Case study

POLYCYTHEMIA RUBRA VERA - A CASE REPORT

Abstract

Polycythemia vera, also denoted as polycythemia rubra vera is a Philadelphia chromosome (Ph)-negative myeloproliferative neoplasm which usually affects 2.5-10 people per 100000 people. Max cases are present in people age 60 years of age, out of which 10% patients are under the age of 40. The below presented case is an original case of 37-year-old female who presented to us with this condition with a history of insomnia, Fronto- parietal headache, a systemic itch that deteriorates after a hot water bath along with loss of concentration from last 6 weeks and early satiety, discomfort in the upper right abdomen and drastic weight loss from previous one month. The blood test depicted markedly increased hemoglobin (23.8g/dl). A bone marrow biopsy was done and it was confirmed that the patient is suffering from PRV. The patient was treated with phlebotomy, aspirin, and Ruxolitinib.

Keywords: polycythemia vera, myeloproliferative disorder, JAK2

Introduction

First ever discovered in 1892, Polycythemia vera (PV), a haemopoietic disorder related to stem cell, is a persistent Philadelphia chromosome (Ph)-negative myeloproliferative neoplasm which shares features

with two other myeloproliferative neoplasms, primary myelofibrosis (PMF) and essential thrombocytosis (ET), in terms of its origin from haemopoietic stem cell, fundamental stimulation of hemopoiesis resulting in overproduction of blood cells which are normal morphologically [1]. These phenotypic characteristics are the repercussions of JAK2 activation, either directly or indirectly. Out of every 1,00,000 people, 2.5-10 are polycythemia sufferers [2]. The average age for a person to develop polycythemia vera is 61 years out of which approximately 10% of the patients are under the age of 40 [3]. The classical sign of Polycythemia Vera is abnormally increased red cell production. Early satiety, weight loss, fatigue, diaphoresis, pruritus, epigastric discomfort, and vasomotor symptoms like dizziness, visual disturbances, headache, and erythromelalgia, are frequent manifestations of polycythemia vera. When discussing about the physical findings, plethora, splenomegaly, hypertension and hepatomegaly are the most common ones [4]. The most common complications associated with polycythemia vera are venous and arterial thrombosis with 16% and 7.5% rates respectively [5,6]. Herein, we present a case report of a patient diagnosed from polycythemia vera.

Case Presentation

A 37-year-old female arrived to the outpatient department and presented with a history of insomnia, Fronto- parietal headache, a systemic itch that deteriorates after a hot water bath along with loss of concentration from last 6 weeks. Also, the patient complaints about early satiety, discomfort in the upper right abdomen and drastic weight loss from previous one month. Except from the fact that she was treated for miliary tuberculosis around 6 years back, there was no other significant medical and medication history. The lady was a housewife and did not smoke and drink. There was no family history to speak of. A general physical examination was conducted which revealed that the blood pressure of the lady was 130/80 mmHg while the pulse was 80/min regular. The patient had stigmata of neoteric weight

loss, but no signs of cyanosis, edema, jaundice or dehydration were present. Facial plethora was observed along with bilateral conjunctival suffusion.

The blood test was done and peripheral blood film was prepared. The reports depicted markedly increased hemoglobin (23.8g/dl) (table 1). The peripheral blood film (Fig. 1) showed numerous RBCs which were normocytic and normochromic. The red blood cell (RBC) indices were normal but eventually the red cell mass is increased. No abnormal or immature cells were present. The level of serum erythropoietin was below the normal accepted limits. While inhaling ambient air, the oxygen saturation was reported to be 95%. and the urine examination were also normal. The electrocardiogram (ECG) and chest X-ray were normal. Biochemical parameters showed normal blood glucose, urea, serum creatinine and liver function tests but mild hepatomegaly and moderate splenomegaly was revealed on ultrasound scan of the abdomen. The signs and symptoms were suggestive of polycythemia Rubra Vera. To confirm the diagnosis, genetic tests were ordered to identify the mutation in the JAK2 gene. Janus kinase 2 gene (JAK2) mutation analysis showed a positive result at 59%. A bone marrow biopsy was also performed on the patient which confirmed the diagnosis of primary proliferative polycythemia or polycythemia Rubra Vera (PRV). The patient went through Periodic phlebotomy (venesection) which is the first line treatment to maintain the red cell mass within normal limits and prevents thrombosis. Around 500-600 mL of blood was removed and venesection was initially repeated every 5–7 days until the hematocrit was reduced to below 45%. Thereafter, venesections were performed at 3-month intervals. Aspirin was indicated for thromboprophylaxis. Hydroxyurea 1000 mg oral daily was used to treat symptomatic splenomegaly and myeloproliferation. Because hydroxyurea was ineffective, she was also given Ruxolitinib 5mg twice a day to help stabilize her blood and function of immune system. Monitoring monthly blood count allowed to enhance the effectiveness of the therapy. Therapeutic phlebotomies were repeated on a regular basis to keep the hematocrit below 45 percent.

