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An unusual presentation of Budd-Chiari syndrome with significance of etiological workup

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INTRODUCTION: Budd–Chiari syndrome (BCS) encompasses a varied group of disorders with common pathology characterized by hepatic venous outflow obstruction which can occur anywhere at the level of the hepatic venules, the large hepatic veins, the inferior vena cava and the right atrium. The term "hepatic venous outflow tract obstruction" is usually applied irrespective of the level f obstruction or the mechanism of obstruction. With the advances in the speciality of radio diagnosis the diagnosis of budd chiari syndrome is easily made. However because of its varied unusual presentations, sometimes it poses a diagnostic challenge for the treating physician. We present a case report of a woman who presented with trivial symptoms and pancytopenia which on further evaluation later turned out to be having chronic budd chiari syndrome. **CASE PRESENTATION**: A 42-year-old female presented to our OPD with history of loose stools and easy fatigability for the last 10 days. On evaluation she had mild ascites and pancytopenia. Her liver function tests were within normal range. She had low serum vitamin B12 and iron deficiency anemia. Her USG hepatobiliary system revealed mild ascites. Computed tomography of her abdomen showed non opacified hepatic veins with marked luminal narrowing of suprahepatic veins with prominent azygous and hemiazygous veins with caudate lobe hypertrophy. Further upper gastrointestinal endoscopy revealed presence of varices which were managed with EVL bands. She was diagnosed as a case of chronic budd chiari syndrome. On thorough history taking it there was history of recurrent abortions for which no prior work up was done. Further investigation revealed deficiency of S, raised homocysteine levels with normal JAK2 mutation and APLA workup. She was then started on anticoagulation and invasive procedures were deferred (stent v TIPS) in view of good network of intrahepatic collaterals. **DISCUSSION:** Budd chiari syndrome have varied presentations ranging from asymptomatic condition detected incidentally (as in our case) to fulminant BCS classical triad of abdominal pain, hepatomegaly, ascites and jaundice. Previously it was the membranous occlusion of IVC that happened to be the main mechanism. However now it is seen that the isolated hepatic vein occlusion is more commonly seen in our country. Also hypercoagulable state being the etiological factor is now more commonly seen than the membranous occlusion of IVC. Both these facts are confirmed by the findings in our case. **CONCLUSION**: since budd chiari syndrome may present as asymptomatic condition, higher degree of suspicion should be kept if any of the signs of liver failure are note on clinical examination. Similarly a thorough and meticulous history is warranted so as to rule out the genetic and acquired causes.

Abbreviations: APLA antiphosholipid antibody;BCS, Budd–Chiari syndrome; CT, computed tomography; EVL,endoscopic variceal ligation;IVC, inferior vena cava;MRI, LMWH, low molecular weight heparin magnetic resonance imaging; OPD, out patient department;TIPS, transjugular intrahepatic portosystemic shunt; UFH, unfractionated heparin;UGIE, upper gastrointestinal endoscopy;USG, ultrasonography; VKA, vitamin K antagonist

Introduction: BCS (Budd–Chiari syndrome) can be defined as group of various disorders which causes obstruction to the flow of blood away from liver at any point starting from the small hepatic venules upto the juncture of IVC and right atrium [1]. However obstruction related to the right-sided cardiac disease is excluded from the definition [2]. BCS is rare but potentially life-threatening condition. BCS is classified into primary BCS and secondary where primary BCS refers to the obstruction within the veins (membranous web or thrombus) whereas secondary BCS implies any extrinsic compression by a lesion that has an origin outside the vein [3,4]. It may take few days to few months or even longer for the development of symptoms. The clinical presentation varies from asymptomatic incidentally detected BCS to acute fulminant BCS [2]. Asymptomatic BCS is seen in

