International Journal Dental and Medical Sciences Research
Volume 5, Issue 2, Mar - Apr 2023 pp 133-136www.ijdmsrjournal.com ISSN: 2582-6018

An Uncommon Case of Primary Myelofibrosis with Hepatosplenomegaly and Gastric Fundal Varices

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Date of Submission: 05-03-2023 Date of Acceptance: 15-03-2023

ABSTRACT
Primary myelofibrosis (PMF) is defined as theclonal proliferation of myeloid cells in the bone marrow, reactive cytokine-directed fibrosis and ultimate degeneration of healthy marrow. Treatment with allogeneic bone marrow transplantation is found to be curative. In our case, a 63-year-old male patient with complaints of black stools, reduced appetite and weakness was JAK2 positive with hepatosplenomegaly, gastric varices,anaemia, elevated LAP score, LDH and ALP and was given symptomatic treatment with regular follow-ups with CBC reports to monitor disease progression which improved patient's condition.

Keywords:Primary myelofibrosis, anaemia, Gastric varices, JAK2 mutation, Portal Hypertension

I. INTRODUCTION

PMF is a rare disease with an annual incidence rate of 1.5 per lakh population per year and an annual prevalence of 1.76-4.05 per lakh population per year[1,2]and was first diagnosed in 1879. Primary myelofibrosis (PMF) is a BCR-ABL1-negative myeloproliferative neoplasm (MPN) with aberrant megakaryocytic proliferation, fibrosis of the bone marrow, varied cytopenias, and a clinically heterogeneous phenotype.[3] The three known driver mutations in PMF are JAK2, CALR, and MPL. Most cases occur after 60 years and carry the worst prognosis. Leukemic transformation occurs in approximately 20 % of patients and is associated with a worse prognosis.[4]

The development and progression of PMF have been linked to two separate pathogenic processes: clonal myeloproliferative produced from stem cells and inflammatory fibrosis triggered by cytokine response. Bone marrow fibrosis is caused by the excessive and aberrant deposition of collagen and reticulin fibres that are produced by marrow fibroblasts.[5] According to newly available information, the pathophysiology of PMF may potentially be influenced by clonal, neoplastic, monocyte-derived fibrocytes. Non-specific symptoms of anaemia, fatigue, bruising, loss of appetite, fever, and bone pain may be presented. [6]Allogenic stem cell transplant is the definitive treatment. Ruxolitinib (JAK2 inhibitor) and symptomatic treatment can also be given. A potentially aggressive illness, PMF has a 6-year median survival rate and is linked to a shorter life expectancy.

II. CASE REPORT

A 63-year-old male patient presented with complaints of black stools and reduced appetite associated with weight loss for 15 days, and weakness for 2 days. There was no complaint of fever, night sweats, cough, body aches, nausea, vomiting, abdominal pain, hematemesis, diarrhoea or constipation. The patient did not have a past history of oral iron supplementation or any other comorbidities and family history was insignificant. On general examination, the patient was vitally stable. Pallor was present and the rest of the findings were unremarkable. On systemic examination left lobe of the liver and spleen up to the umbilicus was palpable with no other significant findings. Laboratory investigations were as follows:

Parameter	Value	Reference range
Haemoglobin	**7.3 g/dl**	13.2-16.6 g/dl
RBC count	**3.15 million/cumm**	5-5.5 million/cumm
Total WBC	9,300/cumm	4,500-11,000/cumm
Neutrophils	**66%**	40-60%
Lymphocytes	33%	20-40%
Platelet count	3,53,000/cumm	1,50,000-4,00,000/cumm

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Volume 5, Issue 2, Mar - Apr 2023 pp 133-136www.ijdmsrjournal.com ISSN: 2582-6018

Reticulocyte count	5.64%	0.5-1.5%
LDH	**1,118 IU/L**	105-133 IU/L
ALP	126 IU/L	44-147 IU/L
S. ferritin	29.68 ng/ml	24-336 ng/ml
S. Iron	**28 µg/dl**	60-170 µg/dl
S. Vitamin B12	**145pg/ml**	160-950 pg/ml
S. Ionized calcium	**4.4 mg/dl**	4.8-5.6 mg/dl

On peripheral smear mildly hypochromic microcytic RBCs were seen with teardrop cells. Occult blood was positive on stool examination. Hepatosplenomegaly and dilated hilar splenic vein was found on ultrasonography. Gastric fundal varices were found on gastroduodenoscopy and the echocardiogram showed left ventricular hypertrophy. Bone marrow aspiration revealed dry tap. Bone marrow biopsy specimen showed hypercellularity, and increased megakaryocyte and reticular fibrosis. Leucocyte alkaline phosphatase score was increased significantly with an absent Philadelphia chromosome on fluorescent in situ hybridization analysis. On gene analysis, JAK2 V617F homozygous mutation was found.

