

Case Report

Polycythemia Vera leading to Jaundice and Marantic Endocarditis, A Case Presentation

Pasricha R^{1*}, Rashidzada S¹, Adiyody J², Dave P¹ and Kuang A¹

¹Department of Medical Education/Family Medicine, Good Samaritan Hospital, USA

²Department of Internal Medicine, Good Samaritan Hospital, USA

*Corresponding author: Pasricha, R, Department of Medical Education/Family Medicine, Good Samaritan Hospital, USA

Received: June 15, 2022; Accepted: September 08, 2022; Published: September 15, 2022

Abstract

Polycythemia vera is an uncommon myeloproliferative neoplasm characterized by the abnormal proliferation and maturation of hematopoietic stem or progenitor cells. It is also known as one of the BCR-ABL1 negative myeloproliferative neoplasms, along with essential thrombocythemia and myelofibrosis. In comparison to essential thrombocythemia and myelofibrosis, polycythemia is driven by JAK2 mutations, specifically JAK2V617F, an activating mutation encoding a tyrosine kinase [1]. This variant mutation is correlated with increased erythropoiesis and myelopoiesis, lower platelet count, higher incidence of splenomegaly, pruritus and thrombotic events.

A 58-year-old male presented to the Emergency Department complaining of pruritus and painless jaundice. Comprehensive blood count revealed an elevated white blood cell count, hemoglobin/ hematocrit, and platelets. Total bilirubin was elevated at 30.3g/dL, with a direct bilirubin of 27g/dL. A Jak-2 mutation was positive, which suggested a diagnosis of polycythemia vera although atypical given his jaundice. An Erythropoietin level was found to be less than 1, suggesting a primary cause of polycythemia vera. In addition, the patient was found to have marantic nonbacterial thrombotic endocarditis on transesophageal echocardiogram. Patient was treated with aspirin to prevent thrombotic events, hydroxyurea and cholestyramine.

The patient's physical examination of profuse jaundice along with an elevated direct bilirubin count of 27g/dL typically does not correlate to a presentation of polycythemia vera. Through further workup, the patient did not demonstrate hemolytic or intrahepatic causes, both intrinsic and extrinsic to the liver, which would have explained the jaundice presentation. This led to a conclusion that the patient's polycythemia vera most likely caused the jaundice presentation.

Keywords: Polycythemia vera; Jaundice; Marantic endocarditis; Thrombocytosis

Case Presentation

58-year-old Caucasian male with a past medical history of renal colic presented with pruritus and painless jaundice, worsening over the past two to three weeks. The patient reports that the pruritus is worse while in the shower. His physical examination was pertinent for scleral icterus and jaundice. At presentation, his labs were significant for a leukocytosis of $27 \times 10^3/\text{mcl}$, hemoglobin of 16g/dL, and platelet count of $444 \times 10^3/\text{mcl}$. Total bilirubin was elevated at 30.3mg/dL, with a predominant direct bilirubin of 27mg/dL. A Jak-2 mutation was positive, which suggested a diagnosis of polycythemia vera although atypical given his jaundice.

The Patient was treated with aspirin to prevent thrombotic events, hydroxyurea and cholestyramine. Liver biopsy revealed chronic inflammation with hepatic cholestasis. Bone marrow biopsy revealed a hypercellular hematopoietic marrow sample, with megakaryocytic hyperplasia. A transthoracic echocardiogram was ordered, as the patient had a loud systolic murmur, as well as to rule out any obstructive causes of microangiopathic hemolytic anemia. An incidental aortic valve mobile density was visualized on transthoracic echocardiogram. A subsequent transesophageal echocardiogram

confirmed the aortic mobile density.

The patient had no risk factors such as intravenous drug abuse or recent dental procedures, which could have explained the etiology of this mobile density as a bacterial endocarditis. The patient did not exhibit any active signs of infection. Thus the diagnosis of a marantic nonbacterial thrombotic endocarditis was established. The patient was discharged from the hospital as symptoms had resolved.

On follow up office visits with hematology/oncology, the patient's jaundice continued to resolve. Testing for BCR-ABL gene mutation to rule out suspicion of chronic myeloid leukemia was negative. Workup for hepatic and biliary causes of elevated direct bilirubin in the setting of polycythemia vera were negative. Cardiothoracic surgery was consulted regarding the patient's marantic endocarditis for which they recommended an eventual aortic valve replacement after the stabilization of the patient's polycythemia vera. Treatment with aspirin and hydroxyurea caused a downtrend in all cell lines, including his complete blood count and bilirubin. This suggested the patient's jaundice was due to the Polycythemia Vera.

Discussion/Conclusion

Polycythemia vera is a panmyelosis pathophysiological process.

Examples of increased bilirubin production include extravascular hemolysis, extravasation of blood into tissues, intravascular hemolysis, or Wilson's disease [2]. An impaired hepatic bilirubin uptake would most commonly be seen in heart failure, portosystemic shunts, Gilbert syndrome, or pharmacotherapy. Impaired bilirubin conjugation can be seen in conditions such as Crigler-Najjar syndrome, Gilbert, neonatal jaundice, hyperthyroidism, or liver disease [3].

