S)

Early recognition and treatment of BCS with systemic anticoagulants can prevent a fatal outcome, such as pulmonary embolism or cirrhosis as observed in the index patient. Incidence of primary APS in male patients presenting as BCS is a rare entity. APS requires anticoagulation to maintain INR of 3-4, and prompt intervention can reduce the complications.

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