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Case Report

Portal Vein Thrombosis and Budd-Chairi Syndrome Due to In-apparent Polycythaemia Vera: Case Report

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ABSTRACT

Portal vein thrombosis (PVT) is an uncommon finding in patients without cirrhosis. The underlying aetiology is challenging and Budd-Chiari syndrome is caused by occlusion of the hepatic veins that drain the liver. It presents with the classical triad of abdominal pain, ascites, and liver enlargement. The main cause of this syndrome is represented by myeloproliferative diseases and, in particular, by polycythaemia vera. The latter may cause multiple splanchnic thrombosis, including portal vein thrombosis, particularly important for its clinical outcomes of ascites, oesophageal varices, collateral vessels genesis, etc. We describe a case of 37 year male presented with severe abdominal pain, abdominal distension due to portal vein thrombosis and budd chairi syndrome caused by polycythaemia vera.

Keywords: Portal vein thrombosis (PVT); Polycythaemia vera (PV); Budd-Chairi syndrome (BCS)

INTRODUCTION

Portal vein thrombosis (PVT) and Budd-Chairi syndrome (BCS) are caused by thrombosis and/or obstruction of the extra hepatic portal veins and the hepatic venous outflow tract, respectively [1]. Portal vein thrombosis (PVT) has a prevalence of 1% in the general population, and is mainly due to liver cirrhosis and myeloproliferative diseases [2] Portal Vein Thrombosis (PVT) in patients with a previously healthy liver is thought to be due to inherited or acquired prothrombotic states [3].

Polycythaemia Vera (PV) is a chronic myeloproliferative neoplasm characterized by clonal proliferation of myeloid cells and an elevated red blood cell mass [3]. PV should also be suspected in patients with the Budd Chiari syndrome and portal, splenic, or mesenteric vein thrombosis [4]. Budd–Chiari syndrome is a very rare condition, affecting one in a million adults [4]. We report a case who was admitted because of the abdominal pain and abdominal distension which we found to be affected by Budd-Chiari syndrome and portal vein thrombosis as the onset of an undiagnosed PV. We also made a brief revision of international literature to try to highlight the main etiopathogenetic and clinical aspects of the disease, and the latest indications for a correct therapeutic approach to this complex patient.

CASE PRESENTATION

37 year old male patient admitted with complains of severe abdominal pain, bilateral lower extremity oedema and abdominal distension since 3 months, His physical examination revealed an alert and oriented individual with no signs of icterus and pallor. He had prominent tachycardia (heart rate 130/min), bilateral pitting pedal oedema and a distended abdomen with the presence of shifting dullness, suggestive of ascites. The remainder of his physical examination was normal with no changes noted on the skin and he had intact arterial pulses in all four extremities.

Laboratory studies determined that he had microcytic hypochromic polycythemia, neutrophilic leucocytosis, hypoalbuminemia , transaminases (Table 1) and Abdomen ultrasound (US) scan which showed thrombus filling lumen of portal vein, abundant ascites, liver with an non-homogeneous echogenicity pattern, increased portal vein diameter (1.64 cm) with few flow signs, and increased spleen volume (longitudinal diameter 15.7 cm) (Figures 1A and 1B). Doppler sonogram confirmed the echogenic structure to be thrombus in the lumen of main portal trunk causing partial obliteration (Figure 2).

Dynamic CECT study showed presence of hypodense filling defect is noted in portal vein S/o thrombus. Presence of ill-defined hypo dense area is noted VI, VII and VIII of liver which remain hypodense in all phase S/o perfusion defect, Splenomegaly, hepatomegaly, mild to moderate ascites. For this, evacuative

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paracentesis was practised and 800 ml of yellow citrine ascites was removed. Physical-chemical, microbiological and histological examination proved negative for exudates or neoplasms. Bone marrow aspiration study revealed panmyelosis with predominant erythroid and megakaryocytic hyperplasia (Figures 3A and 3B).

