Acute/atypical Signs of Budd Chiari Syndrome Secondary to Multi-thrombotic Causes

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Case Report

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Abstract

Budd-Chiari syndrome is a rare medical condition that affects one in a million people and can be caused by various thrombotic and non-thrombotic factors. In rare instances, multiple factors may contribute to its development, with coagulation factor deficiencies being a less commonly implicated cause. This case report presents a case of BCS associated with protein C deficiency and antiphospholipid syndrome (APLS). The patient is a 30-year-old woman who was brought in due to sudden abdominal distension. She had a three weeks history of intractable vomiting and loose stools. There was also a history of repeated miscarriages. The laboratory findings revealed slightly elevated liver enzymes, a positive Anti-β2 GPI screening, moderately decreased Protein C level and activated protein C resistance/FV Leiden. The patient was discharged after 21 days of inpatient treatment with symptomatic improvement.

Introduction

Budd-Chiari syndrome (BCS) is an unusual clinical entity that arises due to thrombotic or non-thrombotic hepatic venous outflow obstruction. Abdominal pain, ascites, and hepatomegaly usually represent clinical presentation. The prevalence of BCS is relatively low, estimated to be less than 1 case per 100,000 individuals in the general population. BCS is rare in Western countries, with a reported incidence of one in 2.5 million cases. However, the prevalence of BCS is higher in Asia, particularly in Nepal, China, and India, where it ranges from 6.8 to 12 cases per 100,000 individuals in China. (1)

There are known to be two types of BCS: Primary BCS and Secondary BCS. The primary is due to thrombosis and obstruction originating in the vein, while external contraction (by a tumour or an abscess) is known to be the reason for secondary causes. (2) There have been many reports about different etiological factors, of which more than one factor may play a role in 25% of the patients. (3) BCS can have various underlying causes, with myeloproliferative neoplasms being the most common culprit (accounting for 39% of cases), followed by JAK2 mutation accounting for 29%, antiphospholipid syndrome (APLS) about 25%, paroxysmal nocturnal hemoglobinuria (PNH) about 19%, protein C deficiency roughly 4%, and protein S deficiency being least common with 3%. (4)

Here we report a case of BCS due to multiple thrombotic causes in a 30-year-old woman brought to the emergency department of Civil Hospital Karachi.

Case Report

A 30-year-old woman was brought to the emergency department of Civil Hospital Karachi by her husband when she developed a sudden onset of abdominal distension. According to her history, she had intractable vomiting and loose stools for three weeks and was treated with intravenous antibiotics, after which her abdomen started distending. There was no active complaint of fever, diarrhea, vomiting, itching and bleeding, although she had mild abdominal discomfort and difficulty breathing. The patient is a mother of 4 children, with three miscarriages at 3, 1 and 1.5 months, respectively. Her last baby was born

in June 2021 through spontaneous vaginal delivery. Her systemic review was unremarkable, and there was no history of alcohol or tobacco consumption relevant to drugs or hepatotoxic chemicals. On examination, the patient was conscious with GCS 15/15. She was of average height with no signs of anemia, jaundice, edema, or coagulopathy. Her abdomen was symmetrically distended, measuring 38.6 inches, with no scar marks or distended veins. There was no visceromegaly; however, shifting dullness and fluid thrill was joyous, showing signs of moderate ascites. The rest of the examination was unremarkable.

Her lab parameters showed cbc and coagulation study in the normal range (white blood cell count of 8.8 × 103/μL (normal range 4–11 × 103/μL) (64.0% neutrophils), hemoglobin of 12.5 gm/dL(normal range 13–17 gm/dL), hematocrit was 40%, and platelet count was 462 × 103/μL (normal range 150–400 × 103/μL), prothrombin time (PT) was 12.1 seconds, international normalized ratio (INR) of 1.16 (normal range 0.8–1.2) and the activated partial thromboplastin time (APTT) ratio was 26.0 seconds). Biochemistry tests showed a slight elevation of liver enzymes (aspartate transaminase (AST) 68 IU/L (normal range 14–63 IU/L); alanine transaminase (ALT) 129 IU/L (normal range < 34 IU/L); alkaline phosphatase (ALP) 292 IU/L (normal range 60–240 IU/L); and, total bilirubin 1.1 mg/dL (normal range 0–1.1 mg/dL) IU/L) and albumin 3 gm/dL (normal range 3.8–5.4 gm/dL), with no jaundice or kidney dysfunction and creatinine being 0.7 mg/dL. The serum level of C-reactive protein was markedly elevated (78.5mg/L). The ascitic fluid study revealed protein 2.5 gm/dL, albumin 1.4 gm/dL, Serum ascites albumin gradient (SAAG) was 1.6, Acid fast bacilli (AFB) and Gram-stain-negative. Serological tests were negative for hepatitis A, B, C, E, and HIV. Serum ferritin and ceruloplasmin are within normal limits. Blood and urine cultures were negative.