15-20% of patients detected on radio imaging. Asymptomatic BCS usually has great network of intrahepatic collaterals and presence of at least one patent hepatic vein. As a result prognosis is better in asymptomatic BCS patients [5]. Acute and fulminant BCS are devoid of the presence of intrahepatic collaterals which helps in distinguishing it from subacute and chronic BCS. The classical triad consists of ascites, abdominal pain and tender hepatomegaly. Other less common manifestations those can be seen are jaundice, encephalopathy, gastrointestinal bleeding which denotes presence of cirrhosis and portal hypertension, more commonly seen in chronic BCS [6]. As far as the geographical distribution is concerned BCS shows variability in terms of the nature of pathological lesion. There is an increased risk of IVC obstruction in the BCS affected Asian and South African population related to the poor living standards. Over a period of time in our country there is decrease in this trend with improvement in the living conditions. Now the latest studies show isolated hepatic vein thrombosis to be more common than IVC occlusion. The most common cause seen in Indian population are inherited hypercoagulable disorders [7-9]. The most commonly reported subtype of BCS in Indian population is of chronic BCS

Most of the patients with BCS have more than one contributory factor for the development of thrombus. Various predisposing conditions can be divided into genetic and acquired. The most common factors are the genetic or acquired hypercoagulable state seen in75% where myeloproliferative disorders are the most common cause [10,11]. Other inherited cause being the polycythemia Vera seen in 50% of the patients. Factor V Leiden mutation accounts for almost 25% of the inherited cases of BCS followed by protein C deficiency [12]. So the primary BCS is characterized by the presence of various contributory prothrombotic markers.

Case presentation:

A 42 years old lady presented to our OPD with history of loose stools and generalised weakness. She was admitted in view of dehydration for observation and fluid management. On clinical examination she had pallor with rest of examination within normal limits. There was nothing to suggest the presence of chronic liver disease in term of ascites, spider nevi, and dilated veins over abdomen. Hematological investigations revealed pancytopenia with rest o biochemical profile including liver function tests to be normal. She was subjected to investigations directed towards pancytopenia where her peripheral smear with reticulocyte count, iron studies, serum vitamin B12 and folic acid levels were done. Immunological workup including ANA was also done. All these investigations were within normal limits except low vitamin B12 and iron studies revealed iron deficiency anemia. Further an ultrasonography of the hepatobiliary system was done which revealed presence of mild ascites with dilated hepatic vein. Clinical history was again sought where the patient revealed history of recurrent abortions in the past, for which was never evaluated. With the possibility of APLA syndrome and dilated hepatic veins a possibility of budd chiari was kept. APLA work was done and contrast enhanced CT abdomen was obtained. Computed tomography of her abdomen showed non opacified hepatic veins with marked luminal narrowing of suprahepatic veins with prominent azygous and hemiazygous veins with caudate lobe hypertrophy. APLA work up came out to be negative. So keeping the possibility of primary, chronic budd chiari syndrome was kept and further work up for hypercoagulable state was sent. Investigations revealed deficiency of protein S with raised Homocysteine levels. JAK2 mutations were negative. An upper GI endoscopy was done which was initially normal and was started on anticoagulation with LMWH overlapped with oral VKA anticoagulant. Vitamin B12 along with iron supplementation was started. She was also started on beta blockers along with diuretics for portal hypertension. She remained stable during the course. A follow up UGIE was done and this time it revealed presence of esophageal varices. She underwent EVL banding and repeat UGIE showed absence of varices. Follow up imaging revealed good network of intrahepatic collaterals in view of which surgical procedure (stenting vs TIPS) was deferred and she was continued on anticoagulation. Currently the patient is doing well with blood normal blood counts; normal homocysteine levels with no signs of portal hypertension. Biochemical results are shown in table 1.

Table 1. Biochemical test results

Test		Result
Complete blood count(CBC)	Hb (g/dl)	8.9
	WBC count (/mm^3)	3800
	Platelets (/mm^3)	68000
Coagulation profile	PT (s)	15.6
	INR	1.8
	aPTT (s)	33.1
LFT	SGOT	28
	SGPT	32
	ALP	56
	Serum total protein	6.8
	albumin	3.2
ANA (IFA)		Negative
Iron studies	Iron (µg/dl)	38 (60-180)
	TIBC (µg/dl)	342
	% saturation	11
Vit B12		198 ng/ml(200-900)
Folic acid		5.2 ng/ml(4-20)
RFT	Urea(mg/dl)	8
	Creatinine (mg/dl)	0.56
Lupus anticoagulant	LA1/LA2 (s)	40/34
Anti cardiolipin antibodies	IgG/IgM	<1/<9.3 (<20CU=negative/<20CU= negative)
Glycoprotein antibody	Anti B2IgG/IgM	<5CU/<1.3CU (<20= negative/<27=negative)
Antithrombin activity		108% (80-120)
Protein C		119 %(70-140)
Protein S		43 % (55- 123)
JAK2 VG17F mutation		Not detected
Serum Homocysteine		15.19 µmol/L(4.44 -13.56)

