

Polycythemia Vera with Janus Kinase2 mutation

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Abstract

Polycythemia vera (PV) is a chronic myeloproliferative disorder characterised by panmyelosis, splenomegaly, and predisposition to venous and arterial thrombosis. Our case was a 54 year male patient who presented with massive splenomegaly, erythrocytosis and bone marrow panmyelosis and positive JAK2V617F mutation. Sensitive and relatively cost effective test of JAK2V617F mutation helped in early diagnosis and treatment of PV with certainty. Patient responded well with phlebotomy. Polycythemia vera is a uncommon myeloproliferative neoplasm which is asymptomatic in majority of patients thus needs early identification and treatment to prevent serious complications of haemorrhage and thrombosis.

Key words: JAK2V617F mutation, Polycythemia vera, bone marrow.

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INTRODUCTION

Polycythaemia vera (PV) is a chronic myeloproliferative neoplasm characterised by unregulated increased production of red cells and haemoglobin without erythropoietin stimulation.¹ It primarily affects adults over 50 years of age and has an annual incidence of about eight to ten cases per million population². A mutation in the Janus Kinase2 (JAK2V617F) gene is strongly associated with 95% cases of polycythemia vera and has a fundamental role in the pathogenesis of polycythemia vera.³

CASE HISTORY

A 54 year old male presented with gradual onset of headache, abdominal distension and on and off fever of

7 months duration. There was no history of smoking and hypertension. The respiratory system and cardiovascular system were normal. Previous investigation showed a consistent rise in haemoglobin and haematocrit. Per abdominal examination showed hugely enlarged spleen and mild hepatomegaly (Fig1). On admission his blood parameters were as shown in table1. Peripheral blood smear showed normocytic normochromic red blood cells, neutrophilic leucocytosis with mild shift to left and platelets singly and frequently in large clumps (Fig2A). Bone marrow aspiration showed panmyelosis with marked erythroid and megakaryocytic hyperplasia (Fig2B). Perls stain did not show any iron stores in the bone marrow. Diagnosis of polycythemia vera was suspected based on clinical examination, blood and bone marrow findings using WHO diagnostic criteria. Further PCR based JAK2V617F mutation analysis was done and positive (homozygous) result confirmed the diagnosis of polycythemia vera and excluded the secondary causes of erythrocytosis. Histopathological examination of bone marrow clot section revealed erythroid and megakaryocytic hyperplasia. Reticulin stain did not show marrow fibrosis. Patient responded to therapeutic phlebotomy. He is under follow up and to date is doing well.



Figure 1

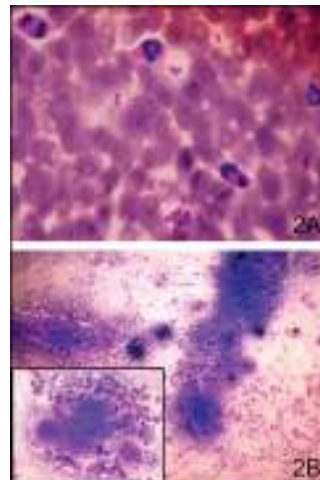


Figure 2A & 2B

Legends

Figure 1: Patient with splenomegaly and mild hepatomegaly (pen markings)

Figure 2A: Peripheral bloods smear showing normocytic normochromic RBCs with neutrophilia and platelets singly and in clumps (Leishman's, x 1000)

Figure 2B: Bonemarrow aspirate showing panmyelosis with prominent erythroid and megakaryocytic hyperplasia. Inset: Bizarre large megakaryocytic cluster (Leishman's, x 200, Inset- x 1000)

DISCUSSION

Janus kinase(JAK2) is a tyrosine kinase involved in the transduction of cellular growth stimuli.JAK2V617F mutation is identified in 95% cases of polycythemia vera resulting in cytokine independent (erythropoietin/thrombopoietin) growth and proliferation resulting in overproduction of erythrocytes thus increasing haemoglobin, haematocrit, red cell mass and higher frequency of major arterial and venous thrombotic complications in addition to platelet mediated microvascular circulatory disturbances.^{4,5} Bonemarrow aspiration in patients with polycythemia vera shows panmyelosis with a relative predominance of the erythroid and megakaryocytic lineages. In classic JAK2V617F positive polycythemia vera there is prominent megakaryocytic clustering composed of large, bizarre megakaryocytes with complex nuclear features.⁶ Patients with JAK2V617F homozygous mutation are bound to have advanced age at diagnosis, higher leucocyte count, haematocrit, larger spleen volume and are likely to display a symptomatic disease with increased risk of thrombosis and hemorrhage and higher rate of evolution into secondary myelofibrosis thus implicating a poor prognosis.⁵

CONCLUSION

JAK2V617F mutation is found in majority of patients with polycythemia vera and enables to diagnose polycythemia vera earlier with more certainty. Our case is presented for its rarity and to highlight the importance of JAK-2 mutation in diagnosis, prognosticating and treating suspected cases of polycythemia vera.

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