Abdominal ultrasonography showed normal measuring liver, spleen and portal vein (1.0 cm) with gross ascites. A focal thrombus was seen at porta hepatis, and color doppler showed no flow, suggesting a thrombus (See Fig. 1). A computed Tomography scan of the abdomen showed a mottled appearance involving the liver with non-visualization of the hepatic vein, and intrahepatic IVC also appeared collapsed. Filling defect within the portal vein and Inferior Vena Cava suggested that the thrombus extends up to the suprarenal region, confirming Budd Chiari Syndrome. (See Fig. 2)

On Autoimmune Workup, Antinuclear antibody (ANA), Anti-Mitochondrial antibody (AMA), Anti-Smooth Muscle antibody (ASMA), Anti-Gatric parietal cell antibody (AGPCA), Anti-SS-A/Ro antibody, rheumatoid factor, anti-double-stranded DNA antibody, anti-Sm antibody, and myeloperoxidase antineutrophil cytoplasmic antibodies were negative. Regarding Antiphospholipid antibodies, the lupus anti-coagulant (1.07) (normal 0.8–1.2)) and anti-cardiolipin antibody were Negative. However, Anti-β2 GPI screening was positive, with IgA and IgG under reference ranges (12.176 RU/ml and 2.062 RU/ml), respectively. However, IgM is 34.261 RU/ml (normal < 20 RU/ml). Her complement level was C3 1.08 g/L (normal range 0.79-1.51g/L), C4 0.11 g/L (normal range 0.16–0.38 g/L), while her Serum IgA level was 3.14 g/L (normal range 0.82–4.53 g/L), Serum IgG level was increased, i.e. 23.1g/L (normal range 7.51–15.6 g/L) and Serum IgM level slightly increased 3.23g/L (normal range 0.46–3.04 g/L). Thrombophilia Workup revealed Protein S in the normal range, 94.2%. At the same time, Protein C levels were moderately

decreased, 46% (normal range 70–140%), as proven that ProC Global/FV, a susceptible test to detect activated protein C resistance/FV Leiden (100%) and protein C deficiency (90%) (5), was also decrease being 0.38 (normal range 0.86–1.1) proving deficiency of Protein C.

The patient was started on Diuretics Furosemide 40 mg thrice daily and Spironolactone 100 mg twice daily. Rivoraxaban10mg was added once a day after the thrombophilia workup, and fluid restriction was advised. The patient was discharged after 21 days of inpatient treatment with symptomatic improvement. On follow-up after six weeks, the patient was clinically stable, and her repeated protein c levels were in the normal range (76%).

Discussion

Budd-Chiari syndrome (BCS) is an uncommon but clinically challenging disorder characterized by the occlusion of the hepatic venous outflow tract, including the small hepatic veins, the large hepatic veins, or the inferior vena cava. (6) This rare disorder has many etiological bases and can be classified as primary or secondary BCS. Primary BCS originates within the lumen of the vein, and the major risk factors include hypercoagulable states and thrombosis, which may be caused by multiple inherited and acquired disorders such as myeloproliferative disorders, protein C deficiency, protein S deficiency, Behcet's disease, antiphospholipid syndrome or IVC webs (more common in Asia). Secondary BCS originates from compression and obstruction external to the vein, such as tumoral invasion, abscess, or cyst. (7) Prothrombotic risk factors are present in 90% of the individuals though 46% have multiple concurrent risk factors. (8) Many other risk factors, such as ulcerative colitis, use of oral contraceptive pills, malnutrition, and pregnancy, have also been identified. However, the cause of BCS remains unknown in numerous cases. In a case series of 164 patients, the etiology was either unidentified or inadequately established in 70.1% of the cases. (9)