	Admittance	Discharge	Reference values
Hemoglobin	17.7 g/dl	15.4 g/dl	13-17 g/dL
Hematocrit	55.6%,	47%	42-54%
Red blood cell count	7.41106	4.71106	4.5-6 × 106 cells/ul
Mean corpuscular volume	75 fl	90 fL	78-95 fL
Mean corpuscular hemoglobin	23.9 pg	32.6 pg	27.0-32.0 pg
Total bilirubin	2.40 mg/dL	0.8 mg/dl	0.20-1.60 mg/dL
AST	60 U/L	30 U/L	10-40 U/L
ALT	79 U/L	30 U/L	9-41 U/L
ALP	305 U/L	230 U/L	80-270 U/L
γGT	111 U/L	55 U/L	8-61 U/L
Albumin	2.3 g/d	3.5 g/dl	3.48-5.39 g/dL
CRP	5.9 mg/L	3 mg/L	0-4 mg/L

AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; γGT: Gamma Glutamyl Transpeptidase; ALP: Alkaline Phosphatase; CRP: C-reactive Protein

Table 1: Abnormal hematochemical parameters in first admission of patient.

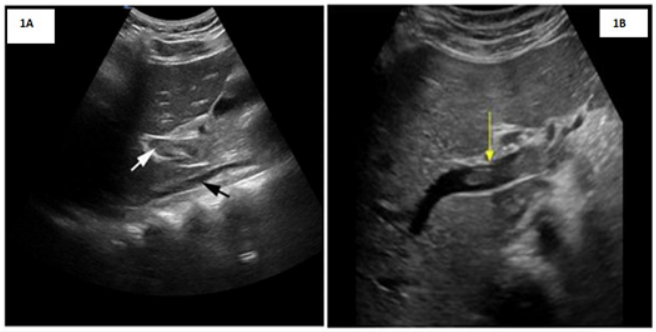

Figure 1: (A-B) Abdomen ultrasound (US) scan which showed thrombus filling lumen of portal vein.

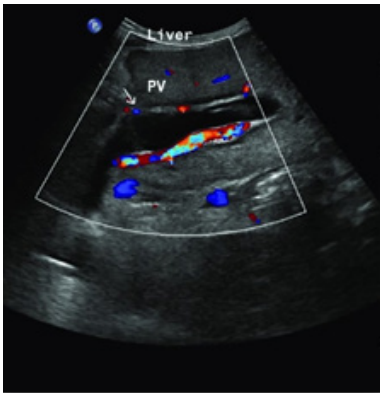

Figure 2: Doppler sonogram show flow around a thmombus

Finally, we requested JAK2 kinase mutation study and FISH for bcr-abl. The patient was found to be positive for mutation in JAK 2 gene resulting in amino acid change Valine in 617 phenyl alanine. FISH for bcr-abl was negative. Serum erythropoietin level was below normal (3.08 mU/ml). Coagulation screening within normal limits, as well as d-dimer significantly positive, S.cerruloplasmin and tumor marker evaluation (a-fetoprotein, CA 19.9, CA 15.3, and CEA,) were normal. Some days later, the patient underwent another abdominal US scan which confirmed the abovementioned findings with, however, in addition the appearance of hepatic veins thrombosis (Budd-Chiari syndrome) and suggesting a hepatic profile compatible with liver stasis. Coagulation screening test were done PT (Prothrombin time) 12.4s, APTT (activated partial thromboplastic time) 35.5s, TT (Thrombin time) 12s, Fibrinogen 200 mg/dl were found to be normal. Meanwhile, according to a differential diagnosis of portal vein thrombosis, we evaluated blood markers of major and minor hepatotropic viruses, human immunodeficiency virus (HIV) types 1 and 2, and thrombophilic disorders (lupus anticoagulant, anti-cardiolipin antibodies, antinuclear antibodies, plasma anticoagulant protein C, protein S, anti-thrombin III and homocysteine). All were within normal range.

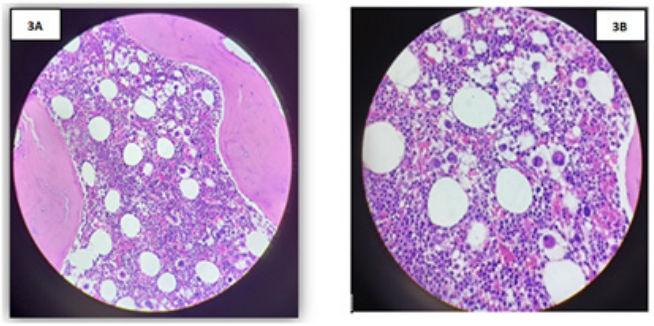

Figure 3: (A-B) Bone marrow aspiration study revealed panmyelosis with predominant erythroid and megakaryocytic hyperplasia