Discussion

Polycythemia rubra vera or Polycythemia vera, is a disorder appertaining to stem cell, marked by an overabundance of red blood cells and the secretion of pro-inflammatory cytokines [7]. Increased red cell mass leads to thickening of blood, increasing the probability of clot formation which further leads to thrombotic complications like splenomegaly, arterial thrombosis hepatomegaly and venous thrombosis. Causes for high level of haemoglobin have been listed in figure 2. The risk of thrombotic events is much greater in people belonging to the age group 65 and older and individuals who previously have suffered from thrombosis. Increased RBC count, may also be accompanied by hiked platelet (megakaryocytic) augmentation and white blood cells (myeloid) [8]. Direct activation of JAK2 occurs via mutation in JAK2V617F or JAK2 exon 12 gene whereas mutation in thrombopoietin receptor, MPL or alterations in ER chaperone calreticulin is responsible for indirect activation of JAK2 [2]. According to the revised WHO guidelines ,2016, to diagnose polycythemia vera there are some major and minor criteria. All three major criteria must be met, or two major criteria plus one minor criterion [9]. The major criteria include (a) hemoglobin > 16 g/dL in women and > 16.5 g/dL in men, or hematocrit > 48% in females and > 49% in males, or red cell mass > 25% above the mean normal projected value, (b)JAK2 exon 12 mutation or JAK2V617F mutation and (c) Hypercellularity for age with trilineage growth (panmyelosis) includes substantial erythroid, granulocytic and megakaryocytic proliferation with pleomorphic, mature megakaryocytes in a bone marrow sample (differences in size). A serum erythropoietin level below the typical reference range is the first minor criterion for diagnosing polycythemia vera. Apart from this, bone marrow is another diagnostic method of importance as it assesses the severity of disease by computing the degree of bone marrow fibrosis [10] and helps in differentiation of PV from other types of myeloproliferative neoplasms [11]. The standard treatment options for polycythemia vera includes phlebotomy, aspirin, and cytoreductive agents like hydroxyurea, Interferon alfa, Ruxolitinib, Busulfan,

Fedratinib. Combination of low dose aspirin and Phlebotomy remains the mainstay of treatment of PV. Phlebotomy is beneficial in maintaining red cell mass within the accepted normal range I.e., maintain the hematocrit < 45%. Aspirin is used in the dose of 81-100mg/day for thromboprophylaxis in PV patients [12]. As per the latest guidelines, patients at high-risk are candidates for cytotoxic drugs and hydroxyurea is the initial drug of choice [13]. Patients who are unable to tolerate hydroxyurea are shifted to Ruxolitinib. Busulfan is reserved for patients above 65 years of age.

CONCLUSION

In PV patients the major aim is to prevent thrombotic complications, which is the prime reason of PV related morbidity and mortality and to maintain hematocrit at <45% which could be achieved by combined periodic phlebotomy and use of pharmacological agents. In the above discussed case, as there was timely diagnosis, the patient was saved from developing life-threatening complications.

HUMAN ETHICS

Consent was obtained by participant in the study.