The classical clinical presentation of BCS includes abdominal pain, ascites, hepatomegaly, jaundice, and leg swelling. (10, 11) About 15–20% of patients are asymptomatic. (7, 10) Furthermore, serum aminotransferase levels and bilirubin levels are elevated. (12) In our case, a 30-year-old woman presented with the main complaints of abdominal distention and associated abdominal discomfort and difficulty breathing. There were elevated liver enzymes and bilirubin, while albumin levels were decreased. Nevertheless, these are nonspecific, and further workup was done to determine the underlying cause.

A radiographic analysis is required to check for the patency of hepatic veins/IVC and is critical to establish a diagnosis. Ultrasonography coupled with Doppler studies are the preferred modality. (13) The ultrasound findings most commonly include hepatosplenomegaly, an enlarged caudate lobe, intrahepatic collaterals, a compressed IVC, and ascites. Computed tomography (CT) and magnetic resonance imaging (MRI) can provide detailed images of the liver and hepatic vasculature to help recognize the underlying cause of BCS and determine the extent of the disease. In our case, abdominal ultrasonography showed a normal-looking liver and spleen with massive ascites. The absence of flow within the hepatic vein on

color Doppler and the lack of visualization of the hepatic vein with the collapsed intrahepatic IVC seen on CT established the diagnosis of BCS.

Some further attempts are required to identify the cause of the hypercoagulable state. An additional autoimmune evaluation was conducted, which revealed elevated antiphospholipid antibodies (Anti-β2 GPI), suggesting antiphospholipid syndrome (APS). This syndrome can be secondary to systematic lupus erythematosus, other connective tissue diseases, malignant tumors, or prolonged drug treatment. (14) However, APS can be primary and occur without any of these conditions (13). This syndrome is clinically associated with recurrent thrombosis, miscarriages, and thrombocytopenia. (15, 16) The association of APS with BCS seems to be rare. Ibrahim. et al. (17) describe a case of primary APS presenting as BCS with positive aCL-IgM (anti-cardiolipin IgM) antibodies and aCLIgA (anti-cardiolipin IgA) antibodies. This is in contrast to our study, where anti-cardiolipin antibodies along with lupus anti-coagulant yielded negative results. A thrombophilia workup was also performed, which demonstrated lowered levels of Protein C.

The ultimate aim of therapeutic interventions in BCS is to relieve portal and IVC hypertension, remove the diseased hepatic vein/IVC, decrease cirrhosis, and prevent a recurrence. Treatment is done stepwise, ranging from medical management to a liver transplant when necessary. Medical management includes anticoagulation, sodium restriction, diuretic therapy, and paracentesis. Trans jugular intrahepatic portosystemic shunt (TIPS) placement has become increasingly popular in patients and has become the option of treatment wherever a shunting procedure is indicated. Angioplasty and stent placement are valuable adjuncts. (18). Our patient was started on anti-coagulants and diuretics and improved significantly with no reports of recurrence.

Conclusion

In conclusion, this case report presents a case of BCS associated with APS and protein C deficiency. Owing to its rarity, BCS is likely to be misdiagnosed or underdiagnosed. Due to this, it is of utmost importance for physicians and clinicians to consider BCS in patients presenting with symptoms of hepatomegaly, splenomegaly, or ascites and perform an extensive workup. To correctly determine the etiology of BCS, it is crucial to assess all prothrombotic factors and an extensive autoimmune workup. Nevertheless, a timely diagnosis and treatment of BCS are vital to prevent long-term complications and improve outcomes.

Declarations

The patient has given their consent to participate in this study and have it published

Ethics approval and consent to participate:

Not applicable as no intervention was performed as a part of the research in any case.

Consent for publication:

Consents were obtained for publication from the patients upon stabilization of their psychotic illnesses.

Availability of data and materials:

Not applicable.

Competing interests:

None to declare.