Broad-spectrum antibiotic therapy was started with cephalosporin plus fluoroquinolones, hydroxyurea, anti-platelet (T. Ecosprin 150 mg daily), phlebotomy (300 ml blood was removed) as well as anticoagulant therapy with low molecular weight heparin (LMWH) and warfarin. Endoscopy upper GIT showed grade I esophageal varices. Later on he was treated with warfarin 5 mg and Propranolol 20 mg daily. Two months later a follow up Color Doppler showed re-canalization of portal vein, a normal hepatic vein flow and development of collateral vessels in hilar and peripancreatic region. The patient continues periodic clinical, laboratory and imaging follow up at the hematooncology clinic of our Institution.

After 6 months patient presented with one episode of hematemesis and abdominal distension in emergency department. Full blood count (FBC) revealed anaemia with haematocrit (hct) of 17%, and platelet count of 3, 55,000 mm3 (Table 2). Furthermore, the patient underwent an urgent upper gastrointestinal (GI) endoscopy revealed multiple bleeding oesophageal varices

occupying the entire diameter of the oesophagus. And oesophageal variceal ligation was performed. Bone Marrow Examination showed mildly hypercellular bone marrow aspirate and imprint smears. Myeloid precursors are well preserved (40%). Erythroid precursors show hyperplasia with macronormoblastic maturation (44%). M: E 0.9:1 Megakaryocytes seen and appear increased in number. PS RBC- Macrocytic normochromic. WBC- Within normal limits. DC: P-68, L-20, M-08, Meta-02, E-02. Platelets- Thrombocytosis. Malarial parasites not seen. Diagnosis of Myeloproliferative neoplasm-Polycythaemia Vera is favoured. Bone marrow biopsy showed bony trabeculae with mildy hypercellular marrow spaces. Megakaryocytes of varying size and shape seen, which appear increased in number and Erythroid precursors hyperplasia and myeloid precursors are well preserved. Reticulin stain-grade 0/1 (As per WHO 2016 classification). Diagnosis of Myeloproliferative neoplasm, Polycythaemia Vera was favoured (MPN -PV). Renal and liver function were normal. Coagulation screening within normal limits as well as d-dimer and tumour marker evaluation (a-fetoprotein, CA 19.9, CA 15.3, and CEA) all within normal limits. Abdominal CT with intravenous contrast showed significant increase in liver volume with parenchymal non-homogeneous density, such as liver cirrhosis, hepatic veins, superior mesenteric vein, splenic vein and spleen-mesenteric confluence failure, showing as inveterate thrombosis, vicarages by various collateral circulations and a large amount of ascites. Echocardiography that was also normal. Patient was received five red cell concentrates and evacuative paracentesis was practised and 1L of yellow citrine ascites was removed. Physical-chemical, microbiological and histological examination proved negative for exudates or neoplasms.

Currently the patient undergoes regular clinical and laboratory follow up in our Department, without further episodes of hepatic decompensation.

	Admittance	Discharge	Reference values
Hemoglobin	5.6 g/dl	13.4 g/dl	13-17 g/dL
Hematocrit	17%,	48%	42-54%
Red blood cell count	1.53106	4.81106	4.5-6×106 cells/ul
Mean corpuscular volume	110 fl	80 fL	78-95 fL
Mean corpuscular hemoglobin	36 pg	33.6 pg	27.0-32.0 pg
Total bilirubin	3.40 mg/dL	0.9 mg/dl	0.20-1.60 mg/dL
AST	80 U/L	33U/L	10-40 U/L
ALT	79 U/L	43 U/L	9-41 U/L
ALP	305 U/L	250 U/L	80-270 U/L
γGT	111 U/L	65 U/L	8-61 U/L
Albumin	2.0 g/d	3.5 g/dl	3.48-5.39 g/dL
CRP	6.9 mg/L	2 mg/L	0-4 mg/L
AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; γGT: Gamma Glutamyl Transpeptidase; ALP: Alkaline Phosphatase; CRP: C-reactive Protein			

Table 2: Abnormal hematochemical parameters in second admission of patient.