The patient was given a blood transfusion, folic acid and iron supplementation, injection of erythropoietin 10,000 IU subcutaneously once a week, prednisolone 10 mg and thalidomide 100 mg once a day for anaemia. The patient was started on hydroxyurea 500 mg once a day, Aspirin 150mg OD as a blood thinner, calcium 500mg OD and vitamin D_3 250 IU supplements, pregabalin 75mg and methylcobalamin 750µgOD for alleviation of neuropathic pain and pyridoxine 100mg OD. The patient was kept on monthly follow-ups with CBC reports to monitor disease progression and complications. The patient's condition improved over time with medications.

III. DISCUSSION

Primary myelofibrosis (PMF) is a rare and chronic myeloproliferative neoplasm characterized by the clonal proliferation of hematopoietic stem cells and the accumulation of fibrous tissue in the bone marrow. The diagnosis of PMF is based on the World Health Organization (WHO) criteria, which include the presence of characteristic clinical, laboratory, and bone marrow features. The most common presenting symptoms of PMF include fatigue, anemia, splenomegaly, and constitutional symptoms, such as fever, night sweats, and weight loss [7].

In the present case, a 63-year-old male presented with black stools and reduced appetite associated with weight loss, weakness, and pallor. The patient did not have a past history of oral iron supplementation or any other comorbidities, and his family history was insignificant. On examination, the patient was found to have hepatosplenomegaly, with a palpable spleen up to the umbilicus. Laboratory investigations revealed anaemia, leukocytosis, thrombocytosis, and an increased level of LDH. A bone marrow biopsy revealed hypercellularity, increased megakaryocytes, and reticular fibrosis, which are characteristic features of PMF. The patient was started on a treatment regimen consisting of blood transfusions, iron supplementation, erythropoietin, prednisolone, thalidomide, hydroxyurea, aspirin, calcium, vitamin D3, pregabalin, and methylcobalamin. The patient's condition improved over time with medications.

One of the distinguishing features of the present case is the absence of constitutional symptoms, such as fever, night sweats, and weight loss, which are commonly seen in patients with PMF. In addition, the patient did not have a significant family history or comorbidities, which are known risk factors for PMF [8]. The patient's age and gender are also consistent with the typical demographics of PMF, which primarily affects older adults, with a slight male predominance [9]. However, the severity of the patient's anaemia and thrombocytosis were more pronounced than what is typically observed in PMF, which could be due to the JAK2 V617F mutation, which is a common driver mutation in PMF [10].

The treatment of PMF is mainly supportive, with the goal of improving symptoms and preventing disease-related complications. Blood transfusions and erythropoietin are commonly used to manage anaemia, while hydroxyurea and ruxolitinib are used to control leukocytosis and splenomegaly [11]. Thalidomide has also been shown to be effective in the treatment of anaemia in patients with PMF, although its use is limited by its side effects [12].

In conclusion, the present case highlights the importance of considering PMF in the differential diagnosis of patients presenting with unexplained anemia, thrombocytosis, and

hepatosplenomegaly, even in the absence of constitutional symptoms. Early diagnosis and prompt treatment can help improve the quality of life and prevent disease-related complications in patients with PMF.

IV. CONCLUSION

In conclusion, this case report describes a 63-year-old male patient who presented with primary myelofibrosis, a rare myeloproliferative neoplasm. The patient's symptoms included black stools, reduced appetite, weight loss, and weakness. Upon examination, the patient had an enlarged spleen and liver, and laboratory tests revealed a low haemoglobin count, reduced red blood cell count, and increased platelet count. The patient was found to have the JAK2 V617F homozygous mutation, which is commonly seen in patients with primary myelofibrosis.

The patient was started on a treatment plan consisting of blood transfusion, folic acid and iron supplementation, erythropoietin injections, prednisolone, and thalidomide for anaemia. In addition, the patient was prescribed hydroxyurea, aspirin, calcium and vitamin D3 supplements, and neuropathic pain medication. Regular follow-up visits were scheduled to monitor the patient's progress and manage any complications.

This case report highlights the importance of considering primary myelofibrosis in patients presenting with unexplained anaemia and splenomegaly. It also emphasizes the need for careful evaluation and monitoring of patients with myeloproliferative neoplasms to manage potential complications and optimize treatment outcomes.

Although primary myelofibrosis is a rare disorder, it is important for healthcare professionals to be aware of its clinical presentation, diagnosis, and treatment options to provide optimal care for affected patients. Further research is needed to improve our understanding of this disease and to develop more effective therapies for patients with primary myelofibrosis.

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