Although the majority of the pathologies mentioned above have a hepatic or biliary involvement, this case presentation illustrates that jaundice is not limited to the mentioned pathophysiological mechanisms. Jaundice secondary to polycythemia vera can be seen in hepatic venous thrombosis, such as Budd-Chiari syndrome. Primary myeloproliferative diseases are the leading cause of hepatic vein thrombosis, and are diagnosed in 20% of cases [4]. Necropsy studies showed a 6% incidence of hepatic vein thrombosis in individuals with polycythemia vera [5]. However, imaging had ruled out this cause through ultrasound and Magnetic Resonance Imaging (MRI). Although increased hemoglobin can cause indirect hyperbilirubinemia through intra- or extravascular hemolysis, the patient's bilirubin was predominately direct. This suggests that the hemolysis due to red blood cell breakdown was not due to the marantic thrombosis endocarditis.

Due to the prothrombotic and hypercoagulability nature of polycythemia vera, there are many clinical manifestations. The clinical manifestations are not limited to transient visual changes, myocardial infarctions, nonbacterial thrombotic endocarditis, pruritus especially following warm shower, cerebrovascular events, erythromelalgia, deep vein thrombosis, superficial thrombophlebitis and gastroduodenal lesions [6].

The pathophysiology of the clinical manifestations of this patient are unclear. Nonbacterial thrombotic endocarditis may initiate from the hyperviscosity of polycythemia vera which in turn causes endothelial injuries. Causes of nonbacterial thrombotic endocarditis include autoimmune disorders, most commonly being lupus, malignancy, and hypercoagulable states. The endothelial injuries lead to platelet aggregation and fibrin deposition [7]. As the thrombus sits on a prior undamaged valve of the heart, it can be easily dislodged and emboli. Compared to infectious etiologies of endocarditis, there are less inflammatory reactions at the valve of attachment [8]. Therefore, it is easier to dislodge nonbacterial valvular vegetation [9].

In this case, the increased hypercoagulability and his viscosity of his polycythemia vera most likely caused the accumulation of a thrombus on the aortic root which was then detected by auscultating

a holosystolic crescendo-decrescendo murmur on the 2nd right intercostal space. Due to this occurrence, CT surgery was consulted and the decision was made for an eventual total aortic valve replacement after the patient's polycythemia and panmyelosis was stabilized.

This case demonstrates the patient's jaundice was due to the polycythemia vera. Prior case reports and research have listed hepatic venous thrombosis as a potential cause; however imaging in this patient had ruled this out. The hyperviscosity of polycythemia vera causes red blood cell injury in the setting of the patient's thrombotic marantic endocarditis, however would not cause a direct bilirubin elevation. The pharmacotherapy utilized on this patient caused a downtrend in all his cell lines with a final bilirubin level below 2gm/dL. This demonstrates an isolated case report in which the jaundice was due to the Polycythemia Vera in the setting of a nonbacterial thrombotic endocarditis.

References

1. Ruggeri M, Tosetto A, Frezzato M, Rodeghiero F. The Rate of Progression to Polycythemia Vera or Essential Thrombocythemia in Patients with Erythrocytosis or Thrombocytosis. *Annals of Internal Medicine*. 2003; 139: 470.
2. Reisman Y, Gips CH, Lavelle SM, Wilson JH. Clinical presentation of (subclinical) jaundice--the Euricterus project in The Netherlands. United Dutch Hospitals and Euricterus Project Management Group. *Hepato-gastroenterology*. 1996; 43: 1190-5.
3. Roy-Chowdhury J, Roy-Chowdhury N, Listowsky I, Wolkoff AW. Drug and Drug Abuse--Associated Hyperbilirubinemia: Experience With Atazanavir. *Clinical Pharmacology in Drug Development*. 2017; 6: 140-146.
4. Janssen HL, Meinardi JR, Vlegaar FP, Uum SHV, Haagsma EB, Meer FJVD, et al. Factor V Leiden mutation, prothrombin gene mutation, and deficiencies in coagulation inhibitors associated with Budd-Chiari syndrome and portal vein thrombosis: results of a case-control study. *Blood*. 2000; 96: 2364-8.
5. Hirshberg B, Shouval D, Fibach E, Friedman G, Ben-Yehuda D. Flow cytometric analysis of autonomous growth of erythroid precursors in liquid culture detects occult polycythemia vera in the Budd-Chiari syndrome. *Journal of hepatology*. 2000; 32: 574-578.
6. Tefferi A. Polycythemia vera and essential thrombocythemia: 2012 update on diagnosis, risk stratification, and management. *American Journal of Hematology*. 2012; 87: 284-293.
7. Carmen Busca-A Angel Robles-M, Luis Ramos-R, Jorge Alvarez. Non-bacterial Thrombotic Endocarditis, Infective Endocarditis: Intech Open. 2019.
8. Deppisch, LM, Fayemi, AO. Non-Bacterial thrombotic endocarditis: clinicopathologic correlations: *Am Heart J*. 1976; 92: 723-9.
9. Rosen P, Armstrong D. Nonbacterial thrombotic endocarditis in patients with malignant neoplastic diseases. *The American journal of medicine*. 1973; 54: 23-29.