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AUTHOR'S CONTRIBUTIONS

Conception and design: SMFZ, BSR

Acquisition of data: SMFZ, AQ

Drafting of the manuscript: BSR, AQ

Critical revision for important intellectual content: MTA

Final approval of the study: AQ, SMFZ, BSR, MTA

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Figures

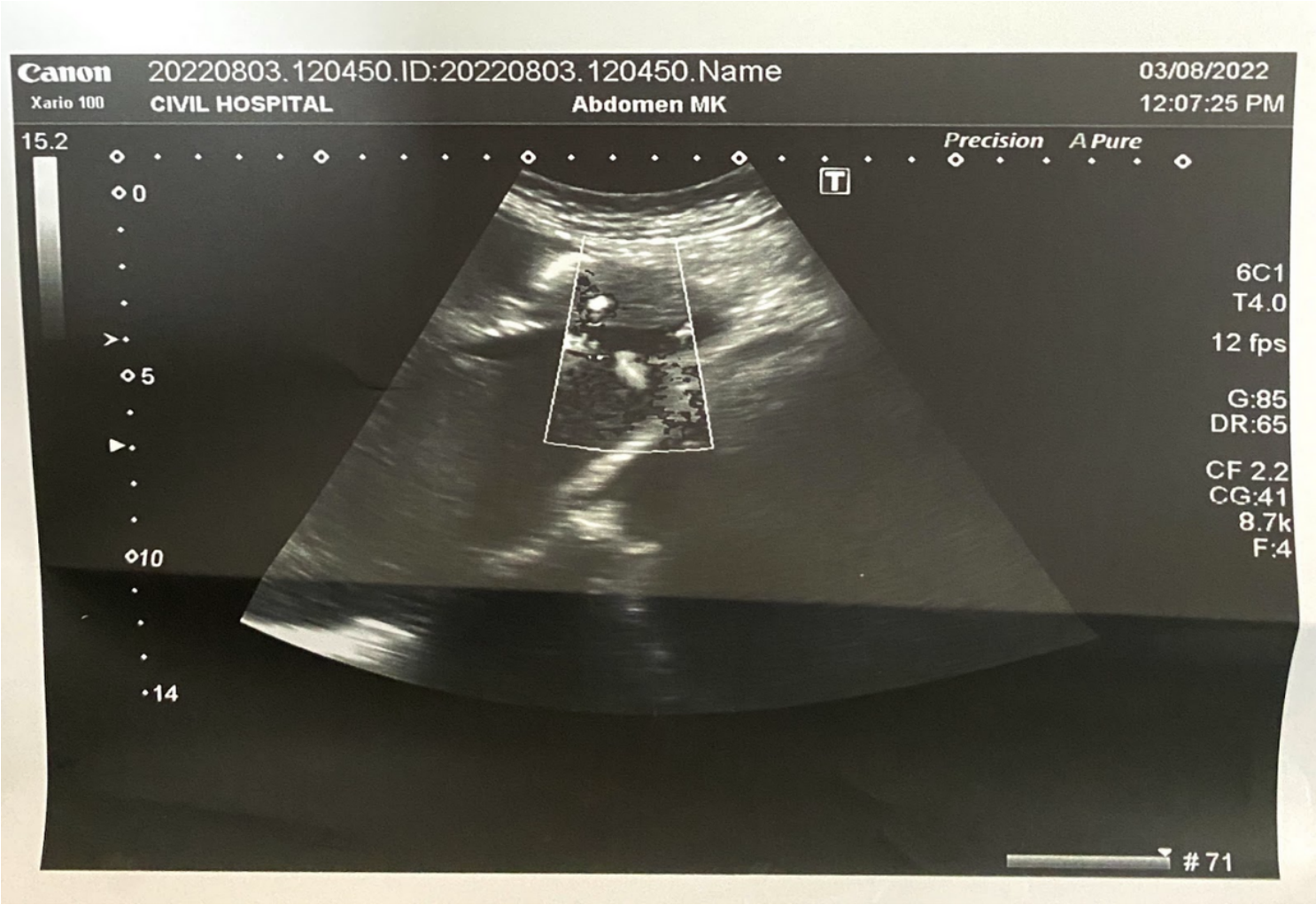

Figure 1

Ultrasound of Abdomen showing coarse texture liver with portal vein thrombosis and gross ascites.

