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Case Report

Polycythemia Rubra Vera Presenting as Acute Coronary Syndrome with Incidental Finding of Left Renal Artery Occlusion

Jenny Koshy[1], Justina Koshy[2], Jeetendra Singh[3], Steffi Thomas[4]

[1]JR- 3, Department of Medicine, Dr. Vasantrao Pawar Medical College, Hospital and Research Centre, Nashik-422003, India

[2]CMO, Yashwantrao Chavan Memorial Hospital, Pimpri, Pune 411018, India

[3]Jeetendra Singh, Professor and Head, Department of Pharmacology, Dr. Vasantrao Pawar Medical College, Hospital and Research Centre, Nashik-422003, India

[4]Steffi Thomas, JR-2, Department of Medicine, Dr. Vasantrao Pawar Medical College, Hospital and Research Centre, Nashik-422003, India

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Corresponding author: Jenny Koshy
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Abstract

Introduction: Polycythemia rubra vera (PRV) is a Philadelphia chromosome (BCR-ABL) negative myeloproliferative neoplasm characterized by clonal stem proliferation of WBCs, RBCs and platelets. Men have a higher preponderance than female with approximately 2.8 per 1,00,000 men and 1.3 per 1,00,000 women being involved with PRV with the typical age at diagnosis being between 60-65 years of age.

Case Report: A 65 year female, hypertensive since 1 year was admitted with complaints of left sided chest pain radiating to the back and left arm not associated with palpitations or diaphoresis. Patient also gave history of dyspnoea on exertion since last few days. On examination the patient had pulse of 78 beats per minute, BP was 150/100 mmHg. There were no other positive findings like pedal oedema, pulmonary crepitations or hepato-splenomegaly. ECG was taken, which showed ST-T changes and T wave inversions in leads I, aVL,V5 and V6 .

Discussion: This case report outlines the investigations and management of a patient who developed ischemic heart disease and renal artery occlusion secondary to the thrombotic events associated with PRV.

Conclusion: Thus, from the case report it is evident that it is necessary to keep rare causes of acute coronary syndrome (ACS) like polycythemia rubra vera as differentials, in the treatment of ACS.

Keywords: Polycythemia Rubra Vera, Acute Coronary Syndrome, Left Renal Artery Occlusion

Introduction

Polycythemia rubra vera (PRV) is a Philadelphia chromosome (BCR-ABL) negative myeloproliferative neoplasm characterized by clonal stem proliferation

of WBCs, RBCs and platelets. [1,2] Men have a higher preponderance than female with approximately 2.8 per 1,00,000 men and 1.3 per 1,00,000 women being involved with PRV with the typical age at diagnosis being between 60-65 years of age. [3] 96% of patients have Janus kinase 2 (JAK2) mutation. [4]

The increase in RBC mass leads to increased hyperviscosity of the blood leading to an increased risk of thrombosis leading to either arterial or venous vascular occlusive events in patients leading to a prominence in coronary and cerebral events. [5,6] Symptoms include headache, dizziness , vertigo, tinnitus, visual disturbances , angina pectoris, intermittent claudication or stroke whereas physical findings include splenomegaly, hepatomegaly, plethora, hypertension etc.[7,8] Elevated haematocrit is the hallmark of polycythaemia with haematocrit being >55 % in approximately 83% of cases. [9] The treatment of choice is Phelobotomy. [3]

We report a case of PRV who presented to us as acute coronary syndrome with complaints of chest pain, high blood pressure and raised hematocrit, RBCs, WBCs and platelets. And on investigations was also found to have left renal artery occlusion.

Case report:

A 65 year female, hypertensive since 1 year was admitted with complaints of left sided chest pain radiating to the back and left arm not associated with palpitations or diaphoresis. Patient also gave history of dyspnoea on exertion since last few days .On examination the patient had pulse of 78 beats per minute , BP was 150/100 mmHg.There was no other positive findings like pedal oedema, pulmonary crepitations or hepato-splenomegaly.ECG was taken , which showed ST-T changes and T wave inversions in leads I ,aVL,V5 and V6 . A provisional diagnosis of Acute coronary syndrome was made. Routine Blood investigations were sent , which revealed a haemoglobin of 16.9gm/dl, red cell count 8.91million /ul ,Hct58.6 %, MCV 65.8fL ,MCH 19.9pg, WBC 50300 platelets10,84,000 .PBS showed RBC morphology as mild microcytic hypochromic with anisocytosis,neutrophilic leucocytosis with shift to left and thrombocytosis .Her creatinine was on the higher side being 1.3 and uric acid was 10.4mg/dl.Erthrocytosis, leucocytosis , thrombocytosis along with a raised haematocrit raised a suspicion of PolycythemiaRubra Vera. Hence JAKV167 was then sent for further confirmation which was positive. Also the cause for a rise in creatinine was evaluated and accordingly a USG abdomen for renal pathology was done, which showed unequal sized kidneys. (left kidney- 7x2.6cm right kidney- 10.3x3.7cm). Further evaluation by Renal Dopplershowed moderately echogenic atrophic left kidney with left renal artery occlusion proximally. Also bone marrow aspiration was done which showed hypercellular marrow with panmyelosis.