DISCUSSION

PV is a myeloproliferative neoplasm characterized by increased red blood cell mass associated with an increased risk for thrombotic events, leukemic transformation, and myelofibrosis [3]. Patients with a sustained elevation of hemoglobin/hematocrit, subnormal serum Erythropoietin (EPO) level, and a JAK2 V617F mutation meet the diagnostic criteria for PV [4]. The goals of care in patients with PV are to reduce the risk of thrombosis, ameliorate symptom burden, and minimize the risk of evolution to post-PV myelofibrosis and or acute myeloid leukemia/myelodysplastic syndrome [5]. Patients should be evaluated for a history of thrombotic events (venous and arterial), PV-associated symptoms (e.g. pruritus, erythromelalgia, bleeding), cardiovascular risk factors, splenomegaly, JAK2 V617F mutation (in peripheral blood or bone marrow), and bone marrow fibrosis [6].

For all patients with PV, maintenance of hematocrit <45% recommended. Some expert recommended hematocrit<45% in men and<42% in women. For all patients with PV, except those with a contraindication to its use, low dose aspirin (150 mg daily) is recommended. For patients with low-risk PV (≤60 years old and no history of thrombosis), the achievement of target hematocrit values by phlebotomy without a cytoreductive agent is recommended [7].

For patients with high-risk PV (>60 years old and or history of thrombosis), phlebotomy plus cytoreductive therapy is recommended. For most patients who require cytoreductive agents (i.e. patients with high-risk PV, and patients with low-risk PV who do not achieve the target haematocrit or symptom control by phlebotomy and aspirin alone), initial treatment with Hydroxyurea (HU) rather than pegylated Interferon alpha, busulfan, ruxolitinib, or other agents is recommended [8,9]

Therefore, at least four forms of Budd-Chiari syndrome can be identified: fulminant, acute, sub-acute, and chronic. Patients with fulminant Budd-Chiari syndrome usually present with jaundice associated with an increase in liver function enzymes, nausea, vomiting, abdominal pain, and, within eight weeks of the onset, hepatic encephalopathy. In the acute form, there is a tendency to rapid and progressive liver parenchyma necrosis, with increase in transaminase, though smaller than that of the fulminant forms, in association with jaundice, pruritus, abdominal pain, and intractable ascites appearance. The subacute forms are certainly the most frequent, and their onset is insidious because ascite and laboratory abnormalities typical of hepatocellular damage are reduced, due to extensive collateral porto-systemic shunt formation. Finally, chronic Budd-Chiari syndrome is evident in patients with previous history of liver cirrhosis, as possible complication. Hepatomegaly is present in all four forms, while splenomegaly and esophageal varices are typical of subacute and chronic disease [10,11].

Pathogenesis may be attributable to a reduction in outflow from the liver leading to hepatic sinusoids and portal vein increased pressure, with a progressive stasis tendency and consequent

hypoxic damage, as well as portal vein thrombosis [12]. A further possible mechanism, related to blood stasis and hypoxic injury, which can promote hepatocellular damage, could be production of free radicals and the resulting oxidative damage [10].

Amitrano et al. reported major bleeding from oesophageal varices as possible acute PVT onset even if they point out this could be due more to underlying, still undiscovered cirrhosis rather than to acute onset of portal vein thrombosis [12].

An Italian study analyzed all the possible causes of death in 192 patients with polycythemia vera. The most important were found to be cardiovascular complicacy (36.4%), including arterial thrombosis (24%), venous thromboembolism (5.2%) and other cardiovascular diseases (7.2%). These are significantly higher than all other causes, including neoplasms (30%), hemorrhages (3.1%), polycythemia evolution (2.6%, spent phase 2.1%, myelodysplasia 0.5%) and all other causes (28.1%, including hepatic failure 2.1%) [13].

CONCLUSION

Although unusual, portal venous thrombosis related events like portal hypertension followed by massive hematemesis may be presentation of PV in previously symptomless patients. All clinicians should be aware of such uncommon associations of PV, caused by heightened viscosity led vascular thrombotic events. Hence we describe a rare gastroenterological presentation of a hematological condition, which provided an unexpected diagnosis. Myeloproliferative disorders should always be considered in the investigation of portal vein thrombosis.

FOOTNOTES

Conflicts of interests: The Authors declare that there are no competing interests.

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