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Table 1. Pathological test results

TEST	**RESULT**	**REFERENCE RANGE**
Haemoglobin	23.8 g/dL	12.0-16.0 g/dL
Haematocrit	0.66	0.36-0.46
RBC	7.86×10^{12}/L	3.5-5.5 x 10^{12}/L
WBC	14.3×10^{9} /L	4.5 to 11.0 × 10^{9}/L
Differential count		
Neutrophils	87%	40% to 60%
Lymphocytes	8%	20% to 40%
Monocytes	4%	2% to 8%
Eosinophils	1%	1% to 4%
Platelets	490×10^{9} /L (103 /mm3)	150-400 x 10^{9}/L

ESR	6 mm/1st hour	≤ 20 mm/hour

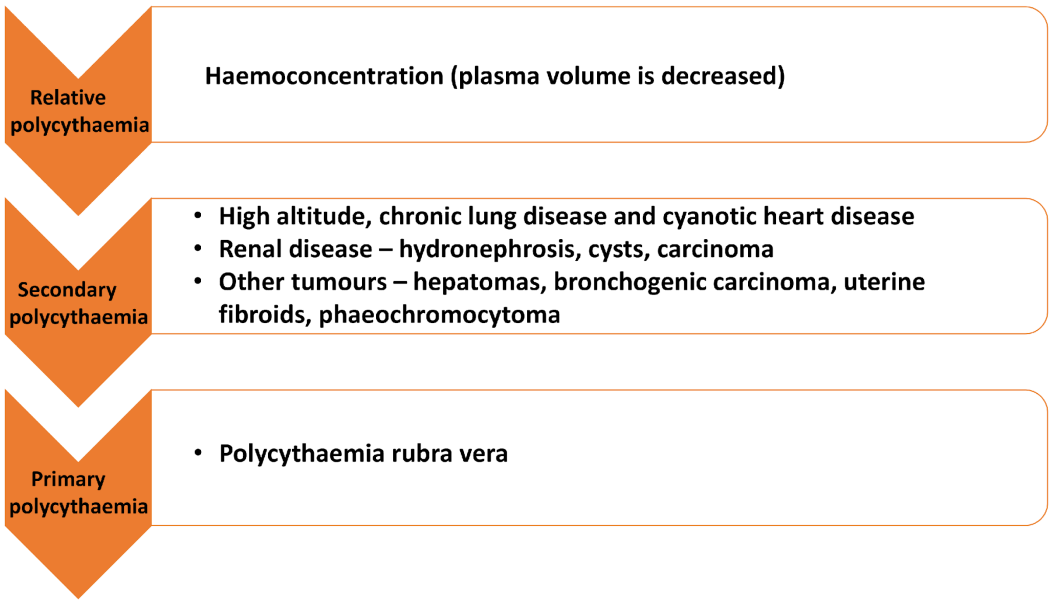

Fig. 1. Causes of high haemoglobin

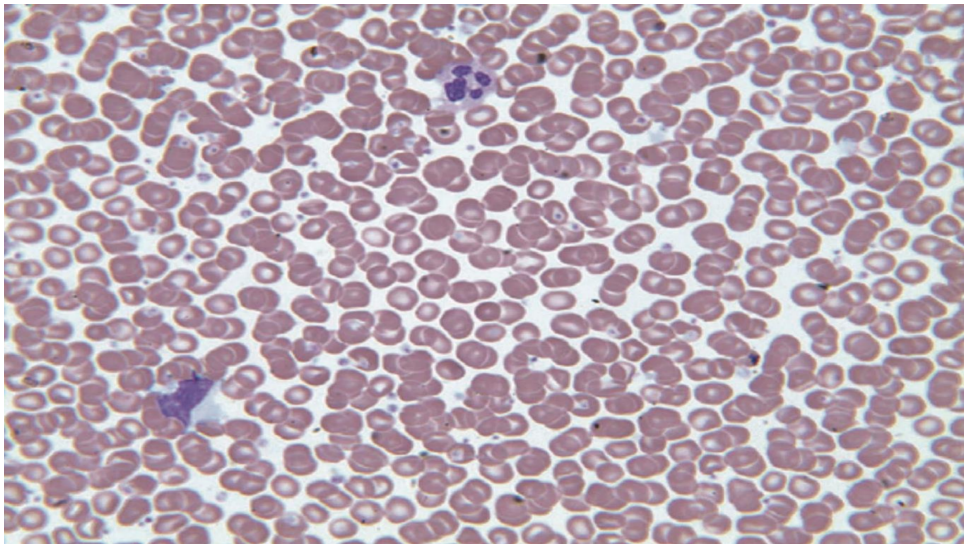

FIG. 2 - Peripheral blood film, clearly depicting elevated red cell count.