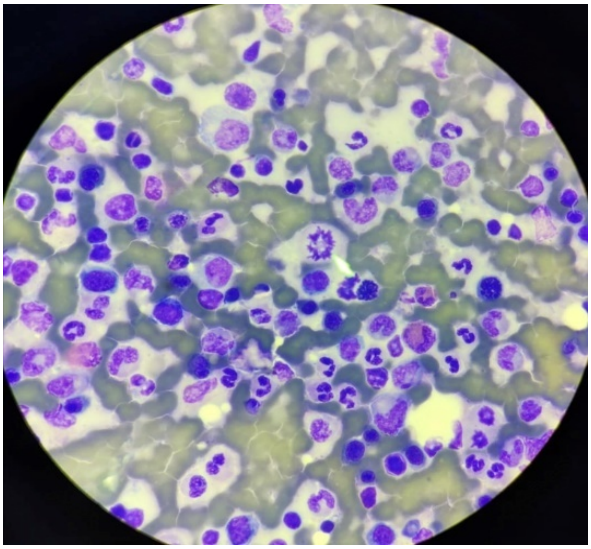

Figure1: Bone marrow showing hypercellular marrow with panmyelinosis.

2D-ECHO was done which revealed mild left ventricular hypertrophy with regional wall motion abnormality seen in distal septum and apex and distal inferior wall hypokinesia with a left ventricular ejection fraction of 40% .(For ACS she was treated with, Tab. Aspirin 75 mg/day, Tab. Clopidogrel 75 mg/day, Tab Atorvastatin 20 mg/day ,Inj. Heparin 5000 four times a day, beta blocker Carvedilol 3.125 mg twice/day, tablet Febuxostat 40 mg once a day and anti-hypertensives.She underwent angiography which revealed Left descending artery diagonal thrombus and she underwent a successful angioplasty with single stent.She was also initiated on Tab.Hydroxyurea 500 mg twice a day. Patient and her relatives were explained about the ailment i.e. polycythemia rubra vera and importance of regular follow up for future needs of phlebotomy.

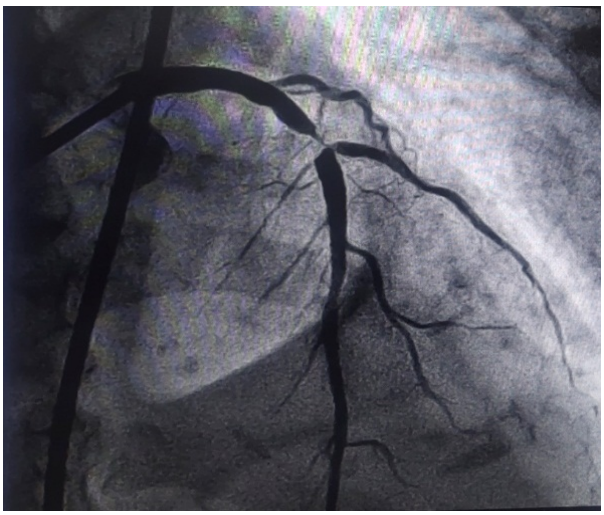

Figure 2: Coronary angiography revealing block in left anterior descending diagonal branch.

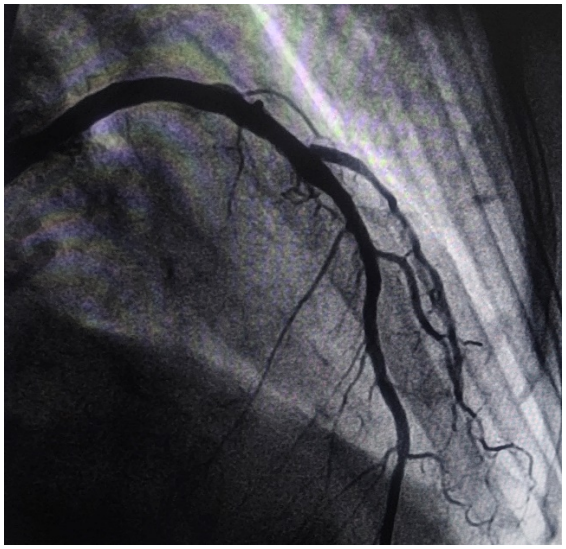

Figure 3: Showing revascularization after stenting.

