

Portal Vein Thrombosis and Budd-Chiari Syndrome as the Initial Symptom of Polycythemia Vera and Hyperhomocysteinemia



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ABSTRACT

Portal Vein Thrombosis (PVT), commonly associated with cirrhosis of liver and thrombophilia, is one of the causes of severe abdominal pain. In the absence of non-cirrhotic non-malignant extrahepatic portal vein thrombosis, Myeloproliferative Disease (MPD) and an underlying thrombotic disorder should always be suspected and investigated. Hyperhomocysteinemia has been well-documented to increase the risk of arterial thrombotic events, peripheral arterial disease, and stroke. It is also a risk factor for deep-vein thrombosis. In the general population, association with portal vein thrombosis is very unusual, and only a few cases have been reported. We describe a case of Polycythemia Vera (PV) and hyperhomocysteinemia presenting with severe abdominal pain due to portal vein thrombosis. The patient underwent phlebotomy and was prescribed life-long anticoagulant, aspirin, vitamin B6, vitamin B12, and folic acid, then referred to a hematologist.

Introduction

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he incidence of PVT among patients without cirrhosis is unclear. It may account for 5-10% of patients with portal hypertension in developed countries and up to a third of patients in devel-

oping countries (because of an increased frequency of infectious complications that predispose to PVT) [1, 2].

Portal Vein Thrombosis (PVT) in patients with a previously healthy liver is thought to be due to inherited or acquired prothrombotic states [3]. There is increasing evidence that hyperhomocysteinemia is a risk factor

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for venous thromboembolic disease (pulmonary embolism and deep vein thrombosis) [4, 5, 6].

Polycythemia Vera (PV) is a chronic myeloproliferative neoplasm characterized by clonal proliferation of myeloid cells and an elevated red blood cell mass [7]. PV should be suspected in any patient with an increased red blood cell mass or increased hemoglobin/hematocrit and an arterial oxygen saturation >92%. PV should also be suspected in patients with the Budd-Chiari syndrome and portal, splenic, or mesenteric vein thrombosis [8].

We report a case who was admitted to the Internal Medicine Department of Imam Khomeini Hospital Complex, Tehran, Iran because of the abdominal pain which we found to be affected by Budd-Chiari syndrome and portal vein thrombosis as the onset of an undiagnosed PV and hyperhomocysteinemia.

Case Presentation

A 42-year-old man presented with the complaints of abdominal pain for 3 weeks. It was dull aching in nature, not associated with nausea and vomiting and not accompanied by hematemesis and melena. He was

afebrile and gave no history of dark urine, headache, seizure, loss of consciousness, and erythromelalgia. However, he had a history of generalized itching (which worsen with bathing). Physical examination revealed ascites and abdominal distention. He was non-icteric. Investigation of organomegaly was impossible due to ascites, and physical examination was otherwise normal. Table 1 presents the laboratory data at initial presentation.

Abdominal Ultrasound (US) showed abundant ascites, liver with non-homogeneous echogenicity pattern, increased portal vein diameter (1.64 cm) with few flow signs, increased spleen volume (longitudinal diameter 15.7 cm), and left liver lobe atrophy due to chronic portal vein thrombosis. Abdominopelvic CT scan revealed mild splenomegaly, mild pleural effusion, liver left lobe atrophy and caudate lobe enlargement (due to chronic thrombosis), collateral mesenteric veins, ascites, and portal vein thrombosis.

Based on imaging data, the patient underwent evaluation of blood markers of hepatitis B, hepatitis C, HIV, and thrombophilic disorders (lupus anticoagulant, anti-cardiolipin antibodies, antinuclear antibodies, anti-dsDNA

Table 1. Laboratory data

Test	Value	Normal Range
WBC	11000 cell/L	4000-10000 cell/L
Hemoglobin	17.9 g/dL	40-43.5 g/dL
MCV	76.9 fL/RBC	80-95 fL/RBC
Platelets	422000	150000-450000 cell/ μ L
ESR (1 hour)	10 mm/h	0-20 mm/hr
Serum bilirubin	1.8 mg/dL	0.1-1.2 mg/dL
Serum total protein	8.1 g/dL	6-8 g/dL
Serum albumin	4.5 g/dL	3.5-5.5 g/dL
Aspartate transaminase	72 U/L	<37 U/L
Alanine transaminase	34 U/L	<41 U/L
Alkaline phosphatase	1041 IU/L	44-147 IU/L
Gamma-glutamyl transferase	9 U/L	9-48 U/L
Serum amylase	39 U/L	<100 U/L
Serum Lipase	27 U/L	<38 U/L

antibodies, and homocysteine). These markers were all within normal limits except homocysteine, which was 41 (NL up to 15). We started combined therapy with Low-Molecular-Weight Heparins (LMWHs) and warfarin until the target International Normalized Ratio (INR) range (INR 2.5-3.5) was achieved. Given the strong suspicion of PV, genotyping for JAK2 V617F was tested and proved positive. Based on all collected data, the patient was diagnosed with Budd-Chiari syndrome due to PV and hyperhomocysteinemia.

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. [7]. Patients with a sustained elevation of hemoglobin/hematocrit, subnormal serum Erythropoietin (EPO) level, and a JAK2 V617F mutation meet the diagnostic criteria for PV [8, 9, 10]. Bone marrow aspiration and biopsy are not required in such patients unless disease evolution is suspected [11]. 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 [11].

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 [9].

For all patients with PV, maintenance of hematocrit <45% is recommended rather than higher target hematocrit values. Some experts suggest a target hematocrit of <45% in men and <42% in women.

Phlebotomy is the mainstay of management of red blood cell mass in PV [11, 12]. For all patients with PV, except those with a contraindication to its use, low-dose aspirin (40, 100 mg by mouth twice 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 [12-16].

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 [17-19].

Hyperhomocysteinemia appears to be an independent risk factor for cerebrovascular, peripheral arterial, coronary heart disease, and venous thromboembolic disease. Hyperhomocysteinemia has been classified as follows: Moderate (15 to 30 $\mu\text{mol/L}$); Intermediate (30 to 100 $\mu\text{mol/L}$); Severe (>100 $\mu\text{mol/L}$) [20]. A reasonable interpretation of the results of trials in primary and secondary prevention is that adequate intake of B vitamins, whether in the diet or from supplements, prevents homocysteine-associated vascular disease [21-23].

Ethical Considerations

Compliance with ethical guidelines

All ethical principles were considered in this article.

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Conflict of interest

The authors declared no conflict of interest.

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