Discussion: BCS refers to hepatic venous outflow obstruction and the obstruction occurring at any level from hepatic venules to the juncture of IVC and right atrium [13]. In our patient the diagnosis was not clear initially. As the patient presented with trivial complaints and there was presence of pancytopenia on investigations. Initial clinical examination was within normal limits. It was then only during the evaluation of pancytopenia the USG hepatobiliary system revealed presence of mild ascites and non visualization of hepatic vein. As the Doppler USG of hepatic outflow tract is the investigation of choice whenever budd chiari syndrome is suspected [14,15]. Also mere non visualization of hepatic veins on real time USG, is not diagnostic of BCS, It becomes prudent to go ahead with the Doppler USG. So the findings which are supportive for the diagnosis of BCS as noted in our patient are: absence of flow or retrograde flow in the hepatic veins. Contrast enhanced CT abdomen revealed non opacification of hepatic veins which is suggestive of the obstruction. But being a non real imaging technique assessment of flow is not possible on CT [16]. So MRI abdomen is a better diagnostic modality with as much sensitivity as of hepatic venography. Another advantage of MRI is its ability to differentiate between acute from subacute and chronic BCS [17].

As far as the etiological work up is concerned it is important to look for any hypercoagulable state. Prior medical history is equally important as in our case was of recurrent abortions. Testing for myeloproliferative diseases include JAK2 mutation assessment and bone marrow biopsy. While looking for other thrombophillias testing of protein C and S, anti thrombin must be done. But the lacuna is that low levels of these factors may be because of any liver disease causing liver dysfunction. So family screening should be done for their presence and the diagnosis of these deficiencies must be made in this context only.

As in our case there was deficiency of protein S for which her family members are to be screened soon. Our patient also had high level of homocysteine that can be explained due to deficiency of vitamin B12 and on supplementation it came down within normal range. Similarly hyperhomocysteinemia is a well known etiological factor for recurrent pregnancy loss. The natural history of BCS is not well known but with the advent of newer therapeutic options, the overall survival continues to increase, reaching five-year survival rates between 80% and

90% [6]. Lifelong anticoagulation is usually recommended in all patients with BCS as there is sufficient evidence that suggest improvement in the overall prognosis of BCS with anticoagulation [18]. When anticoagulation is considered the initial LMWH followed by oral Vit K antagonists are preferred over UFH as the later is associated with higher occurrence of heparin induced thrombocytopenia [19]. For chronic BCS as in our case, the other treatment options are angioplasty, stenting and portosystemic shunting. Since most of the patients present late and the lesion may not be amenable for stenting at that time, so portosystemic shunting and to be specific TIPS is now the standard of care for chronic BCS with recurrent complications despite medical management. In our case because of excellent intrahepatic collaterals and patient being asymptomatic conservative approach was adopted with periodic follow up.

Conclusion: BCS is an uncommon serious condition with varied presentation, warranting great index of suspicion. Since prothrombotic states are invariably present a thorough work-u for the same should be undertaken. All the same, solitary cases, such as in our patient, do not have a predisposing condition(s).Doppler ultrasound remains diagnostic modality of choice for hepatic venous outflow tract obstruction. Treatment includes lifelong anticoagulation with management of complications of cirrhosis. Surgical interventions must be considered on the basis of patient profile and in case of failure of medical therapy wit recurrent complications.

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Ethical approval: as case reports do not require ethical approval or patient consent, provided that there was no intervention and that no patient identifiers appear in the report. Therefore, neither ethical approval nor patient consent was required for this case report. However, written informed consent was obtained from the patient.

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