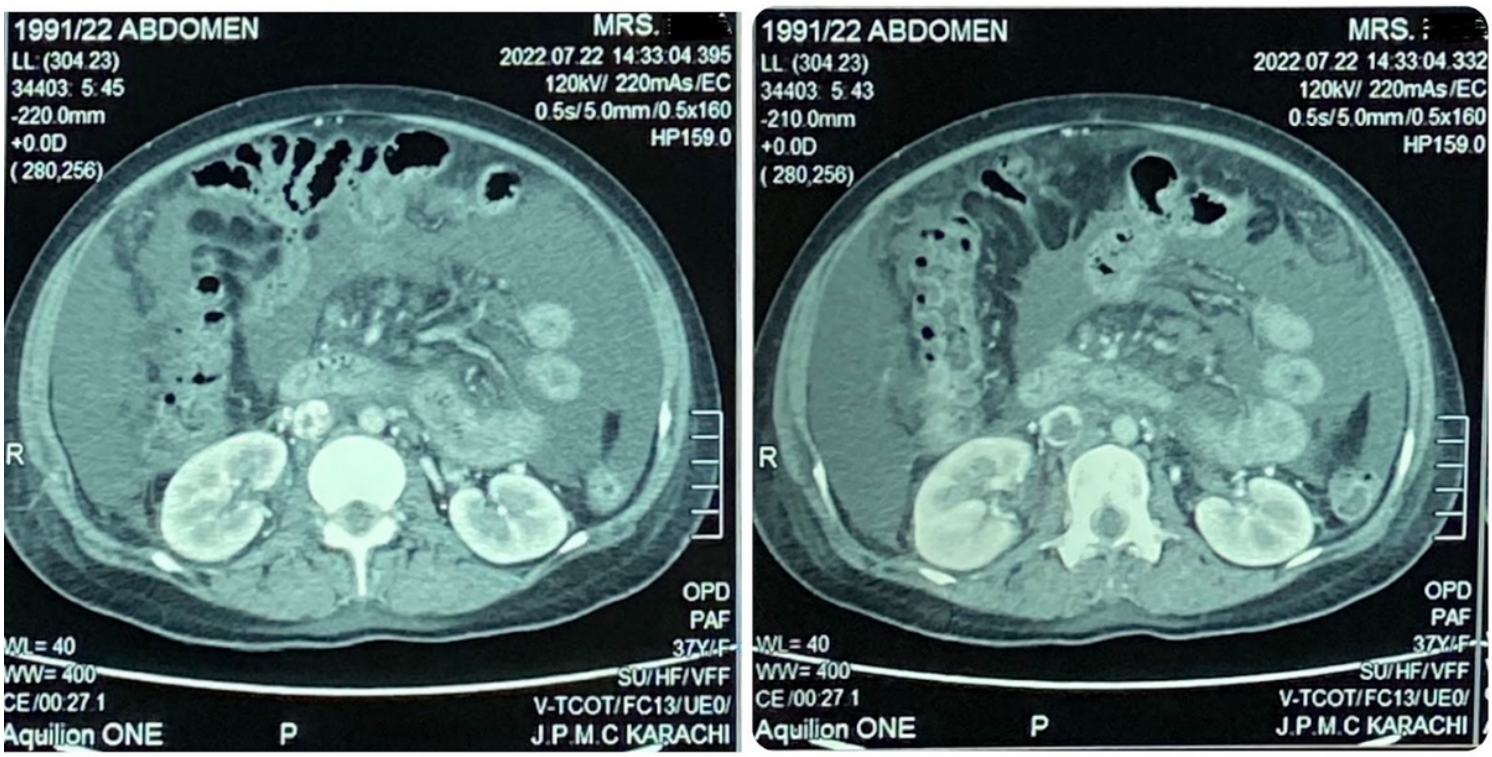

Figure 2

Computed Tomography of the abdomen with contrast shows gross ascites, a mottled appearance of the liver with collapsed inferior vena cava and a filling defect in both the portal vein and IVC.