Discussion:

PRV is a panhyperplastic neoplastic stem cell disorder whose prominent feature is elevated absolute red blood cells accompanied by increased white blood cell and platelets due to uncontrolled abnormal clones of hematopoietic stem cells.[7,8,10,11] It is a relatively rare disorder occurring in around 0.6-1.6 million per million population with a higher predilection in Ashkenazi jews .[3] Though the peak incidence is in the age group of 50-70 years PCV can occur in any age group.[12] Symptoms are present due to increased thrombosis seen in about a third of patients owing to blood hypervicsosity secondary to an increase in the cellular elements of the blood leading to an increased incidence of stroke, myocardial infarction and arterial or venous thrombosis.[5] Also,hypertension is common in these patients. Splenomegaly(75%) and hepatomegaly (25%) is usually present in many of the patients.[13]

Thrombotic complications in polycythemia vera include:-

1)Microvascular complications:-

- Erythromelalgia
- Headache
- Dizziness
- Visual disturbances
- Paresthesia
- Transient ischemic attack

2)Macrovascular complications include:-

a)Arterial thrombotic events:

- Myocardial infacrtion
- Unstable angina
- Stroke
- Peripheral arterial occlusion

b)Venous thrombotic events:

- Deep vein thrombosis
- Pulmonary embolism
- Intra abdominal vein thrombosis
- Cerebral vein thrombosis [14]

The cause of PRV is unknown but many researches are ongoing to define the molecular lesion associated with it. The JAK2 V617F mutation is one identified mutation which leads to pancytosis by turning on the cytokine receptor. [15] As per the 2016 WHO criteria for diagnosing PRV the presence of either all three major criteria or the first two major criteria and minor criteria is required.

Major WHO criteria are as follows:-

1) Hemoglobin> 16.5 g/dl in men and > 16 mg/dl in women or

Hematocrit> 49% in men and 48 % in women or

Red cell mass > 25 % above the mean normal predicted value.

2) Bone marrow biopsy showing hypercellularity for age with trilineage growth (panmyleosis) including prominent erythroid,granulocytic and megakaryocytic proliferation with pleomorphic ,mature megakaryocytes (differences in sizes)

3) Presence of JAK2 V617F or JAK exon 12 mutation.

Minor criteria:

1) Serum erythropoietin level below the reference range for normal. [16]

Other laboratory tests that are often found in these patients include:

1) thrombocytosis

2) leukocytosis

3) leukocyte alkaline phosphatase >100 units/L

4) Hyperuricemia (40%)

5)Prolongation of prothrombin time and activated partial thromboplastin .

6) Elevation of vitamin B12. [10]

The goal of treatment aims at reducing the risk of thrombosis by normalizing red blood cell mass with phlebotomy with the aim to keep the hematocrit less than 45% and suppressing the myeloproliferative activity with chemotherapy with hydroxyurea (in patients older than 50 years).[11]Recently JAK Inhibitors Ruxolitinib has been approved for the treatment of PRV who have an inadequate response to hydroxyurea. Phosphorus 32,interferon alfa and Anagrelide are other therapies reserved for selected patients. Majority of the patients are administered anti platelets like aspirin and clopidogrel.[17,18,19]

This case report outlines the investigations and management of a patient who developed ischemic heart disease and renal artery occlusion secondary to the thrombotic events associated with PRV. The patient satisfied three of the major criterias set by WHO for the diagnosis of PRV and was treated successfully by perfoming phlebotomies to maintain a normal haematocrit and administering hydroxyurea to control thrombocytosis. On discharge she was advised on Tab Hydroxyurea 1000 mg once a day, Tab. Aspirin 75 mg once /day, Tab. Clopidogrel once/day ,Tab .Atorvastatin 20 mg once /day and anti-hypertensives. She was also advised DTPA scan for evaluation of her kidney functions and follow up in OPD after 7 days.

Thus from the case report it is evident that it is necessary to keep rare causes of acute coronary syndrome (ACS) like polycythemia rubra vera as differentials, in the treatment of ACS.

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